London School of Economics and Political Science

The societal costs of Anorexia nervosa in England.

An investigation into the direct, indirect and intangible costs
with particular regard to the role of outpatient services.

Eva-Maria Bonin

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Declaration of Authorship

I certify that the thesis I have presented for examination for the MPhil/PhD degree of the London School of Economics and Political Science is solely my own work other than where I have clearly indicated that it is the work of others (in which case the extent of any work carried out jointly by me and any other person is clearly identified in it).

I warrant that this authorisation does not, to the best of my belief, infringe the rights of any third party.

I declare that my thesis consists of 79,718 words.

Statement of cojoint work

I confirm that versions of Chapter 4 part 2, Chapter 5, Chapter 6 part 2 and Chapter 8 have been published as part of a grant report to NIHR (ISSN 2050-4322). These chapters underwent peer review and benefitted from comments by my co-authors Ulrike Schmidt, Janet Treasure, Ivan Eisler and Jennifer Beecham. Primary data were collected by research teams at the (then) Institute of Psychiatry. All data preparation, methodological considerations, analyses, and write-up are my own.

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Abstract

Anorexia nervosa (AN) is a severe psychiatric illness affecting primarily adolescent females. Although prevalence rates are low, the associated morbidity, mortality and reduced quality of life result in a severe impact on the individual and thought to incur high societal costs. Combining new analyses of a variety of data sources with existing evidence, this thesis examines the societal costs of AN for England, including treatment costs and productivity impacts, and explores why costs may vary based on individual and service characteristics. An estimate of costs for 2010/11 is presented.

The costs of treating AN and variations in costs associated with individual and service characteristics were studied using data from the MCTAAN trial, the Care Pathways Study, and three trials from the NIHR-funded Applied Research into Anorexia Nervosa and Not Otherwise Specified Eating Disorders (ARIADNE) programme. Education attainment and longer-term productivity were studied using data from the ALSPAC and BCS-70, respectively. Results were combined with existing evidence to estimate the societal costs of AN for England.

The costs of treatment vary by service type and service characteristics. Individual treatment costs were positively associated with age and duration of illness, and vary by care pathway. Reporting lifetime incidence of AN was associated with a greater likelihood of being sick or disabled at age 30 (economic activity status). The prevalence of AN was estimated at approximately 12,000 cases, with around 6,000 Years of Potential Life Lost per year. The annual societal costs are estimated at between £80.8 million to £251.8 million.

Policy recommendations include an emphasis on effective and early treatment, to avoid the need for (re-) hospitalisation – a strong predictor of negative patient outcome as well as treatment costs. There is a need to improve data quality in mental health services to build evaluation capacity.

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LIST OF ACRONYMS

ALSPAC	Avon Longitudinal Study of Parents and Children
AN	Anorexia nervosa
ANTOP	Anorexia Nervosa Treatment of Outpatients
ARIADNE	Applied Research into Anorexia Nervosa and Not Otherwise Specified Eating Disorders
ASHE	Annual Survey of Hours and Earnings
AUSD	Australian Dollars
BCS-70	British Cohort Study 1970
BED	Binge eating disorder
BMI	Body mass index
BN	Bulimia nervosa
BP	Bingeing / purging
CAEDS	Child and Adolescent Eating Disorder Service
CAMHS	Child and Adolescent Mental Health Service
CASIS	Carers' Assessment, Skills and Information Sharing
CBT	Cognitive behavioural therapy
CBT-E	Enhanced cognitive-behavioural therapy
CEA	Cost-effectiveness analysis
CEDS-CYP	Community Eating Disorders Services for Children and Young People
CM	Cohort member
CoI	Cost-of-illness
CPRD	Clinical Practice Research Datalink
CPS	Care Pathways Study
CSRI	Client Service Receipt Inventory
CUA	Cost-utility analysis
DASS	Depression Anxiety Stress Scales
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECHO	Experienced Carers Helping Others
ED	Eating disorder
EDE	Eating Disorder Examination
EDE-Q	Eating Disorder Examination, questionnaire version
EDNOS	Eating Disorder Not Otherwise Specified / atypical ED
EDNOS-AN	Eating Disorder Not Otherwise Specified, anorexic type
EDQLS	Eating Disorder Quality of Life Scale
ESA	Employment Support Allowance
EUR	Euro
FCE	Finished consultant episode
FPT	Focal psychodynamic psychotherapy
GBP	British Pound
GBP	Great British Pounds
GCSE	General Certificate of Secondary Education
GL	Greater London

GLM	Generalised linear model
GP	General Practitioner
GPRD	General Practice Research Database
HES	Hospital Episode Statistics
HR-QoL	Health-related quality of life
IAPT	Increasing Access to Psychological Therapies
IB	Incapacity Benefit
ICD	International Classification of Diseases
IFT	Individual-family therapy
IP	Inpatient / inpatient treatment
IT	Individual therapy
MANTRA	Maudsley Model of Anorexia Nervosa Treatment
MAR	Missing at random
MCAR	Missing completely at random
MFDT	Multi-family day treatment
MH	Mental health
MNAR	Missing not at random
NHS	National Health Service
NICAPS	National In-patient Child and Adolescent Psychiatry Study
NICE	National Institute for Health and Care Excellence
NSF	National Service Framework
NS - NS	Non-specialist to non-specialist service
NS – S	Non-specialist to specialist service
ONS	Office for National Statistics
OP	Outpatient / outpatient treatment
OTC	Other cost study
PCT	Primary Care Trust
PDT	Psychodynamic psychotherapy
PoW	Production of welfare approach
QALY	Quality-adjusted life year
QoL	Quality of life
RCP	Royal College of Psychiatrists
RCT	Randomised controlled trial
SDA	Severe Disablement Allowance
SFT	Single family therapy
SMR	Standardised mortality rate
S-S	Specialist to specialist service
SSCM	Specialist Supportive Clinical Management
TAU	Treatment as usual
TAU-O	Optimised treatment as usual
TOuCAN	Treatment Outcome for Child and Adolescent Anorexia Nervosa
US	United States of America
USD	US Dollars
VPF	Value of prevented fatality

VSL	Value of statistical life
WHO	World Health Organisation
WTP	Willingness to pay
YPLL	Years of Potential Life Lost

CHAPTER 1

Introduction to the thesis

CHAPTER INTRODUCTION

Anorexia nervosa (AN) is a severe eating disorder (ED) affecting mostly adolescent girls. AN is a rare disorder: Two-stage studies of at-risk populations typically find a prevalence of up to 1% (Crisp *et al.* 1976; Hoek & van Hoeken 2003; Szmukler 1985), but owing to low overall prevalence as well as differences in methodology and sample population, prevalence rates vary significantly between studies.

Even though prevalence rates are low, the impact on the individual is severe. Patients with ED and sub-threshold ED as well as their carers report lower health-related quality of life than controls, and this impairment can be considerable (Engel *et al.* 2009). Moreover, AN causes distress to families and carers and may affect their psychological well-being (Dimitropoulos *et al.* 2009; Graap *et al.* 2008; Kyriacou *et al.* 2008).

The outcome of AN is poor, with average rates of recovery around 47% and more than 20% of cases becoming chronic (Steinhausen 2002). The prognosis is worse for those with a longer duration of illness, co-morbidity with other psychiatric illness and older age of onset (Berkman *et al.* 2007).

Life expectancy in AN is reduced dramatically – by an estimated 24.6 years for age of onset of 15 (Harbottle *et al.* 2008). The corresponding burden of disease is high: EDs are ranked 4th in terms life years lost to disability in young people aged 15-24 and the metal disorder with the second highest number of life years lost in females aged 15-34 (Mathers *et al.* 2000). Suicide-related standard mortality ratios (SMR; the ratio between observed deaths and deaths expected given the age and sex of the study population) of up to 58.1 have been reported for women with AN (Herzog *et al.* 2000). In fact, suicide may be the most common cause of death in AN, even surpassing the physical consequences of starvation (Pompili *et al.* 2003).

AN is linked to longer term physical problems, such as decreased bone health and risk of fractures, complications at birth and a negative impact on the endocrine and metabolic systems, although the latter are often reversed following recovery (Gendall & Bulik 2005). There is a high probability of co-morbid disorders such as autistic spectrum disorder and attention deficit hyperactivity disorder, obsessive-compulsive disorder, anxiety and borderline personality disorder (for a summary, see 15) and adolescent AN is associated

with higher odds of anxiety and depressive disorders in early adulthood (Johnson *et al.* 2002).

Treatment of AN is costly, in part because treatment often relies on inpatient care (Gowers & Bryant-Waugh 2004). In a census of inpatient beds in England and Wales in 1999, 20% of all child and adolescent beds were occupied by ED patients (O'Herlihy *et al.* 2003b, 2003a), and ED admissions have the longest median length of stay of all adult psychiatric admissions (Thompson *et al.* 2004).

Recently, in England and the UK, there has been a shift from inpatient to outpatient treatment, driven by several developments. In 1998, only 18% of ED units were managed by the NHS, and as a result, inpatient treatment was commissioned to private providers, with money flowing from the public to the private sector (Brown 1997; O'Herlihy *et al.* 2003a; Palmer & Treasure 1999). In response, NHS services were created, mostly in outpatient settings (Palmer & Treasure 1999). At the same time, Specialist ED services are concentrated in the South East of England (O'Herlihy *et al.* 2003b; Tulloch *et al.* 2008) , and 25% of the population live in areas without specialist provision (Royal College of Psychiatrists 2000), while referral from primary care to specialists services may depend on availability of such services within the area (Currin *et al.* 2006). Consequently, setting up outpatient services may facilitate more equitable access to treatment.

Another aspect is a shift in 'treatment philosophy' from a medical view focussing on weight restoration to a more 'holistic' view that includes the family both as a resource for the patient and recipients of support (Eisler 2005; Schmidt *et al.* 2017), supported by a notion that inpatient treatment is associated with negative outcomes and should be avoided except in the most severe cases (Meads *et al.* 2001; National Institute for Clinical Excellence 2004; National Institute for Health and Care Excellence 2017a).

The first (and to my knowledge, so far only) randomised controlled trial in the UK assessing the cost-effectiveness of outpatient treatment compared to inpatient treatment found specialist outpatient treatment to be more likely to be considered cost-effective than inpatient treatment or treatment in general outpatient services on an intention to treat basis (Byford *et al.* 2007a). However, length of psychiatric admissions and costs of secondary health care tended to be higher in general outpatient services compared to both inpatient and specialist outpatient services, suggesting the relationship between treatment setting and costs and outcomes may be more complex.

Even though it is clear that AN has a severe impact on the health care system and people's lives – including patients, their carers, families and partners – to date, there are few attempts at quantifying the economic impact in monetary terms, and there is a dearth of cost-effectiveness studies on treatments for AN (Simon *et al.* 2005; Stuhldreher *et al.* 2012). Cost-of-illness (CoI) studies often form the basis for cost-effectiveness analyses (Hodgson & Meiners 1982), and they are used to measure the impact of a condition in monetary terms, to justify interventions, to assist in the allocation of research funding, to provide a basis for prevention policy and to provide a framework for economic evaluation (Rice 2000). Cost-of-illness studies therefore have the potential to influence both policy and practice, and shape the future research agenda.

While the usefulness of such cost-of-illness studies as an end in themselves has been questioned (e.g. Byford *et al.* 2000; Kennelly 2017; Koopmanschap 1998), they can raise awareness of the burden of disease, especially where there is concern about a lack of effective interventions or a lack of treatment provision. Analysis of variations in costs is particularly useful because this can be used to describe and model trends, and incidence-based estimates showing the costs associated with a condition over the lifetime of an individual can be used in cost-effectiveness studies (Koopmanschap 1998).

This study is limited to estimating the societal costs of AN for England (2010/11). The focus is particularly on filling the gap in information on the costs of treatment in outpatient services. Variations in costs are also explored to contribute to the development of incidence-based estimates that can facilitate economic evaluations, particularly cost-effectiveness analyses. Given the available data, the estimates focus on females with AN.

In this thesis, I contribute towards the effort to establish the costs of mental ill health more widely. Often this cost arises not just from treatment, but from a lack of sufficient and effective treatment. This lack of treatment and support often leads to problems becoming entrenched, resulting in poor outcomes down the line. Showing the costs of a disorder can therefore support an argument for prevention, early intervention, and investment in effective treatments to prevent a chronic course. The economics of mental health have been an area of interest for me for a long time, and I wrote my Master's thesis on methodological issues in estimating the economic costs of suicide (Bonin 2007). Anorexia nervosa and suicide share some common features, in that the individual in question may not conform to the standard assumptions about 'rational' decision making in economic theory. This

thesis grew out of my interest in the economics of mental health, and especially in those conditions that appear to be 'irrational'. As part of my role at the Personal Social Services Research Unit (PSSRU), I have been involved in research on the economics of ED treatment for almost 10 years, and some of the studies in this thesis are the result of this work.

In the remainder of this chapter, I briefly set out the theoretical framework for this thesis and present the research questions to be addressed. These are derived from the survey of the existing literature in Chapter 2. I then provide an overview of the chapters that form the rest of this thesis.

THEORETICAL FRAMEWORK: ECONOMIC COSTS AS SOCIAL COSTS

Economics is the science concerned with efficient allocation of resources, and health economics is therefore concerned with the efficient allocation of resources in the area of health. When considering the efficiency of resource allocation, the perspective of the analysis matters. While sometimes evaluations of interventions to improve health take a health services perspective, this likely omits relevant impacts on other parts of society, such as carers, employers or the patient themselves (Byford & Raftery 1998). Economic evaluation therefore should generally take a societal perspective, and economic costs are conceptualised as 'social costs'. Another view is that the perspective should depend on the type of decision maker to be informed by the analysis. For example, a health and social care perspective may be appropriate for analyses informing decision making within the NHS.

Commonly, three types of economic costs linked to health conditions are distinguished (Hodgson & Meiners 1982):

- Direct costs arising directly from a condition, such as health care expenditure. These should reflect the opportunity cost of a resource.
- Indirect costs that are related to the condition but are not direct cash expenditure, such as productivity losses from lost employment resulting from the condition. These are usually estimated using a human capital or friction cost approach (Koopmanschapp *et al.* 1995).
- Intangible costs[1] are those that are not easily quantified in monetary terms, for example the value of a life lost due to premature mortality or suicide. These can be valued using a human capital approach or willingness to pay methods (Bonin 2007).

Table 1-1 shows examples of each type of costs as they relate to AN.

[1] Please note that many costs that fall under indirect costs, such as productivity losses, are also intangible costs. The intangible costs noted here could also be termed "human costs", see for example (Kennelly 2007)

Table 1-1: Types of costs and examples relating to AN

Type of cost	Examples pertaining to AN
Direct costs	Health care: • Primary care: initial diagnosis and referral; • Secondary care: A & E (medical emergencies, self-harm); medical inpatient admissions (• Tertiary care: Specialist ED services Other community services: • Self-help groups for ED, • physiotherapy (support for weight restoration: body image and awareness, addressing compulsive exercise; addressing the effects of AN: e.g. osteoporosis; managing anxiety: relaxation and massage) Social care: • Social worker, as part of a multi-disciplinary team or as a separate service, e.g. to address safeguarding concerns, advocate for patients detained under the Mental Health Act. • Drug and alcohol services to address addiction Education: • Tutor, EWO Additional expenditure: • Special foods, diet aids, child care
Indirect costs	Lost output: • Education • Career choice, unemployment, reduced work productivity
Intangible costs	Impact on quality of life: • Person with AN, • Impact on carers Loss of life: • Premature mortality from medical complications • Suicide

RESEARCH QUESTIONS

The aim of this thesis is to answer the following overarching questions:

- What are the annual societal costs of AN for England?
- Why do costs vary between individuals?

Based on my survey of the literature, I specified concrete research questions that address several different aspects of the societal costs of AN.

Research questions 1 and 2 investigate aspects of *direct costs*:

- **RQ1:** What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?
- **RQ2:** What services do people use while being treated for AN on an outpatient basis, what are the associated costs, and why do these costs vary?

Research question 3 addresses *indirect costs*:

- **RQ3:** What is the impact of AN on education, employment, income and related outcomes, and for whom?

Research question 4 addresses *intangible costs*:

- **RQ4:** What is the loss of life associated with AN in England?

Research question 5 addresses the totality of *societal costs*:

- **RQ5:** What are the annual societal costs of AN in England?

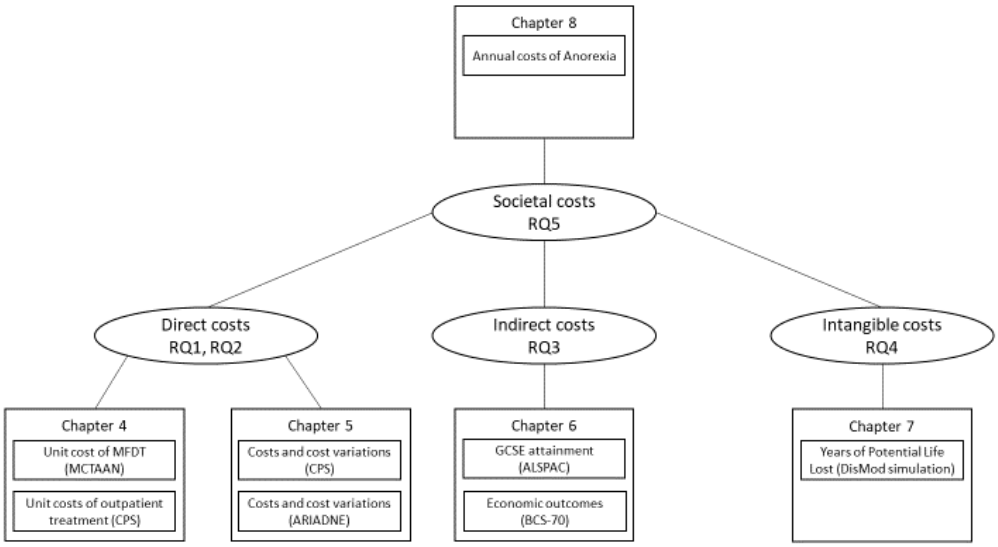
THESIS CHAPTER OUTLINE

The structure of this thesis reflects the concept of economic costs as social costs. The overarching goal is to present an estimate of the societal cost of AN that is as comprehensive as the available data allow, and why these costs may vary. The literature review revealed that there is very little information on the costs associated with AN and at present, no one data source provides sufficient information to construct a comprehensive estimate of costs. To answer these questions, I synthesise available information and fill gaps in the data needed to provide a sound estimate of the costs of AN from a societal perspective using econometric and economic modelling techniques. I explore cost variations based on individual and service characteristics. This thesis therefore consists of a collection of studies exploring different aspects of the societal costs of anorexia nervosa, with a focus on the role of outpatient services.

The empirical chapters (Chapters 4-8) are organised based on the type of cost they explore. Chapters 4 and 5 discuss aspects of direct costs of anorexia (unit costs of services and individual-level costs associated with service use). Chapter 6 explores some of the indirect costs (education and other economic outcomes). In Chapter 7, I estimate the costs associated with avoidable mortality due to AN in terms of Years of Potential Life Lost. Chapter 8 combines parameters from the data and literature review with estimates from the preceding chapters into estimates of the annual costs of AN.

Figure 1-1 shows how each chapter and each element relates to the research questions, and to the components of societal costs: direct costs, indirect costs and intangible costs. This figure will be shown at the beginning of each chapter (or part of a chapter) to indicate which component of societal costs the studies presented in the chapter relates to.

Figure 1-1: Overview of empirical chapters



Chapter 2: Introduction, literature review and research questions

This chapter briefly introduced the policy framework and service developments relevant to the thesis. A structured literature review provides an overview of what is already known on the topics that will be explored in the empirical chapters, identifies gaps in our knowledge and motivates the derivation of the research questions.

Chapter 3: Methods and data sources

Chapter 3 discusses overarching methods used across the empirical studies and describes the data sources used in this thesis.

Chapter 4: Direct cost - Unit costs of ED care

The focus of this chapter is on the direct costs of AN. I present a unit cost for Multi-family Day therapy (MFDT) using data collected for the MCTAAN trial, and unit costs for outpatient treatments estimated from data collected as part of the Care Pathways Study (CPS), with a focus on variation in treatment costs by service-level characteristics.

Chapter 5: Direct costs – Individual-level variations in costs

In this chapter, I use data from the CPS and three trials that were part of the NIHR-funded ARIADNE programme to explore variations in costs associated with service use in people with AN based on individual characteristics.

Chapter 6: Indirect costs - Productivity losses

Chapter 6 focusses on productivity-related impacts of AN in an analysis of the impact of AN on education attainment using ALSPAC data, and a study of longer-term impacts of self-reported AN on employment and related outcomes using the BCS-70.

Chapter 7: Intangible costs – Years of Potential Life Lost

In this chapter, I use the WHO-distributed DISMOD software model the prevalence of AN in England by age and gender, taking into account the incidence and remission from illness reported in the literature. I then calculate life expectancy and Years of Potential Life Lost from AN in England.

Chapter 8: Cost of illness

In Chapter 8, I combine the results of my literature review, publicly available data and the results from Chapters 5 to 7 into a cost-of-illness estimate and present the annual societal costs of AN in England for 2010/11.

Chapter 9: Discussion and policy implications

The final chapter discusses findings from the empirical chapters in the context of existing research, and presents policy implications as well as identifying further questions to inform the future research agenda.

CHAPTER 2

Survey of the literature

CHAPTER INTRODUCTION

In this chapter, I present an overview of the literature relevant to the studies presented in this thesis and highlight some of the conceptual debates and policy questions that frame the delivery of services for AN.

This survey of the literature is not intended to be systematic nor fully comprehensive, but to provide a backdrop to the analyses that follow, and to motivate the research questions to be answered (see Chapter 1). An initial review was carried out in preparing the thesis proposal in 2008 and 2009. This included a scoping search on PubMed and a snowball search from key publications, such as the NICE guidance documents on ED (National Institute for Clinical Excellence 2004), and the (at the time) most recent review of economic studies of AN (CoI, cost-effectiveness and cost studies) available (Simon *et al.* 2005). This was supplemented by a hand search of key journals (International Journal of Eating Disorders and European Eating Disorders Review), expert consultation with colleagues at the IoP and KCL, and grey literature searches using the Google search engine. These initial searches indicated that studies relevant to this thesis were published in journals intended for a clinical audience rather than pure economic journals. Following this initial search, a PubMed alert was set up to monitor new publications with the broad keywords 'anorexia' and 'eating disorder' in the abstract or title. Snowball searches and expert consultations also continued. Additional reviews and systematic reviews were identified, drawn upon and supplemented with additional searches, including reverse searches for citations of key papers. Given that the evidence base on the costs of AN and ED is reviewed regularly (Ágh *et al.* 2016; Crow 2014; National Institute for Clinical Excellence 2004; Simon *et al.* 2005; Striegel Weissman & Rosselli 2017; Stuhldreher *et al.* 2012), conducting an additional systematic review was considered to be a duplication of effort, and would not have made a substantial contribution to knowledge.

In this chapter, I briefly present the aetiology, epidemiology and course of AN, with a view to providing an introduction to the topic and providing a definition of AN that can be applied throughout this thesis. This is followed by an outline of the consequences of AN in terms of health, quality of life, economic outcomes, the effect of families and carers and the impact on mortality. I then discuss the literature on the service response to AN in England – including availability of services, treatment settings and existing economic evaluations - and situate this information in the wider policy context. Finally, I present existing estimates

of the societal costs of AN, both in England and internationally, and summarise the literature indicating why these costs may vary between individuals. A final section discusses the usefulness of cost of illness estimates, identifies gaps in the evidence base to derive my research questions, and highlights the policy relevance and contribution to knowledge of this thesis.

WHAT IS ANOREXIA NERVOSA?

Eating disorders (ED) are severe psychiatric disorders that often become chronic. Anorexia nervosa (AN) is generally characterised by a very low body weight and behaviours and thoughts centred around the avoidance of weight gain, distorted body image and the influence of weight or shape on self-evaluation (American Psychiatric Association 1994; Treasure *et al.* 2010; World Health Organization 1992). Clinical definitions for ED and AN can be found in the Diagnostic and Statistical Manual of Mental Disorders versions IV (American Psychiatric Association 1994) and V (American Psychiatric Association 2013) and the International Classification of Diseases (ICD-10, World Health Organization 1992).

Two subtypes can be distinguished based on behaviours: the restricting type (AN-R) is characterised by low calorie intake, while in the bingeing/purging type (AN-BP), self-induced vomiting or laxative use may compensate for (perceived) over-eating. It is distinguished from the other EDs, bulimia nervosa (BN) and – since their introduction in DSM-V – binge eating disorder (BED).

In addition to these 'full syndromes', Eating Disorders Not Otherwise Specified (EDNOS) is a diagnostic category intended to cover sub-threshold disorders. A meta-analysis by Thomas and colleagues (2009) shows that patients diagnosed with AN-type EDNOS (EDNOS-AN) based on DSM-IV criteria, i.e. with a more lenient BMI cut-off and without the requirement of amenorrhoea (absence of periods), are very similar to more narrowly defined AN.

DIAGNOSTIC CRITERIA

The way in which eating disorders are seen has changed over time. Schmidt (2003) describes a shifting of aetiological models on a spectrum from the biological to the psychological, that eventually locates AN in an ecological framework of risk and protective factors. These

include genetic and neurobiological factors, psychological traits, environmental risk factors and socio-cultural influences. Life stress can be a precipitating factor in both AN and BN, mediated by coping ability and social support.

The current diagnostic criteria for AN under DSM-V are shown in Figure 1. This is a revision of the 1992 DSM-IV criteria, most notably the removal of the criterion of amenorrhoea in females, which brings DSM-V more in line with ICD-10 criteria. A strict weight criterion of <85% of the expected weight for height was removed, in part because it appeared to discourage diagnosis of the full syndrome in practice and inflating the EDNOS category (Micali & Hebebrand 2015).

DSM-IV criteria were subject to several concerns. For example, a study applying DSM-IV and ICD 10 classifications to 226 children aged 7-16 found that over 50% were classified as EDNOS or could not be classified, casting doubt on the usefulness of these systems for children (Nicholls *et al.* 2000). Similarly, DSM-IV has been criticised as "a poor reflection of clinical reality" (Fairburn & Cooper 2011, p. 8) , as an increasing number of cases tended to be classified as EDNOS, rather than 'full syndrome', i.e. AN or BN (Schmidt 2003). This was considered problematic because patients with EDNOS were a diverse population that could not easily fit into a diagnosis of AN or BN, but the disorder presented as severe and persistent so that a classification of 'subthreshold' did not seem appropriate (Fairburn *et al.* 2007). DSM-V appears to address this issue to some extent, with a comparison of classification of diagnoses for 215 new patients entering an ED service based on DSM-IV vs DSM-V finding an increase in proportion of diagnoses of AN from 30% to 40% of patients, and a decrease in the number of EDNOS cases from 62.3% to 32.6% of patients (Ornstein *et al.* 2013).

Figure 2-1: DSM-V criteria for Anorexia nervosa

DSM-V criteria for Anorexia nervosa

- Restriction of energy intake relative to requirements, leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal or, for children and adolescents, less than minimally expected.
- Intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at a significantly low weight
- Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight

Two subtypes:

- Restricting type: During the last three months, the individual has not engaged in recurrent episodes of binge eating or purging behaviour (i.e. self-induced vomiting, or the misuse of laxatives, diuretics, or enemas). This subtype describes presentations in which weight loss is accomplished primarily through dieting, fasting and/or excessive exercise
- Binge-eating/purging type: During the last there months the individual has engaged in recurrent episodes of binge eating or purging behaviour (i.e. self-induced vomiting, or the misuse of laxatives diuretics, or enemas).

Beyond the shifting diagnostic classifications, there has been criticism of the current focus on EDs as "socially reinforced behaviours" (Lutter *et al.* 2016, p. 17), and it has been suggested that genetic and other biological research should inform these criteria (Bulik *et al.* 2007; Micali & Dahlgren 2016). This reinforces the idea that there shift from a psychosocial to a neuropsychiatric or neuropsychological model of AN (Herpertz-Dahlmann *et al.* 2011), and there are calls for research to improve our understanding of the biological causes of AN and AN-related behaviours – bingeing, purging, restriction and exercise (Lutter *et al.* 2016).

'SYNDROME' OR BEHAVIOURS?

While diagnostic manuals, such as the DSM-V or the ICD-10 offer strict clinical criteria for diagnosis (Schmidt 2003), attention has been paid to these different behaviours associated with EDs. For example, a latent class analysis seeking to empirically categorise individuals with ED revealed four classes (Keel *et al.* 2004):

- Restricting AN
- AN and BN with multiple methods of purging
- Restricting AN without obsessive-compulsive behaviours
- BN with one method of purging (self-induced vomiting)

Another study of a general cohort of adolescent females revealed six classes (Swanson *et al.* 2014b):

- Asymptomatic;
- Shape and weight concerns;
- Overeating without loss of control;
- Full and subthreshold BED;
- Full and subthreshold purging disorder;
- Full and subthreshold BN.

These studies highlight that classifications may more usefully be broken down along broad behaviours than diagnostic classes. Among these behaviours, purging (and vomiting in particular) is associated with traits associated with risky behaviours (Reba *et al.* 2005), negative later outcomes (Solmi *et al.* 2015) and lower quality of life (Engel *et al.* 2009). Binge eating is similarly associated with lower quality of life (Latner *et al.* 2008). Participants with restricting AN, on the other hand, have reported better quality of life, and positive social feedback to weight loss and control has been cited as a possible reason (Mond *et al.* 2005). This points to a potential for variation in the societal costs of ED and AN by presence of different ED behaviours.

MODELS OF MAINTENANCE AND TREATMENT

There are several competing theoretical models for explaining maintenance of ED, and these models guide the approach to psychological treatments developed for AN.

The transdiagnostic approach to treatment of ED states that EDs (anorexia and bulimia nervosa as well as EDs not otherwise specified) share several maintenance factors, even though the clinical features may differ (Fairburn *et al.* 2003). It developed from the model of cognitive behaviour therapy for BN, which focussed on over evaluation of eating, shape and weight as a core maintaining factor of BN. This theory was extended to include four additional maintenance factors: clinical perfectionism, low self-esteem, mood intolerance and interpersonal difficulties. It is argued that EDs share the same psychopathology, based around over-evaluation of eating, shape and weight, leading to weight control behaviour and in some cases compensatory behaviours. In addition, it is common for people to transition from one ED to another (Helder & Collier 2010), so that the different ED diagnoses are regarded as different states within the ED category.

In contrast to this model, there is evidence that restricting AN in particular is distinct and a maintenance model combining intra- and interpersonal factors has been proposed (Schmidt *et al.* 2006). Four factors in the maintenance of AN are suggested:

- Obsessive-compulsive personality traits and perfectionism;
- Avoidance;
- Pro-anorectic beliefs;
- Responses of close others.

The last aspect highlights the reciprocal relationship between carer well-being and ability to respond appropriately to the person with AN, and to the severity of the illness and its outcomes. The treatment approach therefore focuses on including carers in the process, especially for young people. This is the theoretical approach underpinning several of the clinical trials that provided data for this thesis.

RISK FACTORS

The literature on risk factors of AN is vast (Bulik *et al.* 2005, 2006; Fairburn *et al.* 1999; Favaro *et al.* 2006; Fragkos & Frangos 2013; Hinney *et al.* 2004; Holland *et al.* 2013; Jacobi *et al.* 2004; Krug *et al.* 2014; Micali *et al.* 2014, 2017a; Micali & Hebebrand 2015; Munkholm *et al.* 2016; Nicholls & Viner 2009; Pike *et al.* 2008; Raevuori *et al.* 2014; Steiner *et al.* 2003; Sundquist *et al.* 2016), and while this is an important area of research for prevention science,

it is not the main concern of this thesis. In this section, I therefore briefly summarise the information presented by Schmidt (2003) and Zipfel and colleagues (2015).

While it is generally thought that ED arise from or are supported by social and cultural pressure, weight and shape concerns are not a feature of all ED, and the interplay of risk and protective factors is more complex. Instead, there is a new emphasis on the heritability of and genetic risk for ED. Some of these genetic risk factors are shared with other disorders, such as depression, while others are unique to ED. The influence of genetic factors may increase with age because of the interplay between genetic expression and hormones in puberty. Molecular genetics is another field of enquiry, and several genes linked to neurotransmitters (serotonin, dopamine) have been identified as potentially relevant in determining ED risk.

Perinatal factors may be important, and premature birth has been identified as a risk factor in AN, possibly linked to early feeding problems – another risk factor for AN.

Childhood risk factors shared with other disorders also included perfectionism, negative self-evaluation, as well as adversity including experience of abuse. While dieting was associated with later development of BN, this was not the case for AN. Twin and sibling studies have confirmed these findings.

The conclusion to be drawn is that AN and ED are complex disorders with multiple and interlinked risk factors, and not all of them may be amenable to preventative efforts. This puts an emphasis on effective treatments and interventions to mitigate the potential negative impact of AN and ED on those affected.

EPIDEMIOLOGY

INCIDENCE

There is a perception that AN and ED are becoming increasingly common. In a widely quoted analysis of incidence of AN in Northern Europe, Hoek and colleagues (Hoek 2006; Hoek & van Hoeken 2003) assert an upward trend until the 1970s. The same seems to be the result of several longitudinal studies (e.g. Lucas, Beard et al. 1991). On the other hand, Fombonne's meta-analysis of 16 international case-register and community studies (1995)

concludes that increasing trends over time can be explained by changes in diagnostic methods, availability of services and reporting of incidence. Pawluck and Gorey (Pawluck & Gorey 1998) reviewed 12 studies and found that variability in rates over time could to a large extent be explained by cohort age and in a recent large-scale study, while Hudson and colleagues (2008) fail to find a significant increase in AN over time for the USA.

The incidence of AN in primary care in Britain appears to have been relatively stable over the last 20 years (Currin *et al.* 2005; Micali *et al.* 2013; Turnbull *et al.* 1996). The main source of information on incidence in the UK is the Clinical Practice Research Datalink (CPRD, formerly known as General Practice Research Database; Walley and Mantgani, 1997), which contains data from around 400 GP practices covering approximately 5% of the UK population in contact with GPs. The sample of practices is representative in terms of geographic distribution and practice size, as well as age and gender of patients (Statistics 2000). The database contains anonymised information on incidence, number of contacts with primary care, prescriptions and referrals. The database has been used to study the incidence of ED in England several times (Currin *et al.* 2005; Micali *et al.* 2013; Turnbull *et al.* 1996).

Most recently, Micali and colleagues (Micali *et al.* 2013) studied the incidence of AN, BN and EDNOS in the UK from 2000-2009 and again found the incidence of AN and BN to be stable over time, with a statistically significant increase in the age-standardised annual incidence rate from 32.3 to 37.2 per 100,000 population driven by an increase in EDNOS. The highest incidence group were adolescent females aged 15-19.

Compared to international estimates from similarly developed countries, the UK incidence is low. Hoek and colleagues (1991; 1995) conducted a similar study of general practitioners' records for the Netherlands and found an overall incidence rate of 8.1 per 100 000 person years, and in the longitudinal study conducted by Lucas and colleagues (Lucas *et al.* 1991, 1999) on the population of Rochester, Minnesota, a similar rate of 8.3 was found for the period from 1935-1989.

However, record-based studies generally do not show the true population incidence, but rather the incidence of cases detected by the health care system. Epidemiological studies find that over 50% of ED cases in the community are not detected by the health care system (Hoek *et al.* 1995; Keski-Rahkonen *et al.* 2007). While primary care is often the first point of contact with health services for people suffering from ED, due to the tendency to conceal

the illness associated with eating disorders and difficulty of diagnosis (especially in children), a record-based study is likely underestimate incidence. In 2,881 women from the 1975-179 birth cohorts of Finnish twins (Keski-Rahkonen *et al.* 2007), the lifetime prevalence of DSM-IV AN was 2.2%, and 50% of those cases had not been detected in the health care system. Incidence for age 15-19 was 270 per 100,000 person-years. This is a substantially higher lifetime prevalence and incidence of AN than previously reported. The accuracy of estimated depends on the efficiency and competency of primary care services, and availability of specialist services.

PREVALENCE

The report on Mental Health of Children and Young People in Great Britain (Green *et al.* 2005) estimated a combined prevalence of autistic spectrum disorder and 'other rare disorders' including ED of ca. 1%. For the analysis, data from the 1999 and 2004 surveys were combined to increase the sample base, but a total of only 24 children with eating disorders could be identified, and no separate analysis was conducted. In this case, the low prevalence leads to a gap in information and research into service use and provision for what is a severe disorder associated with high mortality.

Given the low prevalence in the general population, prevalence studies usually rely on two-stage designs of at-risk populations, mostly young females. Owing to low overall prevalence as well as differences in methodology and sample populations – rates vary significantly: Rooney and colleagues (1995) find a rate of 0.1% among females aged 15-29 in a South-west London area, identified by hospital and community health workers. In a study of 540 females aged 16-35 presenting to their GP in Cambridge, one patient with AN was identified (0.2% of the sample). Mann and colleagues (1983) screened schoolgirls aged 15 in a South London area for abnormal eating attitudes and behaviour (i.e. not a clinical diagnosis of AN) and found these to be present in 6.9% of participants. In a Swedish suburban population that asked health and social care personnel to identify patients with ED, the two-year prevalence of AN was 258 cases per 100,000 inhabitants for females aged 16-24, while Kjelsas and colleagues (Kjelsås *et al.* 2004) surveyed 1,987 adolescents aged 14 and 15 in 13 secondary schools in Norway to find a lifetime prevalence of AN of 0.7%.

Hoek and van Hoeken (Hoek & van Hoeken 2003) reviewed several of these two stage studies from Western Europe and the United States and found an average prevalence rate

of 0.3% for young females. This rate has been widely quoted and was used as the basis for the King's Fund report on the societal costs of AN (King's Fund *et al.* 2008) which estimated that in 2007, there were 26,981 people under 35 with AN in the UK.

More recently, several large-scale studies of more general populations have been conducted. A study in Rochester, Minnesota (Lucas *et al.* 1991) found an overall sex and age-adjusted point prevalence rate of 0.15%, but only 39% of these were confirmed cases of AN. The point prevalence for definite cases is only 0.06%. A study of over 30,000 Swedish twins who met full DSM-IV criteria, had a hospital discharge diagnosis of AN or a cause-of-death including AN found an overall lifetime prevalence of AN of 1.20% for female and 0.29% for male participants (Keski-Rahkonen *et al.* 2006).

Another recent study of the general population illustrates the problems associated with low prevalence: No cases of AN were identified in a study of ED in the general population in a South London area (Solmi *et al.* 2016).

Prevalence estimates for the number of young girls with partial syndrome, usually defined by absence of amenorrhea or sufficient weight loss to meet DSM-IV criteria, fall between 4-5% (Button *et al.* 1997; Wakeling 1996). A lifetime prevalence of AN of 1.9% and an additional 2.4% for EDNOS-AN (absence of amenorrhea) were found in a study of 1,002 female Australian twins aged 28-39 (Wade *et al.* 2006). EDNOS cases accounted for 60% of cases in outpatient settings, while AN accounted for only 14.5% (Hoek 2006), indicating that there is an even higher need for services at the sub-clinical level. However, Micali and colleagues (Micali *et al.* 2017b) found a weighted lifetime prevalence in a cohort of 5,542 from the Avon Longitudinal Study of AN of 3.64%, with 1.68% of the binging/purging type, and atypical AN of 1.7% - possibly reflecting the implementation of DSM-V criteria vs DSM-IV in the previous study. It is likely that the change in diagnostic criteria will be reflected in the relative proportions of full syndrome and EDNOS-AN in future studies.

AN in males is thought to be rare, even though some studies (Carlat *et al.* 1997; Larsen *et al.* 2015; O'Dea & Abraham 2002) suggest that rates may be increasing. Currin and colleagues (2005) found a ratio of 1:12 for male to female cases, similar to findings by Hoek and van Hoeken (Hoek & van Hoeken 2003) and Beglin and Fairburn (1992) who reported 1:10. Button and colleagues (2008) found that approximately 5% of patients of a specialized adult ED service in the 21-year period from 1987-2007 were male. In contrast, an American study (Hudson *et al.* 2007) found a lifetime prevalence ratio of 1:3, which is in line with Kjelsås'

figure for adolescents of 2:7 (Kjelsås *et al.* 2004). A ratio of 1:8 seems to be generally accepted in the literature (Zipfel *et al.* 2015). Given that the prevalence of AN is already low in females, prevalence in males is usually estimated via a ratio of male to female cases in two-stage studies or from clinical populations rather than from general population studies. As will be discussed later in this thesis, the low incidence and prevalence of AN in males means that sufficiently large samples for sub-group analyses by gender tend to be unavailable. As a result, most analyses presented here are for females only.

COURSE AND OUTCOME OF ANOREXIA NERVOSA

Given the low prevalence of AN, most studies are relatively small and it is unclear whether they are representative of a wider population with AN. In addition, outcome (improvement, remission, relapse and mortality) will at least in part depend on effectiveness of treatment. Here I summarise key evidence reviews that combine the results from several studies to investigate the course and outcome of AN, supplemented with recent studies relevant to the English context, rather than surveying the full field of individual studies.

One of the most cited studies is a review of 119 English and German language studies summarising the outcome of AN (Steinhausen 2002). Results need to be interpreted with caution due to the heterogeneity of underlying studies. The study found that outcomes differed depending on the length of the follow-up period, with average mortality increasing from 0.9% in studies with a short follow to 9.4% in studies with the longest follow-up (see Figure 2-2). Outcomes differed by age of onset, with a markedly better prognosis for those with adolescent onset (see Figure 2-3). Overall, less than 50% of patients recovered fully, and the overall outcome did not vary by time period, indicating that there was no trend of improved outcome (for example, through more effective treatments) found in this study.

Following a cohort of patients with AN over 12 years, Fichter and colleagues (2006) found an improvement post-treatment, an average deterioration in the first two years, and improvement between years 3 and 12. Average time to remission in a 12-year follow-up study was over 6 years (Herzog *et al.* 1997).

Figure 2-2: Outcome by length of follow-up period[1]

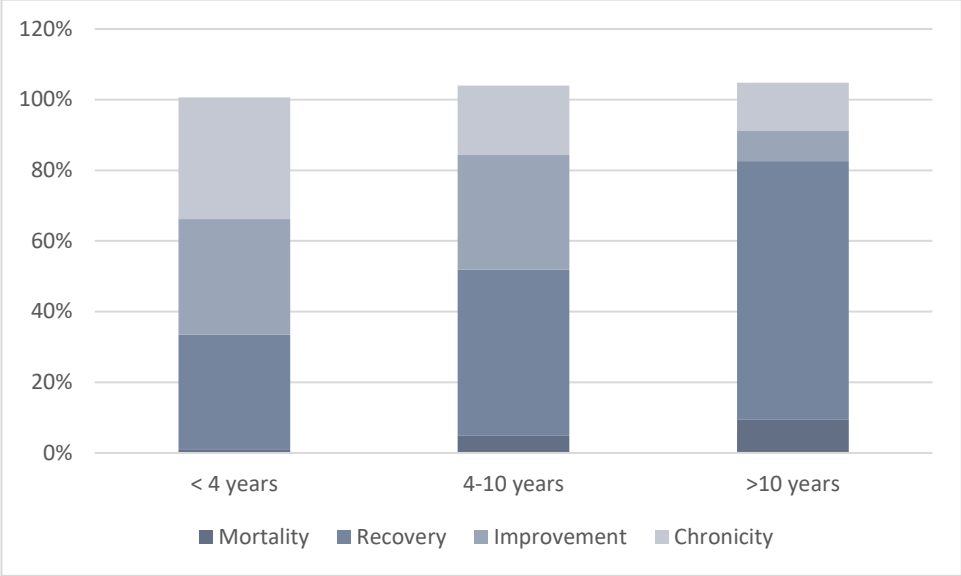
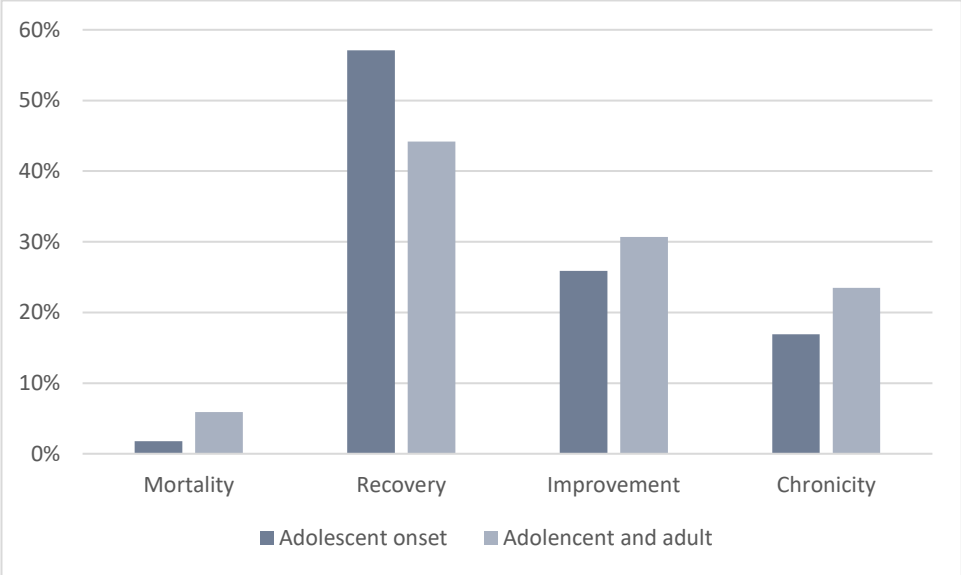


Figure 2-3: Outcome in adolescent onset vs whole group[2]



[1] Data from Steinhausen (Steinhausen 2002), p. 1,286.
[2] Data from Steinhausen (Steinhausen 2002), p. 1,286.

MORTALITY AND SUICIDE

Arcelus and colleagues (Arcelus *et al.* 2011) estimated the standardised mortality ratio[3] (SMR) associated with AN based on 25 studies with a mean follow-up period of 14.2 years at 5.68 (95% CI: 4.17-8.26). As the underlying studies did not include male patients, this ratio applies to females only. This is lower than SMRs previously found (Hoek 2006), and in particular lower than the SMR found in a highly cited study of patients in tertiary care where it was 10.5 (Birmingham *et al.* 2005). A more recent study in the UK used HES data linked to death registrations to calculate the age and sex-specific SMRs for ED between 2001-2009 (Hoang *et al.* 2014). The SMR for AN in patients aged 15-24 was 11.5 (95% CI 6.0-17.0), and 14.0 (CI 9.2-18.8) for patients aged 25-44. For EDNOS, the SMR was 1.4 (CI 0-4.0) for younger and 4.7 (CI 1.4-8.0) for older adults. The SMR for AN was found to be almost twice as high as the SMR for schizophrenia in patients aged 25-44 at 7.3 (CI 6.6-7.9). Overall, the trend in mortality from AN in people who received inpatient treatment seems to be decreasing, e.g. (Lindblad *et al.* 2006).

Mortality from suicide in AN may account for over 50% of deaths (Herzog *et al.* 2000), and the SMR for suicide was 31.0 (CI 21.0-44.0) in a meta-analysis (Preti *et al.* 2011) – much higher than the risk ratio of under 10 found in a previous analysis combining different studies (Pompili *et al.* 2004), and a review of suicide rates in inpatient, outpatient and non-psychiatric settings which found crude mortality rates ranging from 0% to 5.3%, with a combined estimate of 2.5% (Franko & Keel 2006). It follows that the risk of attempted suicide is high, with the prevalence in a cohort of patients in Spanish outpatient services of 8.65% for the restricting type AN, and 25.0% in those with the purging type (Forcano *et al.* 2011) – a finding similar to that of Bulik and colleagues (2008), where 7.4% with restricting subtype and 26.1 % with the purging subtype as well as 29.3% with AN with binge eating had attempted suicide. Measures of depression were elevated in those with suicide attempts. These findings are in line with an earlier study from France, where major depressive disorder and switching from the restricting to the bingeing/purging subtype were associated with an increased risk for suicide attempts (Foulon *et al.* 2007).

[3] The SMR is the ratio between the number of deaths observed in a specific population and the number of deaths that would be expected based on age and sex in a standard population.

WHAT ARE THE CONSEQUENCES OF ANOREXIA NERVOSA?

HEALTH CONSEQUENCES AND CO-MORBIDITIES

The health consequences of AN are wide ranging and complex. Gendall and Bulik (2005) reviewed the literature on the long-term biological consequences of AN. The findings of their review are summarised below.

AN affects reproductive and obstetric health. While there was no difference in infertility, the rate of miscarriages in women with AN was 30% compared to 16%. Between 10%-26.5% of women with a history of AN have caesarean sections, compared to 3% in controls. Premature birth and low birth weight were found in 20% compared to 6% in those without AN.

There were significant negative impacts on bone health, with a higher risk or more severe osteoporosis, osteopenia, premenopausal fracture rates and an increased fracture risk for more than 10 years following diagnosis of AN.

Cancer incidence overall was reduced by 20%, with breast cancer and cervical cancers less common. However, gastrointestinal cancers were more common than expected, as were types of gastrointestinal disease that tend to resolve with refeeding. Bingeing and purging can lead to gastrointestinal bleeding and other problems, while laxative abuse can affect pancreatic function and result in renal failure.

Current AN is associated with endocrine and metabolic problems, such as a reduced resting metabolic rate hypothyroidism and increased growth hormone secretion.

Co-morbid mental health conditions are common in AN. Jordan and colleagues (Jordan *et al.* 2008) report depression in 63% and anxiety in 54% of those affected, while Krug and colleagues (2008) reported affective disorders in 52%. Tobacco and substance use were also common in the same study (34%), with higher risk in the bingeing/purging type of AN compared to the restricting type. There was no increase in alcohol use. Depression is common in AN and is associated with lower quality of life (Winkler *et al.* 2014).

QUALITY OF LIFE

A recent meta-analysis of the health-related quality of life (HR-QoL) in ED (Ágh *et al.* 2016) included 41 studies overall and 18 specifically for AN. Those with ED had lower HR-QoL than those with no ED (Fox & Leung 2009), and those with AN had reduced mobility compared to those with BN and healthy controls (Keilen *et al.* 1994). In some comparisons of AN with BN and BED, there were no significant differences between diagnostic categories but there was a negative relationship between severity of ED symptoms and HR-QoL (de la Rie *et al.* 2007; Padierna *et al.* 2000). A study using a multi-dimensional quality of life instrument (Doll *et al.* 2013) found no differences between the AN group and the comparison group without ED. However, those with BN or BED had lower scores on some sub-domains. This links with a finding by Mond and colleagues (Mond *et al.* 2005), who find that quality of life is lower in those with BN, BED and purging-type AN compared to restricting type AN, and a study by Latner and colleagues (2008), where several purging behaviours (bulimic episodes, laxative abuse, self-induced vomiting) were related to lower general quality of life. This indicates that purging behaviours may negatively affect QoL. AN may also be associated with lower social and physical functioning compared to BN and EDNOS (Bamford & Sly 2009; Latner *et al.* 2008).

An explanation put forward for the fact that some studies do not find an effect of AN on quality of life in patients is that this may be related to positive attitudes towards weight loss (Hay *et al.* 2003). However, a recent meta-analysis finds no evidence for this claim (Winkler *et al.* 2014). The picture of QoL in AN presented by the literature is therefore mixed, but there are indications that QoL is related to purging behaviours, and that AN may affect the physical and social functioning domains of QoL.

ECONOMIC OUTCOMES

AN is associated with long and frequent periods of hospitalisation, where there is alternative provision of education (Tulloch *et al.* 2008). Byford and colleagues (Byford *et al.* 2007a) found that in addition to hospital stays, the young people in their study spent long stretches of time out of education. It seems that in the face of severe illness, education often comes second, although it is a concern to parents (Tierney 2005) and seen as an important determinant of quality of life (de la Rie *et al.* 2005a). For those who remain within mainstream school, special provisions may have to be made to accommodate sickness absences.

There is some evidence that the illness does not affect educational outcomes in the longer term: there was no statistically significant difference between young women with AN and their healthy co-twins 5 years after recovery from AN (Keski-Rahkonen *et al.* 2007), and a greater proportion of patients admitted to hospital with AN had completed post-secondary education compared to controls (Hjern *et al.* 2006). In contrast, Patton and colleagues (2008) found young people with EDNOS-AN more likely to be not in education or employment than cohort members without ED. However, I am not aware of any previous study looking at educational outcomes in AN while controlling for other characteristics, such as socio-economic status.

While few studies on the topic exist, there is some evidence to suggest that the impact of current AN on productivity in adulthood is severe: In a register study of a national cohort of Swedish females born between 1968 and 1977 (N=529,369), 748 inpatients meeting ICD-9 criteria for a main or co-morbid diagnosis of AN were identified and compared to all other participants in terms of health, social and economic outcomes at age 24/25 (Hjern *et al.* 2006). In the group with an inpatient stay for AN, 21.4% were financially dependent on state benefits, compared to 8.6% in the comparison population (risk ration stratified by birth year, socio-economic status, residency and maternal country of birth: 2.6 (95% CI 2.3-3.0). A long duration of inpatient treatment and psychiatric co morbidity were significant predictors of benefit receipt.

In a study from British Columbia, Su and Birmingham (2003) collected survey data collected from inpatients and outpatients in an adult tertiary care ED service and from 40 ED patients throughout the province through a self-help organisation. Of the n=29 respondent recruited through the ED service, 6.9% received income support at the time of the survey and 27.6% had received it in the past. The corresponding figures are 10% and 25% for the n=20 respondents recruited through the self-help organisation. In both groups, around 35% therefore received disability payments either in the past or presently. The total cost of long-term disability modelled based on benefit rates and assumptions about the prevalence of AN in the female population (assumed to range from 1%-2% between ages 15 to 64) was estimated to be in the range of CAD2.5 million to CAD101.7 million per annum, up to 30 times the total annual cost of tertiary care for EDs.

A study using five-year data from the US Medical Expenditures Panel Survey, Samnaliev and colleagues (2015) compared individuals with a current ED to those without ED in terms

of annual health care costs, employment status and earned income. While those with an ED incurred higher health care costs, there was no statistically significant difference in employment rate (OR = 0.67, 95% CI 0.41-1.09), and no statistically significant difference in earnings if employed with a difference in earnings of $2,093 (2011 US$; p=0.48). Results for those with ED with another co-morbid mental health condition were similar, except for significantly lower earnings (difference $19,374, p<0.01).

In summary, while the evidence on economic outcomes for AN is sparse, there is some evidence that there may be a higher probability of receiving disability benefits, and that this is costly when compared on expenditure on treatment. While there is as of yet no evidence that ED affects employment status or wage level (and in fact, there is some evidence to suggest that these are not affected), is less clear how a history of adolescent AN affects adult productivity.

EFFECT ON CARERS AND FAMILY

The role of carers is important to this analysis both because the relationship with the carer plays an important part in the recovery process and because carers carry much of the burden of AN in terms of caregiving. Carers of people with AN experience more distress than carers of people with psychosis (Treasure *et al.* 2001; Whitney *et al.* 2005) The burden of caregiving and other societal costs have not been examined in economic terms.

Carer distress is driven by self-related strains (strain on the carer), and interpersonal strains (strains on relationships) and is higher for mothers than for fathers (Kyriacou *et al.* 2008).

Several qualitative studies have looked at the impact of EDs on other family members. Changes in children with ED are often described as 'alarming', both in personality and behaviour (Cottee-Lane *et al.* 2004) and parents report anxiety about immediate medical problems and the child avoiding social activities.

An ED is often disruptive to family life because it revolves around the disorder to such an extent that the needs of carers and other family members cannot be addressed and social activities are limited (Cottee-Lane *et al.* 2004; de la Rie *et al.* 2005b; Highet *et al.* 2005). The ED can lead to social isolation and put financial strain of the family (Hillege *et al.* 2006). Another factor contributing to carer distress was a lack of support and understanding from close others and indeed health service professionals who often failed to respond to parents'

concerns in the early stages of the disorder (Cottee-Lane *et al.* 2004; de la Rie *et al.* 2005b; Highet *et al.* 2005).

Zabala and colleagues (2009) systematically reviewed quantitative studies about expressed emotion, caregiving burden and psychological distress of carers. Their analysis included 20 studies, 5 focussing on AN only, and 9 including all EDs. All studies reporting measures of psychological distress showed high levels of psychological distress, depression and anxiety. Two studies included in the review compared the caregiving burden of ED carers to carers of psychotic patients (Treasure *et al.* 2001) and compared to healthy controls (Kyriacou *et al.* 2008), respectively, and found that ED carers experienced a higher burden. Zabala and colleagues (2009) note, however, that in both cases, the comparison groups were not well matched. Another study (Santonastaso *et al.* 1997) found that the subjective caregiving burden of carers of AN is higher than for carers of bulimia. In addition, the carers showed high levels of expressed emotion, and this was positively associated with age of the patient and the duration of illness.

While the literature clearly shows a severe impact on the family in terms of caregiving, financial burden and distress, so far, this impact has not been quantified in monetary terms.

TREATMENT OF ANOREXIA NERVOSA IN THE CONTEXT OF ENGLISH MENTAL HEALTH POLICY

Treatment and service development of ED and AN is situated in a broader context of mental health policy. I summarise trends in service development and mental health policy and relate them to service developments in ED. Note that this section does not attempt to detail and critique the available treatment approaches for AN. Instead, it focusses on the policy context and outlines the organisation of services to provide a framework for the analyses that follow.

This section highlights some of the major debates regarding the organisation of services for ED:

- A shift from inpatient to outpatient services;
- The role of specialist services in the treatment of AN;
- Crisis resolution and home treatment teams to prevent admissions and facilitate discharge from hospital.

Table 2-1 lists key policy documents and events in the mental health space up to 2017. Key documents for the devolved nations are also included. Devolution has led to different funding choices and different structures (Greer 2008). While in England, there is more increasing emphasis on provider-based competition and patient choice combined with performance management, the split between purchaser and provider no longer exists in Scotland and Wales. In Northern Ireland, retention of a purchaser/provider split was noted, without the elements of encouraging provider competitions or performance management. Bevan and colleagues (Bevan *et al.* 2014) note that this divergence has not led to a corresponding divergence in health system performance.

With regard to ED, NICE guidance documents apply to England, Wales and Northern Ireland, therefore setting the context for devolved policy and practice. Both Wales and Northern Ireland historically had a lack of specialist ED units, leading to a need for out-of-area treatment (Royal College of Psychiatrists 2012).

An early study (Lemouchoux *et al.* 2001) found that over 20% of the population in Scotland did not have access to specialist NHS ED services, so that private providers were funded to provide care (Carter & Millar 2004). The first specialist ED inpatient unit in Scotland opened in 2009, with other services (including some outpatient services) following suit (Royal College of Psychiatrists 2012). While provision has improved, the Royal College of Psychiatrists concluded in 2012 that further improvements in service availability and improved models of care (such as involvement of GPs, continuity of care and availability of treatment in CAMHS) are required to further reduce avoidable mortality from ED in Scotland.

Table 2-1: Mental health policy in England from 1948

Year	MH policy documents and events	Implications
1948	National Health Service Act	Founding of NHS
1959	Mental Health Act	More stringent admission criteria for asylums
1983	Mental Health Act	Duty to provide "aftercare"
1986	First asylum closed	Process of de-institutionalisation begins.
1990	'National Health Service and Community Care Act	Introduces split between purchaser and provider; implements needs assessment and entitlement to receiving required services.
1998	White paper: 'Modernising mental health services"	£700 million additional funding
1999	National Service Framework for MH	Standards of care, new community-based service models, funding and support for implementation.
	Devolution of NHS Wales	
2000	NHS Plan	Standards of care, new community-based service models, funding and support for implementation.
2001	'National Institute for Mental Health in England'	
2002	Bamford review of Mental Health and Learning Disability (Northern Ireland)	
2003	'Every Child Matters'	Provide comprehensive CAMHS services by 200
	'Mental Health (Care and Treatment) (Scotland) Act	Renewed interest in the rights of patients with ED, with guidance on 'forced feeding' published by the Mental Welfare Commission for Scotland in 2013.
	'National Programme for Improving Mental Health and Well-being. Action Plan 2003-2006' (Scotland)	
2004	NICE guidance on Eating Disorders	
2004	'National Service Framework for Children, Young People and Maternity Services'	Standard 9: Improve standards of care; access to timely, integrated, high quality, multidisciplinary MH services to ensure effective assessment, treatment and support.
2005	'The Mental Health of Children and Young People: A Framework for Promotion, Prevention and Care' (Scotland)	Framework for planning and delivery of integrated approaches to CYP mental health.

Year	MH policy documents and events	Implications
	'Review of Mental Health and Learning Disability' (Northern Ireland)	Lack of local specialist inpatient units leads to treatment being provided outside the country, prompting the prioritisation of development of ED services.
2006	IAPT established	
	'Eating Disorders in Scotland – Recommendations for Management and Treatment'	Published by NHS Quality Improvement Scotland, with recommendations around continuity of care, identification in primary care and referral to specialist services.
	'Delivering for Mental Health' (Scotland)	
2007	'Mental Health Act'	Age appropriate care for under 18s.
	'Better Health, Better Care: Action Plan' (Scotland)	Commitment to faster access to health care locally.
2009	'New horizons: towards a shared vision for mental health'	Prioritises equality, personalisation, destigmatisation and physical health of people with MH problems.
	'Towards a Mentally Flourishing Scotland: Policy and Action Plan 2009-2011'	
	'Eating Disorders Framework for Wales'	Tiered model of service provision implemented for ED. Additional funding of £1m per year for two adult specialist services (Wales)
	First 'Bamford' action plan (2009-11, Northern Ireland)	
2010	'NHS plan for England'	Aims: Increase in funding, address geographical inequalities, improve standards of care and patient choice.
2011	'No Health without Mental Health: Delivering better mental health outcomes for people of all ages.'	Parity of esteem between mental and physical health services.
2012	'Implementation Framework for No Health Without Mental Health'	
	'Health and Social Care Act'	First explicit recognition of "duty towards both physical and mental health" (Parkin & Powell 2017, p. 6)
	'Mental Health Strategy for Scotland: 2012-2015'	
	'Together for Mental Health' (Wales)	

Year	MH policy documents and events	Implications
	Second 'Bamford' action plan (2012-15, Northern Ireland)	
2013	Additional investment in improving CAMHS provision for ED (Wales)	
2014	Health and Social Care Information Centre shows rise in ED admissions of 8%.	
	'Closing the Gap: priorities for essential change in mental health'	Outlines areas for improvement in terms of access to MH services, integrating physical and mental health care, prevention and promotion activities, improving quality of life for people with MH problems.
	'NHS Five Year Forward View'	Proposal to expand access standards to cover eating disorders and a range of other services. Goal: achieve parity of esteem by 2020
	'Social Services and Wellbeing Act 2014' (Wales)	Change in the provision of services for young people to better meet their needs, such as easier access to information, simpler assessments and providing "the right support at the right time". Joint working of the public sector with other organisations.
	'Five year Forward View. Into Action'	Pledge to establish CEDS-CYP.
2015	'Children and Young People's Eating Disorder Access and Waiting Time Commissioning Guide'	Standards and requirements for CEDS-CYP and updated referral pathway.
	'Together for Children and Young People' (Wales)	Multi-agency, multi-disciplinary programme to improve emotional and mental health services for CYP in Wales.
2016	'Five Year Forward View for Mental Health'	Recommendations for improving mental health outcomes and achieve parity of esteem by 2020/21. CEDS pathway to be developed in 2015/16. Call for ED waiting time standard to be model for additional standards. Call to end out-of-area placements.
	'Implementing the Five Year Forward View'	£30 million additional funding to implement CEDS-CYP (2015/16-2020/21)
	'Together for Mental Health Delivery plan: 2016-2019' (Wales)	Commitment to access to appropriate and timely services to reduce the number of out-of-area placements.
	Review of the Welsh Eating Disorder Framework	Key messages arising from the Welsh policy context are summarised: Routine recording of outcome measures is needed to enable evidence based service provision.
2017	Update of 'NICE guidance on the recognition and treatment of ED'	
	'Next steps on the NHS Five Year Forward View'	

Year	MH policy documents and events	Implications
	NHS waiting time standard baseline	
	Publication of 'Mental Health Strategy 2017-2027' for Scotland	Action 22 pledges "support for the development of a digital tool to support young people with eating disorders" to "help ensure that young people with an ED are able to access support in a way that reflects digital lifestyles".
2018	Review of NHS Eating Disorder treatment in Wales	

PROCESS OF DEINSTITUTIONALISATION AND IMPLICATIONS FOR INPATIENT CARE

Gilburt and Peck (2014) summarise the process transformation of mental health services up to the publication of the cross-government paper 'No Health Without Mental Health' in 2011. The publication of 'No Health Without Mental Health' prompts and coincides with an increased focus on mental health services in general, and on ED in particular. I present their argument in what follows.

A process of de-institutionalisation, driven by advances in psychiatry and pharmacology, and changing attitudes towards mental health, started in the late 1980s. This involved moving residents into smaller mental health units or into the community. The transition had cost implications, as for a period, hospital beds still had to be funded alongside the new community services.

Initially, community mental health teams were the predominant service model, but these were found to be insufficiently capable of caring for those with severe and enduring mental health problems and younger people. New service models were implemented, overseen by the new National Institute for Mental Health and leading to both an increase in the workforce and new roles for existing clinicians:

- Assertive outreach teams providing intensive support to people with complex needs living in the community;
- Crisis resolution and home treatment teams to prevent admissions and facilitate discharge from hospital;
- Early intervention teams for psychosis.

After the implementation of the National Service Framework for Mental Health (NSF; Department of Health 1999), it was recognised that the new service models did not always address local requirements –particularly where the new eligibility criteria for community services resulted in unmet needs. Local innovation with a view to improving access to services is now encouraged by national policy, with funding to support implementation of NICE approved treatment for depression and anxiety provided through the flagship 'Increasing Access to Psychological Therapies' programme (IAPT) from 2006. At the same time, the severity of illness of those still treated in inpatient settings has increased, while the

number of acute beds has fallen, putting cost pressures on providers and leading to local concentrations of services. An inability to meet demand for beds has resulted in an increase in out-of-area placements.

AVAILABILITY OF INPATIENT SERVICES FOR AN

The overarching developments in the organisation of mental health services are seen in the service landscape in ED and AN. The severe and often life threatening medical consequences of ED often require hospitalisation, and it has been argued that availability of specialist services is particularly important in the case of ED because their low prevalence means local and general services see too few patients to develop the skills to treat them effectively (Palmer & Treasure 1999). At the same time, early and effective treatment is important, as duration of illness is a predictor of outcome and can prevent the disorder from becoming entrenched (Eisler *et al.* 1997; Steinhausen 2002).

ED cases reflect an overall trend of changing admission and discharge criteria and of increasing severity in those admitted for inpatient care, in. Average age of admission is now higher than in cohorts that pre-date deinstitutionalisation (Collins 2005; Long *et al.* 2011; Morgan & Russell 1975; Russell *et al.* 1987), and the course of illness of inpatients is more severe and enduring.

In terms of the geographic distribution of services, persistent inequalities are found. A survey by the RCP found that in four UK regions covering 25% of the population, there was no specialist provision, and 69% of specialist services were clustered in the South East of England (Royal College of Psychiatrists 2000).

The influential 1999 National In-patient Child and Adolescent Psychiatry Study (O'Herlihy *et al.* 2003b, 2003a) mapped the provision of child and adolescent inpatient units in England and Wales, covering both public and private sectors. One aim of the study was to describe the distribution and characteristics of inpatient mental health units. The study found nine inpatient units supplying 98 beds, or 11% of all mental health inpatient beds. These were predominantly in London (50 beds), the South East (26 beds) and the East (20 beds).

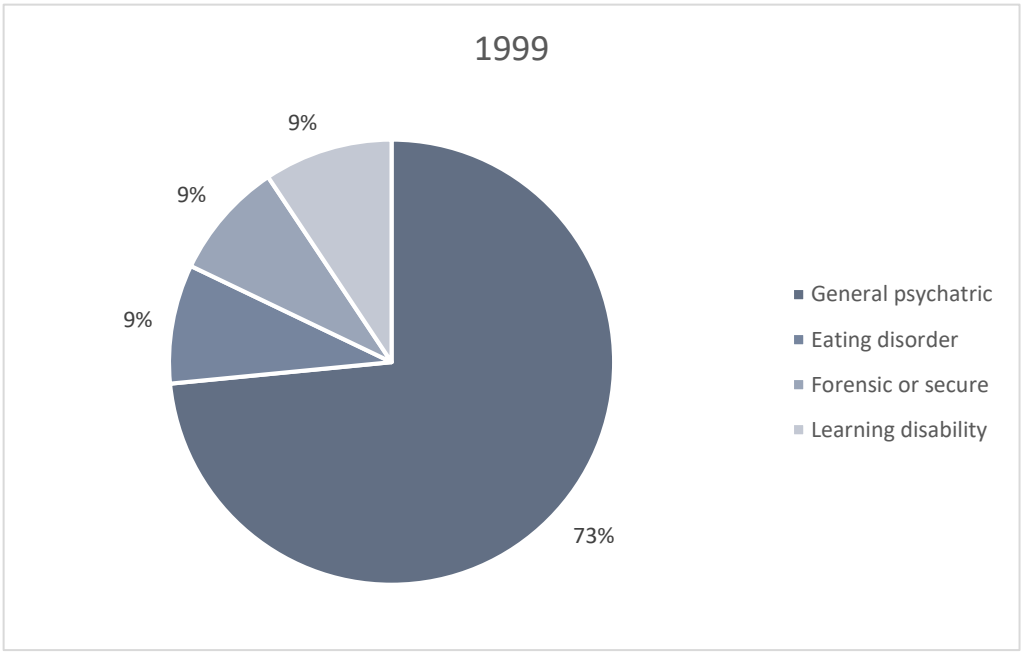
The availability of ED services therefore mirrors the picture for all mental health beds, which are clustered in London and the South East. Eating disorders were the main diagnosis for

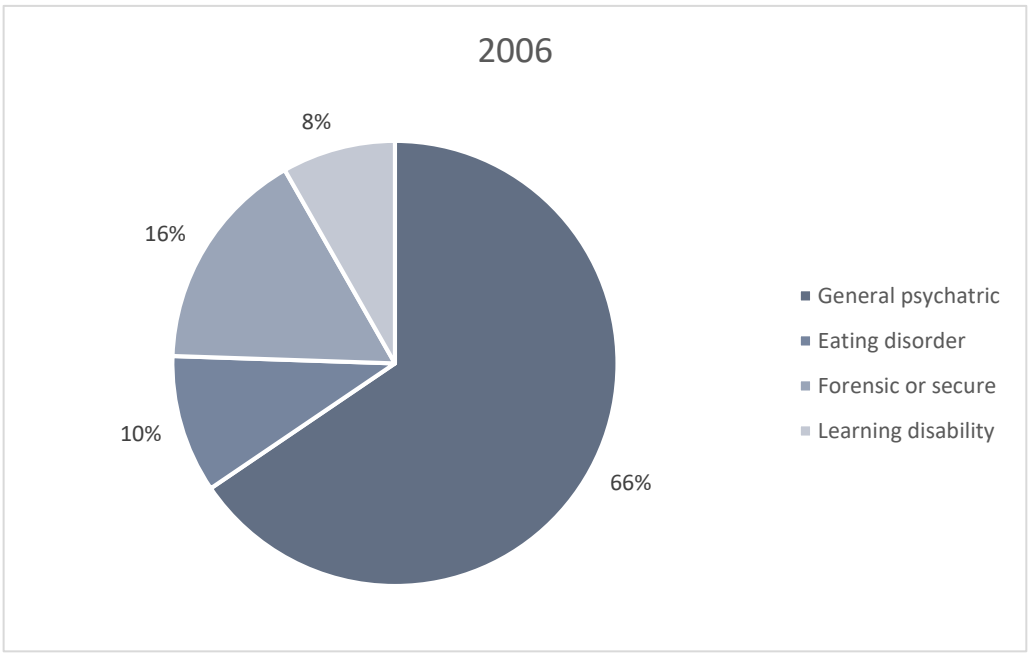
almost a quarter (23.3%, Tulloch et al., 2008a) of young people in inpatient units at the time of the census.

The COSI-CAPS study (Tulloch *et al.* 2008) extended the scope of NICAPS by investigating factors related to treatment outcome such as ward environment and staffing, and estimated unit costs of inpatient care. Eating disorders accounted for 29% of the cohort. It found a 55% increase in specialist ED beds (driven largely by an increase in private sector provision), and that 66% of beds were located in London. This in turn mirrored a national trend where those regions with the highest number of beds per population increased availability more compared to other regions. The proportion of overall beds remained stable (see Figure 2-4).The median admission cost for young people with ED was £37,470 (range £341-122,100; 2007 prices), and average costs in general units were higher than in specialist ED units, with £47,430 compared to £30,370.

The COSI-CAPS study also included a prospective cohort study of young people admitted to general CAMHS units and specialist ED inpatient units. The study found no difference in demographic characteristics of young people admitted to an eating disorder unit compared to those admitted to a general adolescent unit, but those admitted to an EDU had a higher severity of problems and showed a larger improvement from intake to discharge. For those with ED, the change in an ED-specific outcome measure was positively correlated with costs. The authors concluded that specialist units did not produce better outcomes (adjusting for differences at admission), and were not associated with higher levels of patient satisfaction. There were no differences in the average cost of admission.

Figure 2-4: Percentage of inpatient beds by type of unit/ward, 1999 and 2006[1]





The Royal College of Psychiatrists (RCP) undertook a further mapping exercise of services in the UK and Ireland in 2008 (Royal College of Psychiatrists 2012). Questionnaires were sent to members of the Section of Eating Disorders and the Faculty of Child and Adolescent Psychiatry of the RCP, with the aim of capturing all psychiatrists with an interest in ED, and

[1] Data from (O'Herlihy *et al.* 2007), p. 455.

83 valid unique responses from services were received. Of these 83 services, 62 (75%) were in the NHS, with 15 (18%) in the independent and 2 (2%) in the voluntary sector.

Inpatient care for AN was provided by 61 services (74%), while 64 (78%) provided outpatient care, and 40 (49%) provided day care. The number of inpatient beds for ED across child and adolescent and adult services in the UK was 447, with 226 provided by the NHS and 221 by the private sector. Of these, 330 beds (74%) were in specialist EDUs, again almost evenly split between the NHS and the private sector with 166 and 164 beds, respectively. While services remained clustered around London, the geographical distribution improved in England, with an increase in the number of services in the north of England and Scotland. Given that the data are reported for children, adolescents and adults combined, they do not allow us to compare the number of available beds directly to the COSI-CAPS study, which focussed on children and adolescents.

While bed availability and occupancy data are published for the NHS on a quarterly basis [2], these data report on child and adolescent psychiatric beds and adult psychiatric beds overall, without providing a breakdown by specialisation. Moreover, these data do not include beds in the private sector.

THE ROLE OF CHILD AND ADOLESCENT MENTAL HEALTH SERVICES

Child and Adolescent Mental Health Services (CAMHS) are part of the landscape of mental health services in England. They operate under a tiered system (Tiers 1-4) designed primarily to match levels of specialist skill with levels of need (Royal College of Psychiatrists 2005):

- Tier 1 services are provided by generalists such as general practitioners, social workers or teachers.
- Tier 2 is provided by mental health professionals not working in a team environment.
- Tier 3 is provided by multidisciplinary teams and is aimed at young people with more complex mental health needs.
- Tier 4 encompasses highly specialised inpatient, day patient and outpatient services.

[2] https://www.england.nhs.uk/statistics/statistical-work-areas/bed-availability-and-occupancy/bed-data-overnight/; retrieved 20/06/2018

Recent trends have emphasised local autonomy and choice as well as the integration of child and adult mental health services (Callaghan *et al.* 2017).

Despite a commitment to providing appropriate CAMHS services by 2006 in 'Every Child Matters' (2003) and the implementation of the 'National Service Framework for Children, Young People and Maternity Services' (1999), the 2008 final report on the CAMHS review (National CAMHS Review 2008) identified issues around access to services in a timely manner and for young people with persistent problems, driven by access criteria and regional variations in service provision.

A 2005 report highlighted that specialist CAMHS lack the capacity to meet demand (Royal College of Psychiatrists 2005) and recommended treatment of ED in CAMHS Tiers 2 or 3, with Tier 4 reserved for the most severe cases, such as severe ED.

While the 2011 strategy 'No Health without Mental Health' and 'Closing the Gap: Priorities for Essential Change in Mental Health' focussed on early treatment and created the children's IAPT programme, the 'Five Year Forward View for Mental Health' recommendations (2016) concluded that models of care are in practice still under-developed, with mental health problems not adequately supported in primary care and no clear pathways to secondary care in place. In addition, there are efforts to support mental health is schools, with guidance on identifying and supporting pupils published by the Department for Education in 2014 (Parking & Powell 2017), and mental health support in schools is expected to be discussed in a forthcoming Green Paper on mental health.

DETECTION OF ANOREXIA NERVOSA IN PRIMARY CARE AND ONWARD REFERRAL

Within the tiered CAMHS framework, primary care is an important initial point of contact with health services for many people with AN, and often serve as gatekeepers to higher tier care, but the problems identified in the Five Year Forward View are found for people with ED.

Ogg and colleagues (1997) reviewed case records of patients diagnosed with ED in primary care in Glasgow, 34 with DSM-IV diagnoses of AN. 70% of all patients were referred by their GP, and 21% by other specialists. In the five years prior to diagnosis, 71% consulted their GP more than 4 times, with common reasons for consultation being gynaecological

complaints related to amenorrhea or irregular periods, gastrointestinal problems related to ED, or psychological symptoms. Lask and colleagues (2005) also found a high level of primary care consultations up to five years prior to an ED diagnosis in a study of three groups: 19 girls with AN onset under 14, 19 girls with an emotional disorders and 10 girls with no history of mental health problems. Comparisons shown here are made between the group with AN and the non-clinical control group without mental health problems.

On average, those eventually diagnosed with AN had 57.7 consultations (SD 39.5), with 18.6 (SD 12.9) in the five years before diagnosis, 6.7 (SD 5.2) in the year before and 4.6 (SD 2.8) in the six months before diagnosis. The multi-variate analysis of variance showed that there was no significant difference between the three groups in terms of the total number of lifetime consultations (35.9 with SD = 21.7 in the non-clinical group), but higher than the number of consultations in the five years before diagnosis (mean=8.16, SD=6.0), in the year before diagnosis (mean = 1.1, SD = 0.9) and in the six months before diagnosis (mean = 0.58, SD = 0.69).

Those with AN had a greater number of consultations regarding eating, weight and shape, with most of them taking place in the six months before the diagnosis: Over the lifetime, those with AN had 2.53 (SD 1.43) consultations for eat, weight and shape concerns, while in the last six months, it was 2.5 (SD 1.42). The non-clinical control group, on the other hand, reported no such consultations, so that a single consultation about eating, weight and shape concerns was a significant predictor of early onset AN.

But while GPs are likely to see new incident cases of AN first and an increased frequency of contact can be a precursor to diagnosis, a vignette study (Currin *et al.* 2007a) found that females were more likely to receive an ED diagnosis than males, even when description of symptoms was the same, and that diagnosis did not adhere to guidelines. Possible explanations brought forward are a lack of knowledge about ED (Currin *et al.* 2009), and clinical guidelines were often not used in practice (Currin *et al.* 2007b). Gender of the GP also mattered, with female GPs being more likely to diagnose and refer ED to specialist services (Feeney *et al.* 2007). Turnbull and colleagues (Turnbull *et al.* 1996) analysed the GPRD and found that 20% of people presenting with an ED were treated exclusively in primary care, while 93% of those with AN were referred on to specialist care. This has been interpreted as a lack of confidence in or knowledge of treating AN, possibly due to the severity of the illness.

Currin and colleagues (2006) surveyed 3,783 GPs in South London, Kent, Sussex and Surrey and about 1/3 responded. On average, GPs saw 1.9 new cases and more than 50% of GPs had seen a new case in the past year. On average, there were 2.3 consultations before an ED was diagnosed. In contrast to the stepped care approach recommended by NICE (National Institute for Clinical Excellence 2004), there were two distinct approaches to referral. GPs in an area where specialist services existed were both better at identifying ED and tended to refer all ED patients. On the other hand, about 27% of new cases were treated exclusively in primary care. The most common destinations for referral were ED specialist services (22.8% of GP referrals), community mental health services (21.8%), psychiatrists (15.7%) and CAMHS (11%). Delay until treatment commenced was on average 7.6 weeks, mainly because of waiting lists for specialist services or GP counsellors. The two most common suggestions for improving treatment were quick access to specialist services (24%) and training opportunities (24%). The perceived role of GPs was to identify cases, offer a supportive environment and then make a referral. The referral system was perceived as complicated, and there was a concern that specialist care was not available locally. Many GPs mentioned that their knowledge of available services was lacking, and referral behaviour may depend on the (perceived) availability of specialist care.

While Currin's study highlights problems with referrals, Waller and colleagues (2009) found that around 35% of those referred on to specialist ED services were never seen, 50% entered treatment and only half of those who entered finished treatment. This is similar to a highly cited review that found only 34.3% of people with AN were in contact with mental health services (Hoek & van Hoeken 2003).

While some of these studies are now quite dated, it appears from the analysis of current policy recommendations that overall, the picture in CAMHS, including Tier 1 CAMHS, may be improving only slowly, and it is likely that these problems persist, and the recently updated NICE guidance on ED now recommends an immediate referral of suspected ED to community-based ED services (National Institute for Health and Care Excellence 2017a).

OUTPATIENT SERVICES FOR EATING DISORDERS

Gaps in NHS provision had led young people with acute needs being admitted to adult and paediatric wards (Tulloch *et al.* 2008). With reforms to the NHS, the private sector started filling gaps in provision from the 1980s (Treasure 2002).

In a 1999 survey, 82% of ED inpatient beds were managed by the private sector (O'Herlihy *et al.* 2003b), While a later study reported an increase of 69% in the number of independent sector beds from 1999 to 2006, while in the same period, NHS provision increased by only 11%, thus widening the gap in provision from 75% to 82% (O'Herlihy *et al.* 2007). There is also a pattern to be observed that private units appear to be less likely to participate in research studies (House *et al.* 2012; Tulloch *et al.* 2008).

This 'mixed economy', particularly in the area of ED, has led to substantial financial flows from the public to the private sector and increases the cost of treatment (Brown 1997; Treasure 2002). In response, additional NHS services were created, mostly in outpatient settings (Palmer & Treasure 1999).

At the same time, 'treatment philosophy' for AN shifted from a medical view focussing on weight restoration, to a more holistic view that includes the family both as a resource for the patient and recipients of support (Eisler 2005; House 2011). It is now thought that most people with ED can be treated on an outpatient basis (Gowers & Bryant-Waugh 2004). This was supported by a notion that inpatient treatment is not associated with better outcomes than community-based care (Tulloch *et al.* 2008) and may even be lead to comparatively negative outcomes (Meads *et al.* 2001; National Institute for Clinical Excellence 2004).

At the same time, there is a debate around whether the degree of service specialisation contributes to treatment outcome. The TOuCAN trial (Gowers *et al.* 2010) compared the costs and outcomes of inpatient treatment, specialist outpatient treatment and treatment as usual in CAMHS for 167 adolescents aged 12-18 with AN. There were significant improvements after one, two and five years in all three groups, and there was no difference in outcomes when controlling for baseline characteristics. The cost-effectiveness analysis showed that specialist outpatient treatment had the highest probability of being cost-effective. One limitation of this study was that only 65% of patients adhered to the allocated treatment.

House (2011) mapped ED services beyond primary care for all Greater London PCTs and tracked the care pathways and treatment of young people aged 13-18 with AN over 12 months. The aim was to explore care pathways with a view to the effect of service specialisation. Three distinct care pathways were identified based on the first service contact and referral: 1) specialist to specialist service, 2) non-specialist to specialist service and 3) non-specialist to non-specialist service. The non-specialist to non-specialist care pathway

was associated with a lesser degree of continuity of care and higher inpatient admission rates. Participants on this pathway had a higher gain in weight for height, the measure of improvement, which may have been driven by inpatient admissions. As the author discusses, the study results may not be representative of the situation in England because availability of specialist services is higher in London, which may affect the relative importance of the non-specialist to specialist pathway. However, given that previously there was little knowledge about actual care pathways which the differ considerable from the intended care pathway within a PCT, this study is the most comprehensive evidence on service organisation and service use of people with AN in the UK to date.

ECONOMIC EVALUATIONS OF TREATMENTS FOR ANOREXIA NERVOSA

Despite a keen interest in economic evaluations for treatments of AN, there is little empirical evidence available. However, there is no dearth of reviews attempting to identify such studies, and several recent systematic reviews are available. I draw on them to summarise the available evidence on cost-effective treatments for AN, and on economic evaluations of AN treatments more generally.

Stuhldreher and colleagues (2012) helpfully distinguish between cost-effectiveness analyses (CEA) and 'other cost studies' (OCS), with the former including studies comparing at least two treatment options on both outcomes and costs (encompassing also cost-utility analyses and cost-benefit analyses; CUAs and CBAs), and latter being a catch-all term for studies that do not fully meet these criteria, e.g., a cost-consequence analysis, or a study presenting both costs and outcomes but not formally analysing their joint distribution. The authors further pointed to the different approaches available: Conducting an economic analysis or evaluation as part of a clinical trial (usually, this will be a CEA) or other empirical data (usually, this will be an OCS), or performing a model-based analysis.[3] These distinctions will be applied in this section to categorise studies identified in the reviews. In addition, a distinction is made between 'prevention' and 'treatment' – with prevention studies usually focussing on ED more generally, rather than a single disorder.

A systematic review of the cost-effectiveness literature was undertaken as part of the recent review of the NICE guidance on eating disorders (National Institute for Health and Care

[3] More detail on these methods is provided in Chapters 2 and 3.

Excellence 2017a) which identified six studies for inclusion (Agras *et al.* 2014; Byford *et al.* 2007a; Crow & Nyman 2004; Egger *et al.* 2016; Herpertz-Dahlmann *et al.* 2014; Williamson *et al.* 2001). A slightly more recent systematic review (Le *et al.* 2017b) identified three additional studies for inclusion (Aardoom *et al.* 2016; Akers *et al.* 2017; Wright *et al.* 2014). On ad-hoc search of PubMed for additional literature, conducted as part of revisions to the thesis in 2018, unearthed a further two studies (Bode *et al.* 2017; Le *et al.* 2017a). In addition, I drew on several Cochrane reviews to summarise the evidence for different forms of treatment: Self-help and guided self-help (Perkins *et al.* 2006), anti-depressants (Claudino *et al.* 2006), family therapy (Fisher *et al.* 2010), individual psychological therapy on an outpatient basis (Hay *et al.* 2015) and prevention of eating disorders (Le *et al.* 2017c; Pratt & Woolfenden 2002), which did not add to the list of studies.

I summarise the findings of these reviews in Table 2-2, based primarily on Le and colleagues (2017b) and NICE (National Institute for Health and Care Excellence 2017a), and provide more detail on full cost-effectiveness studies of treatments for AN, i.e. those that collect individual-level cost data across multiple cost categories (see Chapter 3 for more detail on the need to capture all relevant costs in an evaluation).

In total, there were five CEAs conducted alongside an RCT (Aardoom *et al.* 2016; Akers *et al.* 2017; Byford *et al.* 2007a; Egger *et al.* 2016; Herpertz-Dahlmann *et al.* 2014), and only two of these (Byford *et al.* 2007a; Egger *et al.* 2016) were RCTs evaluating an intervention to treat AN while also collecting individual-level cost data. Other studies either looked at only intervention costs or intervention costs and narrow health care costs or used average (top down) cost figures, e.g. cost per inpatient stay, average total societal costs) instead of performing bottom-up costing at the individual level and individual-level statistical analyses of cost data.

Table 2-2: Economic evaluations of AN treatment

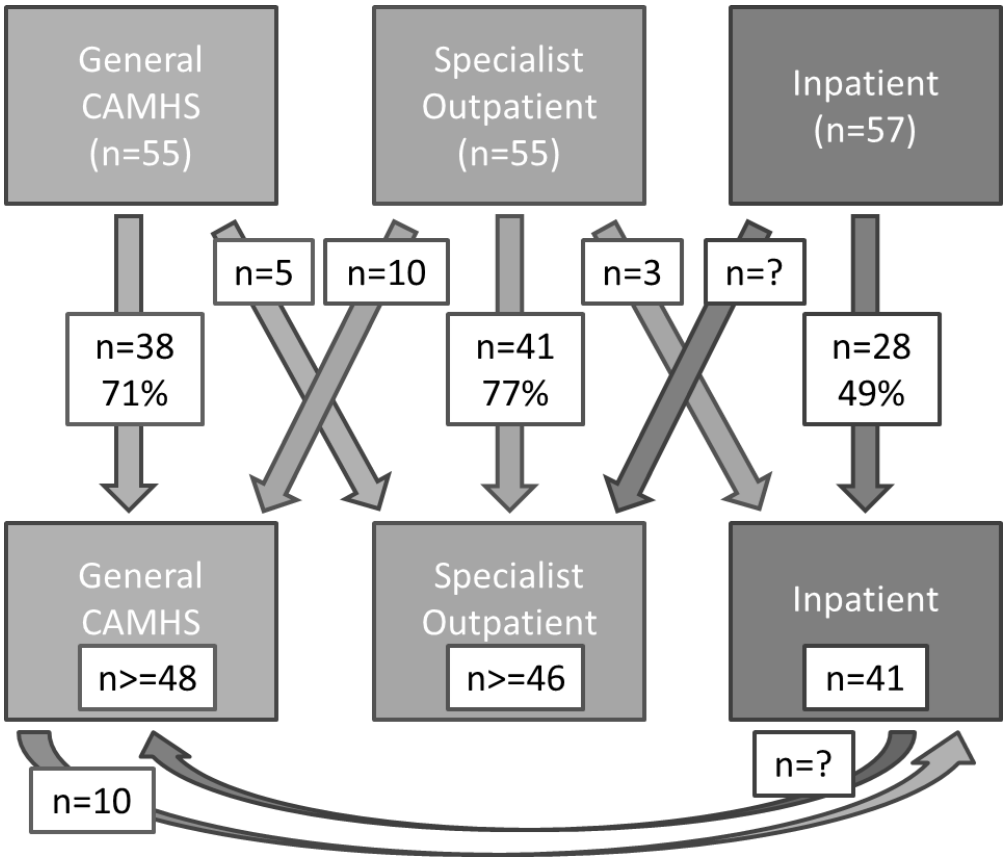
Study and analysis type	Interventions and outcome measure	Country, population	Currency, discount rate and time horizon	Cost perspective, included cost categories	Main findings
Aardoom et al (2016); CUA alongside RCT	Three variants of 'Featback' intervention vs waitlist; QALY	The Netherlands; Females >= 16 with self-reported ED symptoms	2015 € No information 5 months	Societal; Intervention costs, health care costs, productivity losses	Intervention without or with low-intensity therapist support were dominant compared to the waitlist control.
Agras el al (2014); OCS alongside RCT	Family-based treatment (FBT) vs systemic family therapy (SyFT); Percentage in remission	USA; Adolescents 12-18 years with AN	2007 $ (year unclear); Not applicable End of treatment (36 weeks)	Payer; Intervention costs, hospital admissions;	Cost difference FBT vs SyFT -$9,042; Difference in remission rates: 8%
Akers et al (2017); CEA alongside RCT	Cognitive dissonance interventions vs educational brochure; meaningful clinical change in ED symptoms	USA; Females with average age of 21.6 years	2012 $ No rate applied 3 years	Payer (university); Intervention costs only	ICER: US$856 per individual with meaningful clinical change
Bode et al (2017); Model-based OCS (cost-offset)	CBT and focal psychodynamic therapy (FPT) for AN vs optimised TAU; No outcome measures.	Germany; General population with AN.	2014 or 2015 € (year unclear); Not applicable; 12 months	Societal; Individual therapy, inpatient treatment, productivity losses, sickness benefits, early retirement benefits, mortality	Potential savings of € 2.51 and €2.33 per € invested for CBT and FPT, respectively
The Butterfly Foundation (2015); Model-based CUA	Best practice model vs TAU; DALYs	Australia; People with ED	2013 AUS$ (year unclear); 7%; 10 years	Societal; Intervention cost, health care, productivity, employment, welfare	Cost difference: -AUS$57,690 DALY difference: -1.29

Study and analysis type	Interventions and outcome measure	Country, population	Currency, discount rate and time horizon	Cost perspective, included cost categories	Main findings
					Best practice model is dominant. Savings per participant over 10 years of AUS$250,261.
Byford et al (Byford *et al.* 2007a); CEA alongside RCT	Specialist outpatient treatment (SOP) vs inpatient treatment (IT) vs general outpatient treatment (GOT; Morgan-Russel scores (MRAOS)	UK; Adolescents aged 12-18 with DSM-IV diagnosis of AN	2003/04 £ 3.5% 2 years	Public sector; Health care, social care, education	At 2 years: Specialist outpatient treatment dominant. At WTP £0 per point improvement on MRAOS, probability of cost-effectiveness is 78% for SOP, 16% for IP, 6% GOT.
Crow & Nyman (2004), Model-based CEA	Adequate care vs usual care; Years of life saved	USA; Unspecified population with AN	2002 or 2003 $ (year unclear) No discount rate Lifetime	Payer; Intervention costs only.	ICER: US$30,180 per year of life saved (for adequate care)
Eggers et al (2016); CEA alongside RCT	Focal psychodynamic therapy (FPT) vs CBT vs optimised TAU; Recovery, QALY gained	Germany; Females >=16 years with DSM-IV AN and sub-threshold AN	2008 €; Discount rate unclear 22 months	Societal; Intervention costs, health care costs, informal care, travel, productivity losses.	FPT dominant on both outcomes and for direct costs only and from a societal perspective. Probability that FPT is cost-effective <68% vs TAU and <67% vs CBT at WTP of €50,000 per QALY gained. Probability >=85% for cost per recovery >= €10,000 compared to CBT and >=25,000 for TAU.
Herpertz-Dahlmann et al (2014); CEA alongside RCT	Day treatment following short inpatient care vs continued inpatient care; Improvement in BMI	Germany; Adolescent females aged 11-18 with AN	2013 € (year unclear); Not applicable; 12 months	Payer; Psychiatrist, psychologist, inpatient admissions, outpatient visits.	Day treatment is dominant intervention. Difference in average costs per participant and difference in change in

Study and analysis type	Interventions and outcome measure	Country, population	Currency, discount rate and time horizon	Cost perspective, included cost categories	Main findings
				Note: No individual-level cost data collection.	BMI: -€8,367 (p=0,002), 0.46 (p<0.0001).
Le et al (2017a); model-based CUA	Family based treatment (FBT) vs adolescent-focussed individual therapy (AFT) vs no intervention; DALY averted	Australia; Adolescents aged 11-18 with AN of short duration	2013 AUS$; N/A; 6 years	Payer and carers; Intervention cost (including training and supervision), clinical investigations, GP visits, hospitalisation, carer time and travel cost	Mean ICER: FBT $5,089 per DALY averted AFT $51,891 per DALY averted Probability of being cost-effective at AUD$ 50,000 per DALY averted: 100% (FBT) and 45% (AFT).
Williamson et al (2001); OCS	Partial day hospital care vs inpatient care; No outcome measure beyond hospitalisation	USA; People with AN/BN or sub-threshold AN/BN	2000 $ (year unclear); Not applicable; 12 months	Payer; Intervention cost, inpatient admissions	Cost difference -$9,645, p<0.02
Wright et al (Wright *et al.* 2014); Model-based CUA	ED screening vs current practice; Life years with ED avoided and QALY gained	USA Males and females aged 10-17 years	2012 $ 3.5% 10 years	Payer; Intervention costs, health care costs	ICER: US$9,231 per life year with ED avoided; US$57,687 per QALY gained

The TOuCAN trial (Byford *et al.* 2007a; Gowers *et al.* 2010) compared the costs and outcomes of inpatient treatment, specialist outpatient treatment and treatment as usual in Child and Adolescent Mental Health Services (CAMHS) for 167 adolescents aged 12-18 with AN. One limitation of this study was that only 65% of patients adhered to the allocated treatment. Figure 2-5 illustrates patient movement from allocated treatment (top) over the course of the trial (based on Gowers *et al.* 2010), either due to clinical need or due to patient and family preference. It is therefore not surprising that the proportion with a 'good outcome' in each randomisation group was very similar (around 60-67%), and average costs per week over the two-year follow-up period were also similar, ranging from £253 for the specialist OP group to £386 in the general CAMHS group (2003/04 costs).

Figure 2-5: Treatment adherence in the TOuCAN trial



Cost data were collected from clinical records and patient report at the one-year and two-year follow-up. There were significant improvements on the Morgan-Russel scale (Morgan & Hayward 1988), a measure of AN symptoms, after one, two and five years in all three groups, and there was no difference in outcomes when controlling for baseline

characteristics. The cost-effectiveness analysis showed that specialist outpatient treatment had the highest probability of being cost-effective (up to ca. 60%).

More recently, the ANTOP trial (Anorexia Nervosa Treatment of Outpatients) in Germany compared three models of outpatient treatment for adult females with AN: focal psychodynamic psychotherapy (FPT), enhanced cognitive-behavioural therapy (CBT-E), and optimised treatment as usual (TAU-O). Cost data were collected from monitoring data and hospital records (inpatient treatment) over a period of 22 months, and data on other health care services and productivity losses were collected using questionnaires covering a 3-month retrospective period at baseline and at 22 months. Average total costs at 22 months in the FPT group were €21,512 (2008 prices), €24,690 in the CBT-E group and €24,827 in the TAU-O group. Hospitalisation was required for 19% of patients assigned to FPT, 29% of patients in CBT-E and 40% in TAU-O. The contribution of productivity losses from absenteeism and presenteeism to total costs at follow-up was 53% in the FPT group, 52% in CBT-E and 46% in TAU-O. In the FPT group, 35% of patients were recovered at the end of the study, compared to 21% in CBT-E and 12.5% in TAU-O. These results show a trend towards higher hospitalisation rates and associated higher service costs in the TAU-O group, alongside a poorer outcome. Cost-effectiveness analysis employing a net-benefit approach adjusting for baseline variables showed a probability that FPT (compared to TAU-O) would be considered cost-effective of 95% if an additional recovery is valued at €9,825 or more. In a comparison of FPT with CBT-E, the probability reached 85% at a valuation of >=€24,550 per recovery. In the comparison of CBT-E with TAU-O, the probability that CBT-E would be considered cost-effective did not reach values above 90% for valuation values of up to €150,000 per recovery. While the study authors point to uncertainty with regard to their cost estimates (e.g. measurement of productivity losses), another limitation in the context of economic evaluation is using 'recovery' as an outcome, as recovery is likely to be associated with discharge or stepping down of care. Recovery therefore affects both the cost and outcome side of the cost-effectiveness equation.

While the evidence base regarding the cost-effectiveness of AN treatments is growing, there remains a need for robust empirical studies that consider the full range of relevant costs and are able to employ patient-level analysis strategies. Model-based analyses represent an alternative where empirical data are lacking, but best practice recommendations, including transparency about assumptions and addressing issues of uncertainty, need to be followed.

WHAT ARE THE SOCIETAL COSTS OF ANOREXIA NERVOSA?

COST OF ILLNESS ESTIMATES FOR ANOREXIA NERVOSA

As above, I apply the definition by Stuhldreher and colleagues (2012), who define CoIs as a study aiming to determine the costs due to AN for more than one cost category (e.g., inpatient treatment only), and where the analysis is not limited to only one type of intervention or treatment. Studies aiming to determine costs but not meeting the other criteria are referred to as 'other cost studies' (OTCs).

At the time of inception of this thesis, the literature on CoI of AN had recently been reviewed by Simon and colleagues (Simon *et al.* 2005) who found two 'full' CoI studies (Krauth *et al.* 2002; Office of Health Economics 1994), i.e. studies taking a societal perspective, and three 'partial' cost studies estimating the direct costs of ED treatment for inpatient treatment only (Nielsen *et al.* 1996; Rathner & Rainer 1997) and for inpatient and outpatient treatment (Striegel-Moore *et al.* 2000).

A later review (Stuhldreher *et al.* 2012) identified one additional CoI for AN (Mitchell *et al.* 2009). Crow (2014) identified two RCTs collecting broader costs in the health domain over a three-month retrospective period (Stuhldreher *et al.* 2015) and a two-year period (Byford *et al.* 2007a) as well as one study looking at inpatient costs only (Haas *et al.* 2012b).

A further systematic review (Ágh *et al.* 2016) identified another two studies looking at inpatient costs only (Haas *et al.* 2012a; O'Brien & Patrick 2008) and a study reporting costs associated with outpatient family therapy (Lock *et al.* 2008).

Finally, Striegel Weissman and Rosselli (2017) identify a study of the costs associated with inpatient treatment that also considers the costs falling on caregivers in terms of lost work productivity and lost leisure time (Toulany *et al.* 2015) and a study of out-of-pocket expenditure and its relationship to treatment adherence (Gatt *et al.* 2014).

My additional searches, which focussed primarily on full CoI studies for England and included searches of the 'grey' literature, identified two additional CoI studies for England (King's Fund *et al.* 2008; ProBono Economics 2012). Another 'grey' literature study (The Butterfly Foundation 2015) was included in the NICE evidence review on cost-effective treatments for ED (National Institute for Health and Care Excellence 2017b). In the UK

context, the COSI-CAPS study estimated the costs of inpatient stays for ED (Tulloch *et al.* 2008).

It should be noted that there are of course other 'partial' cost studies looking at specific aspects of ED treatment, such as Brown (1997), who investigated the 'mixed economy' of ED treatment, i.e. the growing involvement of the private sector in ED treatment in the UK, studies undertaking simple, often ad-hoc cost analyses of one or several treatment options or service models (Birchall *et al.* 2002; Meads *et al.* 2001). Other studies do not distinguish between different types of ED (de Oliveira *et al.* 2016). There are also studies that report a societal cost estimate (for example, Gustavsson *et al.* 2011), but in fact use data from one other study (Krauth *et al.* 2002) that are used to extrapolate to different contexts.

Table 2-3 shows an overview of the identified 'full' CoI studies, indicating which cost categories were included. While not a CoI study, I also show the study by Byford and colleagues (Byford *et al.* 2007a), as although it covers a selected patient population rather than attempting to calculate total societal costs, it covers the widest range of services and supports and is particularly relevant to the English context.

Table 2-3: Overview of CoI estimates

Study	Country	Direct costs	Indirect costs	Intangible costs
Office of Health Economics (1994)	England	Inpatient treatment General practice	No	No
Striegel-Moore et al (2000)	USA	Inpatient treatment Outpatient treatment	No	No
Krauth et al (2002)	Germany	Inpatient treatment Rehabilitation/convalescence Pension insurance	Inability to work Premature mortality	No
Byford et al (2007a)	UK	Inpatient treatment Outpatient treatment Primary care Social care Voluntary sector Education	No	No
King's Fund (2008)	England	Inpatient treatment Outpatient treatment	Productivity losses	No
Mitchell et al (2009)	USA	Hospital/clinic Health care provider Prescription medication	No	No
ProBono Economics (2012)	England	Inpatient treatment	Unemployment Reduced earnings Premature mortality	Premature mortality
The Butterfly Foundation (2012)	Australia	Hospital Out-of-hospital treatment Medication Out of pocket expenditure: food, travel Carer costs/transfers Other indirect costs Funeral costs	For all EDs: Loss of income Absenteeism Lost home production Presenteeism Premature mortality	For all EDs: Burden of disease

While there has been an increase in the number of CoI estimates available, at the time this study was conceived, no existing study included all types of costs separately for AN, and the spectrum of services and impacts included is often limited. Below, I provide more detail on full CoI studies, first presenting the 'international' estimates and then focussing on estimates for England and the UK, as they are most relevant to this thesis. Prices in 2010/11 £are provided for comparison purposes. These have been uprated using the appropriate GDP deflator to 2010/11 prices and then converted to £[1].

INTERNATIONAL ESTIMATES

Krauth and colleagues (2002) estimated the annual cost of EDs for Germany based on a sample of benefit data from statutory health insurance and statutory pension insurance. The cost of inpatient treatment was based on average hospital charges. A projected 4,618 people received inpatient treatment at a total cost of €59.1m (£56.9m). Rehabilitation measures in convalescence centres (485 cases) cost €2.7 million (£2.6m), rehabilitation (474 cases) €3.1 million (£3m). Productivity losses were calculated based on 1,155 people each losing 78.4 days of work (€8 million; £7.7m), and the discounted present value of future earnings for 214 people who died prematurely due to AN (€122.5 million; £117.9m). The total annual cost of AN was estimated at €195.4 million (£188m; range €115.1 million-€297.4 million; £110.7m-£286.1m) and €5.3000 per person (£50,990). The authors state that this is relatively low compared to the total cost of other conditions such as cardiovascular diseases or obesity; however, the proportion of indirect cost is high at 67%, driven by high mortality rates in a young patient population.

Striegel-Moore and colleagues (2008) searched the 1995 MarketScan insurance database to quantify the use and cost of services in the US. 517 female and 49 male patients were treated for AN (2000). 21.5% of females and 18.4% of males were hospitalized for AN, with an average length of stay of 26 days at a cost of $17,384 (females; £15,433) and 15.6 days at a cost of $8,799 (males; £7,811). The cost of outpatient treatment was $2,344 for females and $1,154 for males (£5,366 and £2,438). The mean annual cost of treatment was $6,045 for

[1] Data from https://data.worldbank.org/indicator/ and https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/371079/Avg-year-20110331.csv/preview

females and $2,746 for males (£5,366 and £2,438). According to this estimate, treatment costs for females with AN are higher than those for schizophrenia ($4,824; £4,283).

A partial CoI study of AN from the US covered inpatient costs, outpatient care, and the costs of drugs based on a claims database (Mitchell *et al.* 2009). This study included a non-ED control group and calculated the additional costs due to AN at $1,288 (£988).

Deloitte Access Economics estimated the annual costs associated with ED in Australia on behalf of the Butterfly Foundation (The Butterfly Foundation 2012). While this estimate was ambitious and includes a comprehensive list of cost categories, beyond health care data there were few empirical data sources so that a lot of uncertainty around the assumptions made to construct the estimate and – except for direct health care costs – it was not possible to distinguish between different types of ED. Table 2-4 outlines the components of the estimate and shows the resulting costs in 2010/11 GBP.

Table 2-4: Australian CoI estimate for AN, in original currency and 2010/11 GBP (£)

Cost category	Cost for AN/ED in 2008/09 AUD	Cost in 2010/11 GBP
Hospital (AN only)	57.8m	38.6 m
Out of hospital medical expenses (AN only)	1.5m	1.0 m
Prescriptions (AN only)	0.5m	0.3 m
Loss of income	5.98bn	4.0bn
Absenteeism and lost home production	1.8bn	1.2bn
Presenteeism	5.3bn	3.5bn
Productivity losses from premature death	2bn	1.3bn
Carer costs	8.54m	5.7m
Other indirect costs	585m	390.6m
Funeral costs	9m	6.0m
Deadweight loss (government transfers and revenue forgone)	9m	6.0m
Burden of disease (intangible costs)	52.6bn	35.1bn

With the exception of the Deloitte estimate (The Butterfly Foundation 2012), none of the international CoI estimates attempt to include intangible costs. The firmest data available are those for inpatient treatment, which is arguably the most important health service cost to capture as it likely accounts for a large proportion of health care costs. There is more uncertainty around estimates of outpatient treatment, and – given the high cost of inpatient

treatment and the shift in 'treatment philosophy' towards outpatient treatment – there is a need to improve data quality with respect to the costs of outpatient services.

UK ESTIMATES

An early study of the cost of EDs in the UK (Office of Health Economics 1994) adopted a health service provider perspective and used data from the National Survey of Morbidity in General Practice and the Hospital Inpatient Enquiry to estimate service use in general practice, inpatient bed days and prescriptions. Intangible costs were not included, and while the intention was to include the costs of outpatient treatment, no information was available so no costs were included. The total cost to the NHS was estimated at £4.2 million per annum €6m in 2010/11 prices). This study has a limited perspective, primarily due to a lack of data availability.

The King's Fund (2008) estimated the service cost and lost employment of AN in the UK. Based on the Hospital Episode Statistic, the costs of inpatient care were estimated to be £2.5 million in 2007/08 prices (2010/11 £2.65m) for people under age 15 and £8m (£8.48m) for people aged 15-34. The cost of outpatient treatment was derived assuming that only 34.4% of all people with AN are in contact with mental health services (following Hoek and van Hoeken), and that outpatient costs are 41% of inpatient costs (following Striegel-Moore et al (2008), or £4.4 million (£4.54m). Lost employment was calculated on the basis that 1,830 people received Incapacity Benefits for EDs. Assuming a weighted annual salary of £19,051 (£20,201), the annual cost of unemployment was £33 million (£35m). The total cost was £48m (£50.9m) per annum, with 69% due to lost productivity.

ProBono Economics (2012) put together an estimate of the costs associated with ED. Their estimate included the costs of inpatient and outpatient treatment, primary care and private healthcare, well as lost earnings, disease burden and premature mortality. Generating a highest and lowest estimate, they estimated the range of costs of ED to be between £1.26bn and £9.6bn in 2011/12 prices (£1.24bn and £9.47 in 2010/11 prices, respectively); much of it due to intangible costs and productivity losses.

The King's Fund study and the ProBono Economics study both draw on HES data to estimate the number of inpatient days. They then applied assumptions to determine the number of days provided to children and adolescents vs adults (King's Fund: ¾ of inpatient days in for people under age 35; ProBono Economics: The total costs of adult admissions

are about twice as high as those for children). Unit costs are then applied, and while both use PSSRU unit cost data from 2006 and 2009/10 respectively, there was a large difference in estimates at £213 and £503 (in 2010/11 prices), respectively. This demonstrates that even though similar data sources were used, large differences in estimates can still arise, with a King's Fund estimate of inpatient costs of £11m and a ProBono Economics estimate of £49m – although the latter estimate is unable to differentiate between AN and BN (both estimates shown in 2010/11 prices). Data quality declines as we move further 'outward' from inpatient costs, so that productivity losses are estimated purely on assumptions (rather than empirical evidence) about unemployment and productivity reductions, and usually drawn from different mental health problems such as depression. It is unclear whether these data are applicable to AN.

Similar to the picture presented by the international studies, there is great uncertainty around the costs of outpatient treatment. The King's Fund estimate is based on the ratio of outpatient costs to inpatient costs found by Striegel-Moore for the US (Striegel-Moore *et al.* 2000), while ProBono Economics base their estimate on unpublished HES data (ProBono Economics 2012, p. 19). This points to the large gap in our understanding in the costs of outpatient care for AN.

When looking at estimates from different countries it is important to keep in mind that costs depend on the organisation of the specific health care system, prevailing approach to treatment and insurance arrangements, so that the results may not necessarily be comparable on a like-for-like basis. This explains at least some of the variance between the different estimates, although Striegel Weissman and Rosselli (2017) report that even US estimates varied from $127 to $8,042 per patient[2], and there is a large amount of heterogeneity of methods, perspectives and assumptions. As a result, Striegel Weissman and Rosselli in 2017 arrive at the same conclusion as Stuhldreher did in 2012:

> "(A) comprehensive evaluation of all costs associated with eating disorders are still lacking, as are studies that utilize an appropriate non-disorder comparison group for estimating excess costs due to an eating disorder" (Striegel Weissman & Rosselli 2017, p. 52).

[2] As it is unclear what the price years is for these costs, I am unable to uprate these consistently.

WHY DO COSTS VARY?

The production of welfare approach explores whether the level of cost is related to the observed change in clinical outcome, adjusting for patient characteristics[3]. The question this approach answers is therefore whether there is a significant relationship between resources invested and outcomes achieved.

One early study of service use in AN, Button and colleagues (1997) tracked 100 consecutive patients referred to an eating disorders service; 21 had a diagnosis of AN. There was no statistically significant relationship between service consumption, measured as therapy sessions, inpatient admissions and correspondence, and outcome at follow-up. Time in contact was almost significant, with a longer contact time predicting a poorer outcome. A diagnosis of AN and working part time were predictors of longer time in contact with the service and more correspondence.

In the more recent COSI-CAPS study (Tulloch *et al.* 2008), the costs of inpatient admissions were not significantly associated with quality of life or mental health scores, nor were they associated with BMI at admission.

Inpatient care is a significant contributor to the total costs associated with AN. Inter-individual variation in total hospital costs is typically (and perhaps trivially) driven by length of stay. Length of stay appears to vary significantly between international studies, as do costs per stay. A US study found an average of 26 days in a system where outpatient treatment appeared to be the norm at a cost of $17384 (Striegel-Moore *et al.* 2000), compared to 50 days at a cost of €12800 in a German study (Krauth *et al.* 2002).

Recently, studies using micro-costing approaches in costing inpatient stays have made it possible to look at variations in cost per day as well as cost per stay.

Haas and colleagues (2012b) studied the hospital costs associated with ED admissions to a Berlin hospital in 2006-2009. AN was associated with higher costs than BN or ED-related obesity. A co-morbid personality disorder and a unit decrease in admission BMI in AN predicted increased hospital cost. In another study, lower admission BMI and personality and behaviour disorders were positively associated with costs (Haas *et al.* 2012b). These

[3] More on the production of welfare approach in Chapter 3.

studies were motivated by the impending introduction of a tariff system for reimbursement and the question whether a single tariff should apply to all ED.

Lower BMI was also a significant predictor of higher hospital costs in a recent Canadian study (Toulany *et al.* 2015), where a unit increase in BMI was associated with a 15.7% decrease in costs.[4] In an analysis of the US Medical Expenditures Panel Survey (Samnaliev *et al.* 2015), comorbid mental health problems were associated with a non-significant trend towards higher costs.

Stuhldreher and colleagues (2015) found that women commencing outpatient treatment who reported a hospital stay in the preceding three months had four times higher costs than those without a hospital stay. Predictors of total costs in those reporting outpatient treatment only were whether the disorder was of the binge-purging type, whether duration of illness was greater than six years and whether at least one mental health comorbidity was present. BMI was not associated with total costs. For women with a hospital admission, a higher BMI at baseline, i.e. after hospitalisation, was associated with higher costs. The authors stipulate that an increased weight gain is associated with a longer hospital stay.

A study using data from the US Medical Expenditure Panel Survey estimated the difference in annual health care costs, employment status and income, comparing participants with and without ED (Samnaliev *et al.* 2015). Health care costs were larger for the ED group. The impact of mental health comorbidity was significant for annual earnings.

[4] This study also investigated variations in caregiver costs in terms of lost work productivity and lost leisure time, and found higher BMI and younger age to be negatively associated with these costs.

CONCLUSIONS

ON THE USEFULNESS OF COST OF ILLNESS STUDIES

Economics is the science concerned with efficient allocation of resources, and health economics is therefore concerned with the efficient allocation of resources in the area of health. One of our tools is economic evaluation, which involves comparing two alternative courses of actions in terms of both their costs and their impact on health (Drummond *et al.* 2015). Cost of illness studies (CoI) focus only on the costs, and are therefore not a form of evaluation. There is a longstanding debate in the literature about whether their construction is a useful pursuit.

Koopmanschap (1998) summarises the debate around the usefulness of CoI studies in the context of health policy. The primary point of criticism is that – as pointed out above – CoI studies alone do no aid in the evaluation of healthcare programmes because they themselves do not include information on effectiveness. However, CoI studies can be combined with information on effectiveness into cost-effectiveness analyses using economic modelling techniques that combine information from a variety of sources where no single source (such as individual-level data on costs and effects from an RCT) is available (Drummond *et al.* 2015). It is further argued that CoI estimates can help to prioritise conditions where future economic evaluations may be useful. On the other hand, this may lead to prioritisation of programmes for diseases that are already expensive.

Kennelly (2017) suggests that CoI estimates may simply miss the point, as most health care expenditure is effective and there is no compelling reason why there should be less of it.

In my view, a large cot of illness may be caused by underinvestment in prevention or treatment, resulting in a large burden, for example in terms of lost productivity or excess mortality, that could be avoided with provision of additional (effective) interventions.

Moreover, CoI studies can usefully highlight major cost components contributing to total costs, and explain trends or project costs as part of scenario analysis.

Byford and colleagues add that "simply identifying an area of high expenditure does not provide enough information to suggest inefficiency and waste and so should not automatically take precedence for further scrutiny" (Byford et al., 2000, p. 1135). They

further argue that CoI estimates do not help determine how much of the cost could be saved, as diseases will not be completely eradicated, and it is unclear whether prevention will be cheaper than the CoI. Low prevalence condition with a high cost to individuals that are amenable to prevention may result in lower societal CoI than high prevalence conditions.

This argument points us in the direction of perhaps calculating a cost per person with a condition, in addition to a societal figure, as the point is well taken and raises important questions around equity – particularly where investment in health care is primarily from funds raised by general taxation.

This adds further to the argument that CoI studies – while they may have some intrinsic value – are at best a first step towards economic evaluation. As mentioned above, economic evaluation such as cost-effectiveness analysis requires information on both costs and effectiveness. The distinction between 'incidence-based' and 'prevalence-based CoI estimates (see above) is important when discussing the usefulness of CoI estimates.

Incidence-based CoI studies that model or describe the course of an illness over time for an individual and attach costs to 'health states' (e.g. the costs associated with service use in the year prior to diagnosis of AN, or the costs associated with productivity losses as a consequence of early-onset AN) can provide the 'cost' side of the cost-effectiveness equation. In such a model-based economic evaluation, the costs associated with the course of AN without the intervention being evaluated or a second, comparator intervention, would be compared to the intervention under study.

Figure 2- 6 shows a simplified model of the course of illness for AN. A discussion of individual-level modelling approaches can be found in Chapter 3.

Here, three possible 'states' are available:

- Never AN: An individual never goes on to have AN.
- Current AN: An individual is currently diagnoses with AN.
- No longer AN: An individual who had AN is no longer affected.

In a model with 'Markov periods', which is a simple form of economic model that is used here as an example, individuals are assumed to spend a specified amount of time in a state, for example, a one-year period.

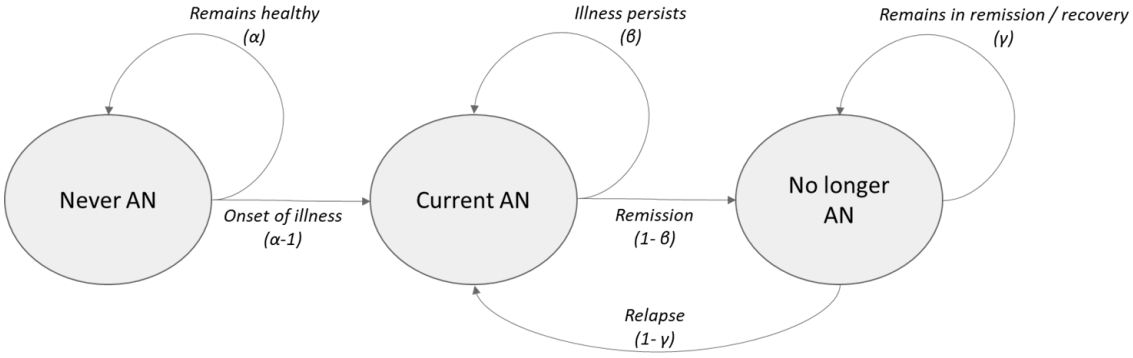
In addition, there are six 'transitions' with their associated 'transition probabilities' (where pairs such as α and 1-α add up to 100%):

- Remains healthy: An individual without AN in period t still does not have AN in period t+1 (α).
- Onset of illness: An individual without AN in period t has AN in period t+1 (1-α).
- Illness persists: An individual with AN in period t still has AN in period t+1 (β).
- Remission: An individual with AN in period t no longer has AN in period t+1 (1-β).
- Remains in remission/recovery: An individual with AN in period t and no AN in period t+1 is still without AN in period t+2 (γ).
- Relapse: An individual who was in remission from AN in period t+1 has AN in period t+2 (1-γ).

Individuals move between 'states' via 'transitions', from one period to the next. There is a 'transition probability' attached to each transition. In addition, costs are attached to each state and each transition.

For example, the costs associated with individuals never having AN may be assumed to be zero, as no additional costs due to AN arise in this case. As shown above, costs increase in the year prior to diagnosis due to an increased frequency of GP visits. The transition 'onset of illness' therefore could be associated with these costs. While no data are available for the 'No longer AN' state, i.e. no empirical cost data are available for those who have are in remission or recovery, we can assume for the sake of argument that in this state, costs are higher than in the 'Never AN' state due to the longer-term consequences of the condition, but lower than in the 'Current AN' state as there is no need for treatment.

Figure 2-6: Schematic state-transition model of the course of illness for AN



The simplest way of approaching model-based economic evaluation would be to determine how an intervention changes transition probabilities. A successful treatment, for example, might improve the chance of remission, i.e. increase the transition probability for 'remission'. Holding all other transition probabilities equal, costs for an individual receiving this intervention would be lower, as they are more likely to enter the less costly state ('No longer AN').

A preventative intervention, on the other hand, may increase the probability that individuals 'remain healthy', i.e. remain in the 'Never AN' state, and therefore reduce the transition probability for 'Onset of illness'. All else remaining equal, costs will again be lower as we have assigned a zero cost to the 'Never AN' state, and the intervention has increased the probability of remaining in this state.

The example above looks at the potential for using incidence-based CoI estimates for model-based economic evaluation for AN, but general CoI studies that cover more than one condition can provide comparable estimates and therefore allow for the comparison of relative savings from interventions across these conditions (Koopmanschap 1998).

- Reflecting on the arguments surrounding the usefulness of COI estimates, prevalence-based CoI studies have several, but perhaps more limited, uses:
- Raising awareness for the burden of a specific disease, especially where there is concern about a lack of effective interventions or a lack of treatment provision;
- Prioritising future efforts where the costs of several conditions are estimated on an equivalent basis;

- Identifying the relative size of contributors to total costs to determine where the burden of disease falls. This is relevant both in terms of who might fund additional interventions, but also for equity considerations where caregiver burden or personal expenditure are concerned in a publicly funded health care system;

Incidence-based CoI studies on the other hand can be used directly in cost-effectiveness or disease modelling studies to describe trends when analysed in the context of demographic or technological developments.

In practice, CoI studies are used to justify interventions, assist in the allocation of research funding, provide a basis for prevention policy and to provide a framework for economic evaluation. In addition, CoI studies are successfully used by policy and decision makers to justify budgets (Rice 2000), suggesting a pragmatic motivation for their continued use.

As a result, cost-of-illness studies have the potential to influence both policy and practice, as well as shape the future research agenda.

The implementation of cost-effective alternatives to inpatient treatment across the country should be a priority to ensure equitable access and adequate treatment (Department of Health 1999; Green *et al.* 2005; Tulloch *et al.* 2008). One piece of evidence needed to facilitate this is a sound CoI estimate, and cost-effectiveness analyses building on it. A CoI estimate that can disaggregate costs and consider unmet need can help us understand the 'paradox' (Striegel Weissman & Rosselli 2017) of high costs coupled with infrequent treatment and high levels of unmet need in AN.

POLICY RELEVANCE AND CONTRIBUTION TO KNOWLEDGE

A lot has been written about Anorexia nervosa, but given the low prevalence, the ethical and practical difficulty in conducting clinical trials with a severely ill population, and a shifting understanding of the illness and its aetiology, significant gaps in the knowledge remain about how best to approach treatment for this severe condition. Economic evaluation can play a part in aiding decision making.

There is a clear demand for a cost of illness estimate for Anorexia nervosa to help in understanding the condition and its complex interplay with services (Striegel Weissman & Rosselli 2017).

Particular gaps in the evidence base have been identified:

- There is a dearth of information on service use and costs beyond inpatient care.
- Given a shift from inpatient to outpatient care, information on the costs of different forms of outpatient treatment is required.
- Few existing estimates include indirect costs, such as lost employment, and little is known about the impact of AN on these outcomes.
- Few existing estimates consider the costs of disability and mortality associated with AN.
- Little information is available about why costs vary between individuals.

The aim of this thesis is to answer the following overarching questions:

- What are the annual societal costs of AN for England?
- Why do costs vary between individuals?

Based on my survey of the literature, I specified concrete research questions that address different aspects of the societal costs of AN.

Research questions 1 and 2 investigate aspects of *direct costs*:

- **RQ1:** What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?
- **RQ2:** What services do people use while being treated for AN on an outpatient basis, what are the associated costs, and why do these costs vary?

Research question 3 addresses *indirect costs*:

- **RQ3:** What is the impact of AN on education, employment, income and related outcomes, and for whom?

Research question 4 addresses *intangible costs*:

- **RQ4:** What is the loss of life associated with AN in England?

Research question 5 addresses the totality of *societal costs*:

- **RQ5:** What are the annual societal costs of AN in England?

This thesis contributes knowledge by providing a comprehensive estimate of the societal costs of AN for England, with a particular focus on outpatient services.

It picks up several strands of debate around the treatment of ED, namely how to bring about an even greater shift from inpatient to outpatient treatment, and whether there is a benefit to service specialisation. Given the recent trends in mental health policy, namely the 'Five Year Forward Plan' and the 'Five Year Forward Plan for Mental Health', and the resulting commitment to implementing a waiting time standard for ED that will require the implementation of (cost-) effective services, this thesis is potentially more relevant now than it was upon its inception.

CHAPTER 3

Methods and data

CHAPTER INTRODUCTION

In this chapter, I discuss the methods employed in conducting these studies and describe the primary and secondary data sources used in this thesis. Given the wide range of topics covered and methods, I focus here on a discussion and critical assessment of the overarching methods relevant to the thesis, and justify the choice of approach. Specific analysis models and hypotheses are detailed in individual chapters, as appropriate.

Since no one dataset exists that could be used to meet the aims of this thesis – to present an estimate of the societal costs of anorexia in England, and explore why these may vary, in this thesis, I draw on a variety of data and employ a range of methods to answer my research questions. In addition to feeding into the estimate of societal costs, each study contributes to the knowledge base, because it fills a gap in the evidence regarding the costs of AN.

The thesis consists of six empirical studies using seven datasets (Chapters 4-6), in addition to three studies applying decision modelling approaches (Chapters 7 and 8). Table 3 1 provides an overview of the relationship between research questions, chapters, data and methods of analysis.

This thesis builds on work carried out in the context of my employment as a researcher in the Personal Social Services Research Unit (PSSRU) at the London School of Economics, and particularly as part of the NIHR-funded ARIADNE programme (RP-PG-0606-1043). The final report underwent peer review and has now been published (Schmidt et al. 2017). This includes versions of the studies presented in Chapter 4 (part 2), Chapter 5, Chapter 6 (part 2) and Chapter 8 (part 1) that have been revised and extended for this thesis.

The programme was led by Prof. Ulrike Schmidt at the Institute of Psychiatry (IoP). The economic component of this programme was led by Prof. Jeni Beecham (PSSRU) and consisted of

- Cost-effectiveness analysis alongside several clinical trials,
- Modelling the social costs of AN and
- Estimating savings to society from changing models of care.

Within that programme, I was responsible for developing the cost-of-illness model described above, perform analyses of service use, costs and cost-effectiveness, calculate the costs associated with current care pathways and develop a prediction model showing the impact of the implementation of cost-effective treatments on the social costs of AN.

Primary data for the ARIADNE programme were collected by researchers at the IoP. I was responsible for liaising with the research workers and conducting the analyses as described above, in particular building the cost-of-illness model. For the PhD, additional data were used to augment the models.

The Care Pathways Study (CPS) is a health services research and naturalistic cohort study that was part of the ARIADNE programme. Data for this study were collected by Dr Jennifer House. I was responsible for extracting data and carrying out the analyses presented here.

The MCTAAN trial was led by Ivan Eisler (IoP). Liaison and quality assurance during the data collection and entry phase were carried out by myself and Jennifer Beecham. I am responsible for the unit cost work and data analysis.

The analysis of the BCS-70 as part of the ARIADNE project was conceived by Jennifer Beecham, but I was responsible for the detailed analysis plan, study design and carrying out the analysis.

Data access for ALSPAC was facilitated by Dr Nadia Micali (University College London) through the NIHR-funded project 'Adolescent eating disorders and related behaviours: longitudinal course and risk factors'. I was solely responsible for the design and analysis of the study using ALSPAC data presented here.

Table 3-1: Relating research questions to chapters, data sources and methods

Research question	**Thesis chapter**	**Data source**	**Principal method of analysis**
RQ1: What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?	Chapter 4	Part 1: MCTAAN study	Economic costing of intervention and descriptive analysis.
		Part 2: Care Pathways Study	Additionally, analysis of variation using regression.
RQ2: What services do people used while being treated for AN on an outpatient basis, what are the associated costs, and why do these costs vary?	Chapter 5	Part 1: Care Pathways Study	Regression analysis in an expenditure function framework.
		Part 2: Three ARIADNE RCTs	
RQ3: What is the impact of AN on education, employment, income and related outcomes, and for whom?	Chapter 6	Part 1: ALSPAC	Regression analysis using linear, logistic and generalised linear models.
		Part 2: BCS-70	
RQ4: What is the loss of life associated with AN in England?	Chapter 7	Life tables for England and parameters from literature review.	Decision-analytic modelling in a Markov framework.
RQ5: What are the annual and lifetime societal costs of AN in England?	Chapter 8	Results from Chapters 4-7 and parameters from literature review.	Cost-of-illness estimate building on decision trees.

WORKING DEFINITION OF ANOREXIA NERVOSA

To estimate the costs associated with AN, it is essential to define what we mean by AN. As outlined in Chapter 2, different definitions for AN exist between the two major diagnostic classifications, DSM-IV and ICD-10. While most of the studies reviewed predated the introduction of DSM-V, evidence is now emerging that uses the new definition. But in addition to the shifting classifications used to identify the 'full syndrome', the fact that the EDNOS group of EDs is much larger than the full syndrome group means that a focus on strict criteria risks disregarding a large part of the costs and morbidity associated with AN and related disorders. As the literature revealed a heterogeneity of definitions used across different studies, in this thesis, what is considered 'AN' is any of the following:

- AN based on DSM-IV criteria;
- AN based on DSM-V criteria;
- AN based on ICD-10 criteria;
- AN-type EDNOS based on the above;
- Self-report of AN.

More detail on the most relevant definitions is provided in Chapter 2.

DATA SOURCES

Here I describe the datasets that were analysed using statistic and econometric techniques to obtain novel results. I do not discuss those data sources that were used to perform basic calculations. The latter includes sources such as the Hospital Episode Statistics (HES), data obtained from the Department for Work and Pensions (DWP) and other routine data sources such as life tables published on an ongoing basis by the Office for National Statistics (ONS).

The data used can be broadly divided into two categories: Those used to analyse service use and associated costs, and those used to investigate productivity-related outcomes. The first come from four clinical trials and a health services research study (primary data), while the latter come from two large UK cohort studies (secondary data).

ARIADNE PROGRAMME

The NIHR-funded programme provided data on three RCTs and a study of care pathways for young people with AN. The final report for this programme has undergone peer review through NIHR and was recently published (Schmidt *et al.* 2017).

The programme included three randomised controlled trials (RCTs), namely, CASIS (interventions for carers), MOSAIC (outpatient therapy for adults with AN) and iMANTRA (relapse prevention in severe AN) that collected information on participant service use. These service use data are used in this thesis to look at the services used by people with AN, the associated costs, and variation in costs by patient characteristics (Chapter 5, part 2; answering RQ2)

GUIDED SELF-HELP INTERVENTION FOR CARERS (CASIS)

The CASIS trial (Carers' Assesment, Skills and Information Sharing; Goddard et al., 2013) investigated whether the addition of a guided self-help, skills training intervention for carers (Experienced Carers Helping Others; ECHO) to inpatient care provided an additional benefit to carers and patients. Patients (aged 12 and over with a primary diagnosis of AN; n=178) and their carers (n=268) were recruited from 15 inpatient services in the UK and randomised to either ECHO or treatment as usual (TAU). The ECHO intervention consisted of self-help materials (book, DVDs) and 10 telephone coaching sessions. Data were collected at baseline, 6-months and 12-months.

The following outcomes relevant to the economic analyses presented here were measured in patients:

Primary:

- Relapse, defined as readmission to inpatient care or a drop of 2 points from discharge BMI (measured monthly)
- Depression, Anxiety and Stress Scale-21 (DASS-21; Lovibond & Lovibond 1995), a 21-item scale measuring the psychological concepts depression, anxiety and stress where higher scores represent higher levels of morbidity.

Secondary:

- Wold Health Organization – Quality of Life Questionnaire (short version; WHO-QoL-100; The Whoqol Group 1998), a self-report measure of quality of life (QoL) in four domains: physical health, psychological, social relationships, environment. This is measured on 5-point Likert scales in 24 areas. Two additional items ask about overall QoL and general health.
- Eating Disorder Examination (EDE; Fairburn & Cooper 1993), a semi-structured interview with four subscales (dietary restraint, eating concern, weight concern, shape concern) and a global score (mean of the four subscales). A questionnaire version with similar properties to the interview is available (EDE-Q; Luce & Crowther 1999).

To support an economic evaluation, a Client Service Receipt Inventory (CSRI; Beecham & Knapp 2001), covering a retrospective 6-month period was completed by patients and carers. This thesis is concerned with the patient data only.

While there were no differences in BMI, patients in the ECHO group experienced lower levels of ED symptoms and improved QoL at 6 months. Carers saw a greater reduction in caregiving time and a small to moderate reduction in carer burden. Full results for the trial have been published (Hibbs *et al.* 2015).

OUTPATIENT THERAPY FOR ADULTS WITH BROAD AN (MOSAIC)

The MOSAIC trial (protocol (Schmidt *et al.* 2013) compared the Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA (Schmidt *et al.* 2006) with Specialist Supportive Clinical Management (SSCM) in outpatient with DSM-IV AN or EDNOS-AN in a multi-centre RCT. Participants (adults aged 18-65) were recruited from four specialist ED services in the south of England. 72 were allocated to MANTRA and 70 to SSCM. Both interventions consist of 20 sessions over a 12-month period.

Data were collected at baseline, 6-months and 12-months. This included the following outcome measures that were considered relevant for the analyses in this PhD:

Primary outcome measure:

- Body Mass Index (BMI; kg/m^2) at 12 months

Secondary outcome measure:

- EDE or EDE-Q
- DASS

In addition, a CSRI covering a retrospective 6-month period was developed to support an economic evaluation.

The trial found that there were no differences in clinical outcome between the two treatment groups, with patients showing improvements on all measures. However, patients found MANTRA to be more acceptable and credible than SSCM. Full details of the trial, including measures and results are published in (Schmidt *et al.* 2017).

RELAPSE PREVENTION IN SEVERE AN (IMANTRA)

The final ARIANE study generating data used in this PhD was a feasibility trial that randomly allocated 41 inpatients treated for AN aged 16 or above from seven UK specialist ED units to receive e-mail guided self-care based on MANTRA (iMANTRA) or treatment as usual (TAU).

Outcome measures included

- BMI
- EDE or EDE-Q
- DASS
- WHO-QoL

Again, a CSRI was completed at baseline, 6-months and 12-months.

While there were no differences between groups at 6 months, the iMANTRA group showed higher BMI and lower DASS at 12 months and a slightly lower readmission rate of 22.7% compared to 31.2% in the TAU group. Full details of the feasibility study can be found in the ARIADNE report (Schmidt *et al.* 2017).

CARE PATHWAYS STUDY (CPS)

The Care Pathways Study investigated the impact of different service contexts on treatment outcome (House *et al.* 2012; House 2011). The study consisted of

- A naturalistic health services research study (service-level recruitment and data collection), and
- A retrospective cohort study (patient-level recruitment and data collection).

A list of potentially eligible services was compiled and key contacts within services were identified by IoP researchers. Those contacts were asked to complete a questionnaire providing service-level information on service specialisation, service organisation and treatment practice with regard to adolescent ED that was designed by researchers at the IoP and the PSSRU.

Services were included if they were:

- Within the catchment area of a Greater London PCT (GLPCT)
- Located outside Greater London but accepting referrals from GLPCTs
- Provides secondary or tertiary mental health care to adolescents (age 13-17)
- Provided by NHS or private sector

44 services were identified and 40 agreed to participate but 3 subsequently failed to provide the data needed to be included, so that 37 services participated in the study.

Three main intended care pathways were identified:

- Specialist Child and Adolescent Eating Disorder Services (CEADs);
- General CAMHS with a specialisation or special interest in ED (Specialist CAMHS);
- General CAMHS with no specialisation in ED, referred to as 'non-specialist CAMHS'.

The analysis of patient-level data revealed that sometimes the actual care pathways differed from the intended care pathways. The identified *actual* care pathways (by specialisation of the first service) were:

- Specialist to specialist
- Non-specialist to specialist
- Non-specialist to non-specialist
- Private services

Patients identified through participating services were included if they

- Had an initial contact or re-contact after a treatment break of at least 6 months with a participating service between 01/12/2006 and 30/11/2008
- Were adolescents (age 13-17)
- Had a primary diagnosis an eating disorder (ED)
- Were registered with a GP from a GLPCT

378 unique cases meeting all inclusion criteria were identified and 93 with a known diagnosis of AN or EDNOS-AN consented to be part of the study. Care pathways data were available for 90 patients.

The main finding of the study was that direct access to specialist services led to higher referral rates, lower admission rates, and greater consistency of care (Schmidt *et al.* 2017).

I use data on services to investigate treatments provided in outpatient services and their costs (Chapter 4, part 1; answering RQ 1), and data on 84 participants to explore the treatments received and their costs by care pathway as well as variations in costs (Chapter 5, part 1; answering RQ 2).

MCTAAN STUDY

This study is not part of the ARIADNE project but is funded by The Health Foundation and lead by Prof Ivan Eisler (IoP). A randomized controlled trial compared Multiple Family Day Treatment (MFDT) with manualized outpatient family therapy over a 12 months period.

Outpatient family therapy can in many cases be a substitute for inpatient treatment even for severe AN (Eisler *et al.* 2007) . Multiple family day treatment is an intensive form of treatment consisting of a one-week day programme for up to six families, followed by four to five further days at four to eight-week intervals. Individual family meetings take place between group meetings as required. The focus is to prevent hospitalisation. A randomized controlled trial will compare MFDT with manualized outpatient family therapy over a 12 months period. Primary outcomes are BMI and EDE global score. Outcome and CSRI data were collected a baseline (pre-treatment), three months, 12 months (end of treatment) and 18 months (6 months follow-up). While it was envisaged to recruit 200 patients in total,

actual numbers fell short with only 165 entering the study. This study was funded by The Health Foundation and lead by Prof. Ivan Eisler.

UK COHORT STUDIES

To estimate the productivity-related costs arising from AN, it is necessary to have data on people with the condition, as well as a suitable comparison group. Causality is difficult to establish in a cohort design. To determine an association between AN and differential outcomes relative to this comparison group, the two groups must be as similar as possible (and ideally, the same) in all potentially relevant aspects except exposure to the condition, or if any differences can be taken into account in the statistical analysis. This means that a comparison group should be as similar as possible in terms of demographic and socio-economic characteristics and other variables relevant to AN and the outcomes under investigation, or that at least differences can be assessed based on the available data.

In addition to suitability for answering the research questions, the following considerations went into selecting data sources:

- Data are freely accessible, or access can be obtained without additional funding
- Data have not been analysed with respect to the research questions

It should be noted that the data review was conducted in the early stages of this thesis, and the decisions made with regard to data selection reflect availability, quality and publication record of the data at the time.

BRITISH COHORT STUDY

The British Cohort Study (Centre for Longitudinal Studies 2015) BCS-70 includes over 17,000 babies born in the UK in one week in April 1970 and is representative of the UK population. Currently, data are available for seven sweeps up to age 38, so that people can be tracked well into adulthood. The use of the data for this study has been registered with the Economic and Social Data Service (UK Data Service 2014) and access is free of charge.

No formal diagnosis of ED is included in the BCS-70, but at age 30, there is a set of questions asking:

- Whether the participant ever had an ED (lifetime ED);

- Age when the participant first had an ED (age of onset);
- Whether the participant had an ED in the previous 12 months (current ED);
- Type of ED.

The BCS-70 data has been successfully used to study risk factors of lifetime ED (Nicholls & Viner 2009). In the cohort, 111 women with AN can be identified – a prevalence of 1.9%, which is in line with expectations. At the time the study was designed, data were also available on outcomes up to age 34 and include information on education and qualifications, employment status and income.

The data allowed me to estimate earnings forgone by those with AN, and this is used in the CoI estimate to show the longer-term costs of AN.

AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN

The Avon Longitudinal Study of Parents and Children (Golding *et al.* 2001) ALSPAC is a prospective study of pregnancy and child development, collecting data on mothers, partners and children. The initial sample consists of 85-90% of women living in Avon who were expected to give birth between April 1991 and December 1992, or 14,472 pregnancies. Later, an attempt was made to recruit those who did not initially join the study, and the total sample includes 15,224 foetuses. While a representative sample was envisioned, the study has a shortfall in less affluent families and ethnic minority mothers compared to the population of Britain (Bristol University n.d.). Data are currently available up to age 16, and the data for age 18 is expected to become available in early 2012.

Previous research into AN with the ALSPAC data has focussed on the mothers of the study children, specifically on the impact of pregnancy on EDs (Micali *et al.* 2007b) and the impact of maternal EDs on perinatal outcomes (Micali *et al.* 2007a), post-partum depression (Micali *et al.* 2011) and breast feeding (Micali *et al.* 2010). This demonstrates the feasibility of researching AN using ALSPAC data.

The NIHR-funded project 'Adolescent eating disorders and related behaviours: longitudinal course and risk factors' was carried out by Dr Nadia Micali (King's College London), and data access for the analysis of ALSPAC presented here was facilitated through this study. An application for access to the data up to age 16 is was drafted and accepted by the ALSPAC team. As part of the project, questions about eating behaviours and BMI were

included in the ALSPAC sweeps at ages 14, 16 and 18. The researchers have since used these data to obtain clinical diagnoses of ED. The focus of their project was on risk factors contributing to adolescent EDs, and particularly the transgenerational effect of maternal EDs. At the time of my data application, a study of ED and pregnancy had included 12,252 mothers, 237 of whom reported a history of AN – a 'lifetime' prevalence of 1.7% with an average age around 27. This inspired confidence that a sufficient number of young people with AN could be identified to conduct this study.

A NOTE ON SELF-REPORT DATA

Much of the work in this thesis relies on self-reported data, either in the form of service use data collected using CSRIs, or from the large cohort studies.

When it comes to service use, self-reported data are sometimes considered less reliable than, for example, medical records. However, since there is no one central source of service use data covering different agencies in the UK, data would have to be collected from each agency, potentially in different geographical locations – and the full spectrum of agencies that would need to be included may not be known to researchers without consulting with participants. A study comparing self-report data and GP records on service contacts and found that while GP records were more accurate when it came to GP contacts, they were less reliable in reporting contact with other services, such as hospital or community-based services (Byford *et al.* 2007b). Total costs calculated based on the service use reported from both sources were similar. Another study found a high level of agreement between self-report data and GP records(Patel *et al.* 2005)..

A practical consideration is that participants are likely to be in contact with a wide range of services in diverse geographical areas and that service use patterns will differ between individuals. Without asking participants, the specific services will be unknown. For these reasons, collecting data from each agency is often not feasible, and the CSRI approach is likely to provide similar or at least adequate results with much less resource input (Beecham & Knapp 2001).

Similarly, sometimes concerns are raised about the reliability of self-reported diagnoses or symptoms. While for physical health problems with well-defined criteria, such as diabetes, there tends to be good agreement between self-reported diagnoses and clinical diagnoses

from records (Berg *et al.* 2012). Self-report can be less successful due to differences between (self-) perception and physical measurement, such as in the case of 47% of adolescents reporting to be 'very overweight' when they were not in one study (Goodman *et al.* 2000). Self-report measures may also lead to misreporting due to carelessness in completing them (Kaminska & Foulsham 2016). On the other hand, self-report may reduce socially desirable responding, i.e. under-reporting of undesirable behaviours and over-reporting of desirable behaviours (Edwards 1958).

Research specific to reporting of ED has been conducted, and a meta-analysis of studies comparing the interview and the (self-report) questionnaire versions of the Eating Disorder Examination found that these were correlated, with participants consistently reporting higher levels of symptoms on the self-report measure (Berg *et al.* 2012). Disagreement was noted on the binge eating subscale, where more episodes were reported in the interview version. The authors suggest that the two instruments measure similar concepts, but are not inherently the same. The choice of informant may also matter. A study comparing ED symptom reports collected from young people and their parents as part of the ALSPAC (Swanson *et al.* 2014a) concluded that adolescents were more likely than parents to report bulimic symptoms, while parents were more likely to report thinness. This suggests a role for multiple informants in capturing the range of ED symptoms. While the study above compared two versions of the same assessment tool, a comparison of simple questions such as "Have you ever had anorexia?" and "Has anybody ever suspected that you might have an eating disorder" performed better than clinical subscales in identifying AN in a community sample (Keski-Rahkonen *et al.* 2006).

On balance, self-reported measures of ED are convenient and less resource intensive than clinical interviews, and there is evidence to suggest that they perform adequately, and simpler questions may perform better than questionnaire versions of clinical assessments.

COSTING METHODS

PERSPECTIVE OF ANALYSIS

When analysing the economic impact of social policies, a key consideration concerns the perspective adopted for the analysis (Drummond *et al.* 2005). Deciding on a perspective in this context means deciding whose views have standing when it comes to decision making

about investment of public funds. A common distinction is between public sector costs, focussing on public sector budgets, and societal or social costs, which – in the context of cost-of-illness studies – include the perspective of everyone who bears a 'cost' from an illness.

Due to data limitations and resource constraints, cost analyses often adopt a narrow perspective. NICE, for example, generally recommends a health and social care services perspective be used in health technology assessment (National Institute for Health and Care Excellence 2013, 2014). The thesis however is situated within the theoretical context of economic decision analysis, which requires the consideration of full economic costs and benefits of each decision option. First formalised by Pigou (1932), the concept of externalities is relevant for our choice of cost perspective. An externality occurs when a cost or benefit resulting from a choice is borne by a party other than the decision maker. An example of an externality in the context of anorexia nervosa might be a choice taken by service commissioners to shift the focus of treatment from inpatient treatment for AN to outpatient treatment, a health and social care perspective will only take into account the impact of this decision on health and social care services. Say this hypothetical decision is neutral in terms of patient outcomes such as recovery and survival, and saves money, leading analysist to conclude that this is in fact the superior service model. However, a shift towards outpatient services means patients will spend more time out of hospital, potentially increasing the amount of time requiring informal care provided by parents, family and spouses. A societal perspective would incorporate and value this additional burden placed on caregivers, and thereby 'internalise' the externality into the decision-making process. Potential cost savings to the health care system may be outweighed by the increased burden to caregivers when taking a societal perspective.

While the analyses presented in this thesis are limited both by data availability and resource constraints, the ambition is to discuss the costs of AN from a societal perspective, and this is done wherever possible.

DIRECT COSTS

PRINCIPLES OF UNIT COSTING

In this thesis, I follow the definition of a 'unit cost' used by Beecham (2000), where a unit cost is the cost per unit of activity or output.

Beecham (2000, pp. 12-15) sets out the principles of unit costing, reflecting economic theory outlined above.

- Unit costs should be inclusive, i.e. include resources needed to provide all components of a service. This includes both fixed costs, i.e. those costs that do not depend on the output or service produced such as overheads, and variable costs, i.e. costs that change with outputs produced such as salary costs and on-costs, regardless of the budget or source providing these resources.
- Unit costs should be developed in such a way that they match service use and allow for accurate costing of services received. For example, an ED service may provide a variety of sessions, ranging from brief weigh-ins with a nurse to one-to-one therapy sessions with a consultant. These are very different in terms of resource implications, and providing an overall unit cost for a generic intervention with this service would not reflect actual resources received by the client.
- Unit costs should be based on the principle of long-run marginal opportunity costs. Economic costs include both 'accounting costs' – costs that might be reflected in a public-sector budget – and 'opportunity costs' – the benefit forgone from not investing in the next best alternative. In other words, not only the immediate monetary expense needs to be considered, but also the value of the benefit forgone by choosing one option over another. 'Marginal cost' refers to the cost of supporting an additional patient in the service, whereas the focus on 'long-run' costs such as capital investment in buildings highlights the need to consider the implications of service expansion.

Additionally, Beecham & Knapp (2001) highlight the importance of retaining variations in costs between different service users, different facilities or different geographies.

MICRO-COSTING: TOP-DOWN VS BOTTOM-UP APPROACHES

In addition to applying the principles outlined above, there are two broad approaches to estimating unit costs:

In the top-down approach, all relevant expenditure is added and divided by the corresponding unit of activity. This approach is comparatively simple to apply and can be most appropriate where an average cost – such as the average cost per person receiving treatment through an ED service – is required, but does not facilitate analysis of variation in costs, for example for patients requiring additional support beyond a standard intervention or by patient characteristics, nor does it allow for consideration of regional variability.

In contrast, using the bottom-up all resources required to provide an intervention or service are described and costed. The monetary value of those resources is then linked to the unit of activity. This approach tends to be more accurate and versatile, as it can be linked to individuals, thus retaining variability between patients and between sites.

Beecham (2000) sets out the process for estimating unit costs for a service or intervention using a bottom-up approach:

- Comprehensively describe all service or intervention elements;
- Estimate the cost implications (costs) and
- Identify relevant activities (units);
- Calculate the total costs and costs per unit ('unit cost').

For the purpose of this thesis, the bottom-up approach is employed where the available data allow, namely in the development of unit costs of outpatient treatments and in the exploration of variation of individual-level total cost.

COSTING SERVICE USE

The costs associated with service use by people with AN were calculated by attaching unit costs to instances of service use. The two main sources for unit costs in health and social care in England are

- PSSRU unit cost volume (Curtis 2011)

- NHS reference costs (Department of Health 2011)

These resources were used for convenience, and to maximise consistency across different costing studies by using the same source of unit cost data. Where no unit costs were readily available, they were estimated using an equivalent approach that employs the principles set out above (Beecham 2000; Berridge *et al.* 2002).

INDIRECT COSTS: PRODUCTIVITY LOSSES

Productivity is based on the production function, where output is a function of capital, labour and technology. Productivity is a measure of output per unit of input. Productivity loss is therefore the value of lost output (Zhang *et al.* 2011). In this section, I briefly outline the concepts related to productivity losses and discuss the main methods available to value such losses in economic terms.

CONCEPTS

Absenteeism

Absenteeism is a reduction in output due to work days lost. In AN, this may be due to acute illness or hospitalisation, doctor visits or – in the case of carers or parents – due to increased time spent providing informal care. Additionally, productivity losses may arise from excess mortality, but capturing the 'value of life' poses additional challenges, which I discuss below.

My analysis of BCS-70 data presented in Chapter 6 did not show a significant effect of AN on the probability of employment at age 30. However, there was a significant effect on economic activity status, with women with AN more likely to be sick or disabled. Productivity losses are therefore measured as output foregone due to additional disability (see Chapter 8 for details).

Presenteeism

Presenteeism measures a reduction in productivity while at work, that is, the difference in output in the presence of a condition compared to output in the absence of the condition. Given the complexity of many modern jobs, especially in non-manual, non-industrial settings where outputs cannot be easily defined nor counted, and the complexity of an impairment resulting from a mental health problem, studies of Presenteeism generally rely on self-report measures rather than routine data (Schultz & Edington 2007).

Losses from presenteeism are then calculated using the same estimate of productivity as for the calculation of absenteeism, and applying the average reduction in productivity to this estimate. To my knowledge, there is no estimate available for AN, but the loss due to depression, sadness or mental illness has been estimated at 15.3% (Goetzel *et al.* 2004).

No individual-level data on presenteeism were available for a representative sample of people affected by AN, so that an estimate of costs due to presenteeism was not included in the estimate of societal cost.

Underemployment

Underemployment denotes the fact that illness can lead to changes in employment status, such as early retirement, reduced working hours or loss of job (Zhang *et al.* 2011). In addition, an illness may affect choice of job or prevent an individual from working in a job at a level matched to their qualifications and skills. Lost output is calculated as the differential between expected and actual output.

As with presenteeism, no data were available to estimate the productivity losses resulting from underemployment for this thesis.

Days of education missed

If productivity losses can be framed as output forgone, and productivity is related to level of education (see below under Valuation methods how productivity can be measured through the proxy of wages), then days of education missed are relevant to a full assessment of productivity losses arising from AN. The study of ALSPAC data presented in Chapter 6, Part 2 includes a self-report measure of days of school missed due to illness over a two-week period. While results are presented for an analysis of whether AN is associated with an increased number of school days missed or associated with an increased probability that an absence occurred, the valuation challenge outlined below means that these cannot be directly measured.

VALUATION METHODS

Human capital and friction cost approach

Productivity losses from absenteeism, presenteeism and underemployment are usually valued under the human capital approach. The human capital method places a value on lost output by calculating the sum of discounted expected future income. The theoretical

justification for this approach is that the market wage is equal to the marginal product of labour in a competitive market (Zhang *et al.* 2011), and therefore represents the opportunity cost of lost output to society.

The approach can be criticised because of its potential to discriminate against groups that face structural disadvantages in the labour market, such as the economically inactive, women or members of ethnic minorities as well as people with mental health problems. Using actual wage rates can, in this case, lead to lower estimates of the societal costs associated with an illness, and especially such conditions that are more likely to affect those groups. The use of average wage rates has therefore been suggested as a means of assessing the loss of productivity that would be averted in the absence of the condition in question.

Another criticism that led to a refinement of the human capital approach is that, in an environment where unemployment is above the frictional level, an absent worker would eventually be replaced by another, and the approach therefore over-estimates productivity losses due to, for example, diminishing returns to labour at the level of the firm, i.e. other employees performing essential tasks during short absences to avoid loss of output (Koopmanschap 1998). The friction cost approach (Koopmanschapp *et al.* 1995) was proposed to address this problem. Friction costs include the cost of hiring and training a new worker, either from the unemployed or an internal labour pool, as well as lost production or the extra cost occurring for maintaining production during the friction period. The friction cost approach has itself been subject to criticism, for example in that a friction cost that is lower than the wage rate would be at odds with neoclassical theory which states that wages equal the marginal product of labour (Johannesson 1996).

Valuing non-market production

Another issue that is linked to criticism of the human capital approach is that it disregards unpaid work, such as housework and caregiving. The inclusion of informal care in economic evaluation can impact on findings to the extent that a conclusion regarding cost-effectiveness may be reversed upon inclusion alongside a healthcare perspective (Goodrich *et al.* 2012).

To determine a 'shadow price' for these activities, the opportunity costs of lost time spent on unpaid work needs to be developed. Several options have been proposed for an approach based on opportunity costs (Francis & McDaid 2009):

- Market wage forgone based on an individual's likely earnings;
- Average wage;
- Minimum wage.

Alternatively, 'replacement costs' can be used, i.e. valuing the output produced in terms of the cost of purchasing an equivalent service on the market. An example may be the cost of child care or the cost of hiring a nurse or caregiver.

Valuing lost education

The value of lost education in terms of days of school missed can be conceptualised in several ways.

Lost education can be conceptualised an intermediate outcome in the process of producing human capital, measured in terms of education qualifications. With this approach, the number of days missed would need to be (causally) linked to education qualifications. While absence from school has been found to be a predictor of lower education outcomes (Ou & Reynolds 2008), valuing one day of absence in terms of lost income based on a reduction in education attainment would require establishing and quantifying a causal relationship of the marginal impact of one day missed on education outcome.

Another valuation approach taken is to measure the value of one day of absence via the proxy of productivity losses of a parent or guardian (Smith *et al.* 1997). Arguably, both approaches should be combined, and also include the costs associated with alternative school provision and out-of-pocket expenditure, such as childcare.

INTANGIBLE COSTS: THE ECONOMIC 'VALUE OF LIFE'

Intangible costs are those that cannot be directly measured, and that do not convert into monetary values in a straightforward way. This includes impacts of an illness on quality of life and on life itself.

Attempting to measure the 'value of life' is sometimes seen as inappropriate, the argument being that there is an inherent value to life that cannot and perhaps s*hould* not be quantified in monetary terms. It is this characteristic of 'life' that makes it the prime example of what is considered an 'intangible' concept. While the debate around whether we should measure the value of life lost is interesting and important, for this thesis, I shall simply argue that

even considering the potential pitfalls and given the limitations of our methods, it would be even more contentious to disregard the loss of life resulting from a condition in any CoI estimate, and the value of loss of life averted can be included on the 'benefit' side of economic evaluations. There are, however, issues around measurement, and I summarise the different approaches available below.

HUMAN CAPITAL APPROACH VS WILLINGNESS TO PAY

There are two main categories of methods used to measure intangible cost (Bonin 2007; Landefeld & Seskin 1982; Mishan 1971):

- Productivity-based approaches which measure output foregone, usually in terms of years of productive life lost combined with estimates of earnings lost – essentially the human capital approach.
- Willingness to pay (WTP) – based approaches which use methods of preference elicitation to determine. The latter provide a more general measure of value of life and usually employ some kind of risk-wage trade-off setting to obtain an estimate.

Willingness to pay measures may provide a more general measure and reduce bias. However, their application is not without challenge. One criticism that deserves to be highlighted is that willingness to pay is not necessarily related to ability or intention to pay (Zhang *et al.* 2011). This means it is conceivable that the sum of all economic losses from life years lost can total more than, for example, Gross Domestic Product, nullifying the use of CoI estimates in aiding decision making (Kennelly 2017).

PREFERENCE ELICITATION

The Treasury Green Book for appraisal and evaluation in central government (HM Treasury 2003) updated 2011, pp. 57-58 currently recommends the use of 'willingness to pay' or 'willingness to accept' approaches, i.e. market based approaches. These break down into 'stated preference' and 'revealed preference approaches (Fujiwara & Campbell 2011):

- Stated preference approaches involve presenting participants with different scenarios and asking them either how much they would be willing to pay (contingent valuation), or to choose a most preferred option among different variations of a good or scenario (choice modelling).

- Revealed preference approaches elicit valuations by observing market behaviour.

Please note that there are additional problems around aggregating individual preferences to obtain a social value, which are not discussed here.

VALUE OF PREVENTED FATALITY

One pragmatic approach to estimating intangible cost is the Value of Statistical Life VSL (Viscusi & Aldy 2003). This approach estimates the willingness to pay (WTP) for a reduction in risk by analysis. Incremental changes in wages alongside corresponding changes in risk of death within the labour market are analysed to determine the Value of Prevented Fatality (VPF). Alternatively, stated preference approaches can be employed. It is important to note that this is not the 'value of a life lost'. A VPF of £1 million corresponds to a reduction in risk of one in 100,000 being valued at about £10 to an average individual. A frequently highlighted problem with these estimates is that market behaviour is not solely driven by the avoidance of mortality, and that stated preference approaches require the assessment of small incremental changes – something people are known to struggle with (Zhang *et al.* 2011).

An estimate of VPF for the UK was developed by the Department for Transport (Department for Transport 2007). This is a VPF of around £1.43 million (2005 prices) and consists of

- A WTP estimate of the 'human costs' of a fatality, both in terms of the loss of enjoyment of life and the impact on family and friends - £936,380.
- Lost output due to injury, including salary oncosts such as national insurance contributions – £490,960.
- Direct costs of the fatality - £840.

COST PER QUALITY-ADJUSTED LIFE YEAR

A 'de-facto' valuation of life years lost is the WTP threshold applied by National Institute for Health and Care Excellence (NICE). We might consider this cost-effectiveness threshold, i.e. the highest amount that should be paid per quality adjusted life year (QALY; a year of life lived at full health), of £20,000 to £30,000 (Devlin & Parkin 2004; McCabe *et al.* 2008) an example of a 'stated preference' at the societal level.

While the preference weights for the underlying QALYs were derived using trade-offs between years liven in various different health states, the monetary valuation is as (Appleby *et al.* 2007) point out, not based on evidence. Further, in practice the threshold appears to be applied inconsistently and a more accurate ceiling value may be £45,000 (Devlin & Parkin 2004). Recently, there have been efforts to obtain an empirical estimate of the CE threshold based on the argument that there is a relationship between health care expenditure and health outcomes (Martin *et al.* 2008). By relating changes in overall NHS expenditure to changes in mortality for different programme budget categories, an empirical CE threshold can be estimated (Claxton *et al.* 2015). Based on 2008 expenditure data and 2008-2010 mortality data, the central estimate for the CE threshold is £12,936, with an 89% chance that it is smaller than £20,000 and a 97% chance that it is under £30,000 – and therefore almost certainly lower than the current figures.

This finding contrasts with the preliminary results from a study attempting to obtain social valuations of QALYs (Baker *et al.* 2010), which find a value around £25,000 per QALY using revealed preference methods. This difference in the threshold highlights the difference in approach, which represents a move from valuation based on individual preferences to a model that values health and life by the proxy of resources required to maintain them. The latter approach provides a more 'rational' way of valuing health that emphasises the trade-offs required – i.e., if more is spent on health, less can be spent elsewhere. An avenue for further exploration may be to establish whether the difference between the 'empirical' valuation and the 'preference-based' valuation indicate a potential preference for (irrational?) 'over-spending' on health care.

CONCLUSIONS

It is clear that estimating a monetary value for life itself is conceptually difficult. For the purpose of this thesis, which seeks to contribute to the development of economic evaluations for interventions for AN, I chose a pragmatic approach in selecting an existing estimate to apply to life years lost. Given that the thesis is situated in the field of health economics, the most relevant value appears to be the NICE WTP threshold. Even though it may be argued that this underestimates the value of what is measured – especially in the context of much higher values applied in other areas of appraisal for government policy – this is the value that best reflects the preferences of decision makers and funders. While this

can be seen as a departure from a strict societal perspective, this will give credibility to the estimate and link it directly to decision making within the NHS.

DATA COLLECTION FOR COST ANALYSIS

While most of the data used for the analyses presented in this thesis were from secondary sources (ALSPAC, BCS-70, public sources such as the Office for National Statistics and Department for Work and Pensions), four sets of data were collected as part of clinical trials and a cohort study:

- Service-level information on resources for providing Multi-family Day Therapy (MCTAAN trial);
- Service-level information on resources for providing outpatient ED services as part of the Care Pathways Study;
- Patient-level information on service use from clinical records (Care Pathways Study);
- Information on service use alongside three clinical trials as part of the ARIADNE programme.

The data collection instruments were developed in collaboration with the various clinical research teams and Professor Jennifer Beecham.

1) SERVICE INFORMATION SCHEDULE FOR MCTAAN

A Service Information Schedule (SIS; Sleed *et al.* 2004) is used to record information on resources needed to provide an intervention or service. This again reflects the principles of economic costing above, which require a broad perspective that includes all resources – regardless of the budget, or whether these are paid (such as regular staff) or in-kind contributions (such as volunteers or trainees).

The topics covered by the SIS are the same across interventions, as all cost categories need to be addressed:

- What staff are involved in providing the intervention?
- What are the salaries and on-costs for staff involved?
- How much time do staff spend on providing the intervention?

- How much time is spent preparing for the intervention, in supervision and feedback, and travelling to the intervention venue?
- What non-staff resources are required to provide the intervention? This includes additional room hire as well as materials, child care if offered, or snacks provided to participants.

However, implementation of the principles of the SIS will vary depending on the intervention or service being costed. Development of the SIS can be described an application of the process of unit cost estimation, reflecting step one of the process – describing all components of the intervention or service. The SIS for MCTAAN is attached as Appendix 1.

2) SERVICE-LEVEL QUESTIONNAIRE FOR THE CARE PATHWAYS STUDY

For the Care Pathways Study, a service-level questionnaire for service managers was developed by Jennifer Beecham, Eva-Maria Bonin and Jennifer House. This applied the principles of the SIS, but aimed to match data that would be collected as part of the routine administration of outpatient services to minimize the burden of data collection.

The questionnaire covered the following information for the 2007-08 financial year:

- Medical, nursing and other staff working in the service
- Amount of time dedicated to adolescent ED
- Referrals of adolescents with a primary diagnosis of ED overall, AN and BN
- Total number of adolescents assessed and treated by the service (overall)
- Expenditure on staff salaries and oncosts
- Other expenditure such as travel and subsistence
- Clinical and office expenditure,
- Capital costs and
- Overheads.

The full questionnaire is attached as Appendix 2.

3) SERVICE USE FROM PATIENT RECORDS

The main CPS collected patient-level data on a cohort of adolescents from participating services.

The patient-level data provides the following information relevant to the economic analysis:

- Patient socio-demographic characteristics
- Patient clinical data (weight and height)
- Treatment received within each outpatient service along the care pathway:
- Number of assessments
- Number of individual or family sessions
- Number of group, dietic and medical outpatient sessions
- Number and type of outpatient appointments for physical tests
- Number of telephone calls
- Number of psychiatric reviews
- Number of inpatient days for ED or other reasons

The data were re-entered to better suit the needs of the economic analysis, showing the total number of service contacts for each individual within each service along their care pathway.

4) SERVICE USE FROM CSRI

Information on patient service use was collected alongside several clinical trials involving people with AN. These data were used to describe service use and estimate and analyse associated costs.

The Client Service Receipt Inventory (CSRI; Beecham & Knapp 2001) is an instrument for collecting service use data on a broad range of services and participant characteristics and can be used to collect self-reported data. This allows services and interventions to be costed according to the principles of economic costing, as providing an intervention paid for by one agency may reduce the need for services provided by another, and therefore to analyse the impact of interventions on different agencies.

The main sections of the CSRI are as follows:

- Background and client information
- Accommodation and living situation
- Employment history, earnings and other personal resources
- Service receipt
- Informal care and additional expenditure

While self-report measures are sometimes seen as inferior to medical records, there is no one, central source of service use information across different agencies. A study comparing patient self-report and GP records showed that the overall costs obtained from both sources were similar, but (perhaps not surprisingly) that while GP records are more accurate when it comes to GP contacts, they are less reliable than self-report when it comes to the use of other resources, such as hospital and community services (Byford *et al.* 2007b). Another study found high agreement between self-report and GP records (Patel *et al.* 2005). A practical consideration is that participants are likely to be in contact with a wide range of services in diverse geographical areas and differ between individuals and that without asking participants, the specific services will be unknown. For this reason, collecting data from each agency is often not feasible, and the CSRI approach is likely to provide similar results with much less resource input (Beecham & Knapp 2001).

DATA ANALYSES

THE NEED TO INCLUDE CONFOUNDING VARIABLES

To attempt to establish causality when estimating the impact of AN on later outcomes such as education attainment, employment and income using data from individual-level observational studies, the methods need to be capable of accounting for any other potential influences on the outcome.

Confounders are factors that impact both on the exposure (AN) and the outcome (economic outcome). For example, behavioural difficulties may be associated with a higher risk overdeveloping AN, and higher levels of behavioural difficulties could also be associated with a higher risk of lower attainment.

Covariates are related only to the outcome, without affecting the relationship between the exposure and the outcome. These are often genetic or biological factors. For example, symptoms of AN may resolve with age, even in the absence of intervention.

The methods presented here can account for confounders and covariates. The concrete confounders and covariates included in the analysis models are detailed in the relevant empirical chapters.

LOGISTIC REGRESSION

Logistic regression is a suitable choice where outcomes (or dependent variables) are binary, i.e. can either take the value zero or one. For example, if the outcome of interest is whether a young person has obtained 5 good GCSEs or not, the probability that this is the case (meaning the binary variable takes the value one) for any one individual i is p_i, and the probability that this is not the case (meaning the binary variable takes the value zero) is $1 - p_i$.

p_i, can be written as

$$p_i = F(x_i) = \frac{1}{1 + \mathrm{e}^{-(\beta_0 + \beta_1 x_i)}}$$

Where X_i represents the vector of factors associated with the outcome – the co-variates and confounders in the analysis model. β_0 is the intercept in a linear regression equation, and $\beta_1$is the regression coefficient on x.

The logistic function g is a linear combination

$$g\big(F(x)\big) = \ln\left(\frac{F(x)}{1 - F(x)}\right) = B_0 + B_1\bar{X}$$

This equation can be exponentiated to yield

$$\frac{F(x)}{1-F(x)} = \mathrm{e}^{\beta_0 + \beta_1 x}.$$

The value of a binary outcome variable *y* given *X* is

$$y_i = p_i + \varepsilon$$

The error term ε follows a binominal distribution with a mean of zero and a variance of $p_i(1 - p_i)$.

The likelihood function

$$l(\beta) = \prod_i^n p(x_i)^{y_i}[1 - p(x_i)]^{(1-y_i)}$$

consists of the product of the probability of a positive and the probability of a negative outcome and is then maximised for β that best fit

$$y = \begin{cases} 1 & \beta_0 + \beta_1 x + \varepsilon > 0 \\ 0 & else \end{cases}$$

The odds can be described as

$$\frac{p(x)}{1 - p(x)} = \exp(\beta_0 + \beta_1 x) = \mathrm{e}^{\beta_0}\left(\mathrm{e}^{\beta_1}\right)^x$$

If both outcome (dependent) and predictor (independent) variable are binary, as is the case when modelling the impact of anorexia (vs no anorexia) on attainment of 5 good GCSEs (vs fewer than 5 good GCSEs), this can be expressed as an odds ratio for a unit change in *x*:

$$OR = \frac{-\frac{F(x+1)}{1 - F(x+1)}}{\left(\frac{\bar{f}(x)}{1 - F_{(x)}}\right)} = \frac{\mathrm{e}^{\beta_0 + \beta_1(x+1)}}{\mathrm{e}^{\beta_0 + \beta_1 x}} = \mathrm{e}^{\beta_1}$$

The odds ratio ranges from zero to infinity. An odds ratio of 1 denotes an equal chance of the outcome variable taking the value one for both groups (anorexia vs no anorexia), i.e.

there is no difference in the chance that members of either group will achieve 5 good GCSEs. An odds ratio <1 means that the chance of achieving the outcome is lower for people with anorexia, and an odds ratio >1 means that the chance is higher for this group. An OR of 0.5 would be interpreted as those with AN being only half as likely as those without ED to achieve 5 good GCSEs, while an OR of 2 means they would be twice as likely.

The same principle is applied for categorical/nominal variables with more than two categories. One category is chosen as the 'reference category', and parameters are estimated to denote the odds ratio relative to this reference category. This type of model will be used both in Chapter 5 where some explanatory variables are categorical or ordinal (e.g. social class at birth), and in Chapter 6 where in addition, the predictor in the ALSPAC study is a nominal variable with three levels (no ED, AN, other ED). Where a categorical variable is used as a predictor, an F-test is performed post-hoc to determine whether the category of interest is different from the reference category (in this case: whether AN cases are different from those without ED).

For continuous independent variables or co-variates, the coefficient denotes the change in the log odds related to a one-unit increase in the continuous variable. For example, in Chapter 6, the coefficient on the (scale variable) number of days absent from school due to illness in a model where 5 good GCSEs is the outcome provides the change in the outcome variable for any one-unit change in the scale variable. If the coefficient is 0.9, an additional day of absence leads to a 10% reduction in the (relative) chance of achieving 5 good GCSEs.

In all cases, the interpretation of the parameters β_1 is simple: the odds or odds ratio increase by β_1 for each unit increase in x_i.

WORKING WITH COST DATA

EXPLORING VARIATION IN COST DATA

Theoretical underpinning: Production of welfare approach

The production of welfare (PoW) approach originates in the evaluation of social care services and applies the methods and vocabulary of the general theory of production to the area of welfare. This provides a theoretical framework for analysing the relationship

between inputs (the means of production) and outputs (in this case, welfare). Or, put differently, analysing welfare as a quantifiable production process dependent on a set of different 'inputs'. In the following section, I summarise the salient points of the production of welfare (PoW) approach as presented by Davies & Knapp (Davies & Knapp 1981) pp. 3-19 and point out how it applies to the analysis of treatment and outcomes in AN.

The term 'welfare' in this context is used in a general sense and may refer to a broad range of outcomes. Moreover, the 'production process' that converts inputs into welfare indicators may differ between alternative welfare dimensions examined. One of the challenges is therefore to define the distinct (but possibly interacting) factors that constitute welfare and are to be measured, and then finding a valid construct to measure them. In the context of health care, the output of interest is most likely is a (mental) health outcome or quality of life.

The PoW approach distinguishes between three different types of inputs which explain variations in individual outcomes:

- Resources, or tangible and direct inputs such as staff, buildings and other physical elements endogenous to a health service.
- Non-resources, or intangibles endogenous to the service, such as staff attitudes and other characteristics of service environment.
- Quasi-inputs, or intangibles that are exogenous to the service, such as patient characteristics and experiences prior to service contact.

Table 6: Production of welfare approach and application to AN

PoW	**(aspect of) welfare**	**Resources (endogenous, tangible)**	**Non-resources (endogenous, intangible)**	**Quasi-inputs (exogenous, intangible)**
AN	Improved symptomatology; improved quality of life	Hospital bed days, staff time	Ward climate	Patient characteristics (age, personality)

Endogenous inputs are those that can be influenced by a service provider. Quasi-inputs on the other hand highlight the role of the patient in the production of her own welfare. The basic premise of PoW can be summarised as follows:

> "Outputs are determined by the levels and modes of combination of resource inputs and non resource inputs, given the exogenously determined values of quasi-inputs" (Davies & Knapp 1981, p. 8)

This can be stated in the form of a production function:

$$Y_i = f(X_{1i}, \dots, X_{ni})$$

where Y_i is the outcome of interest and X_{ji} are the inputs for person i.

Outcomes, such as improved health, are therefore 'produced' by combining resource and non-resource inputs. Different resource combinations may produce differential outcomes. Where the aim is to link changes in outcomes (here: health) to the resources invested, the cost estimate should be as broad as possible and include a wide range of services (Beecham 2000; Beecham *et al.* 1991; Knapp 1998), linking back to the principles of economic costing described above.

Cost functions

A related concept is that of cost and expenditure functions. In economic analysis, the relationship of interest is often that between resource use (as measured by costs) and outcomes. The model can be re-stated in the form of a cost function because

> "(…) there is an obvious causal link between resource inputs (summarised by costs) and the final outcomes (or product) of the care system, but this relationship will be mediated by the intermediate outcomes and the different combinations of non-resource inputs." (Beecham 2000, p. 32)

The cost function can be written as

$$C_i = f(M_{1i}, \dots, M_{ni}, Y_i)$$

where C_i are the costs, M_{ji} are the mediating factors and Y_i is the outcome for person i. In the cost function approach, the relationship between costs and outcomes can be explored, linking back to the production of welfare approach (Beecham *et al.* 1991; Knapp 1998). Here, service costs are used as the dependent and outcome variables are used as explanatory variables (controlling for patient characteristics) in a regression-type framework. The cost function therefore explores whether cost variations are associated with outcomes. It is often

the case that instead, costs vary based on demographic characteristics, or that much of the variance in costs remains unexplained due to unobserved variables.

In this thesis, I use baseline data to explore variations in costs. The analysis cannot claim to be a full cost function approach, as an 'outcome' in that framework is a change brought about by resource investment. Instead, I explore predictors of baseline costs within a regression framework to provide information on potential mediators that need to be considered in future analyses as well as information on why and for whom baseline costs may vary.

CHARACTERISTICS OF COST DATA

There are some well-known problems associated with cost data that influence the choice of analysis approach and estimation models. Two papers in particular have summarised these issues, and provide an overview of the approaches available to address them.

Dunn and colleagues (2003) write for a general audience wishing to critically assess the methods used in economic evaluation, while Kilian and colleagues (2002) provide a more technical overview and show the implications of different approaches in a modelling study applying them to the same data. The following sections summarise the characteristics of cost data, the issues resulting from them and approaches suggested to address them as discussed in these papers.

Distribution of cost data

While ordinary least squares regression assumes a normal distribution, raw cost data are often positively skewed with a long right tail because by definition, the lowest possible value is zero and empirically, most participants incur low (or even zero) costs while a small number of participants – for example, those with long hospital stays – incur very high costs.

Heteroscedasticity

Another feature of cost data is that the assumption of homoscedasticity of residuals is often violated, i.e. their variance increases with the value of the observations. In an OLS context, the estimator is still unbiased but does not minimise mean square error, and therefore variance estimate will be inconsistent.

Zero- and low-cost cases

Another common feature of cost data is a number of participants with zero or very low service costs, and a number with markedly higher costs. This suggests that there are often two distinct 'types' of patients represented in the data, and it may be useful to account for this clustering in the analysis.

Sample size for economic evaluation

Most clinical studies are powered for the analysis of outcomes rather than an economic analysis. Cost data – especially when taking a broad perspective – are usually characterised by large standard deviations, which (all things being equal) increases the required sample size for a given level of power. As a result, clinical studies are often underpowered with regard to the economic evaluation. Given the small sample sizes in some studies presented here, and the fact that cost data often do not follow a normal distribution, standard parametric methods (t-tests) will be supplemented by non-parametric methods (bootstrap; Efron & Tibshirani 1993) to explore cost differences.

APPROACHES FOR ADDRESSING THE CHARACTERISTICS OF COST DATA

There are several options for addressing this problem that have been explored in the literature by various authors (Kilian *et al.* 2002; Knapp 1998).

Ordinary Least Squares with bootstrap

A common approach for dealing with the problem of heteroscedasticity is to apply the non-parametric bootstrap to an ordinary least squares regression (Efron & Tibshirani 1993). While several approaches to bootstrapping are available, one that is easily implemented within STATA and allows for standard errors that are heteroscedasticity consistent is the pairs bootstrap, i.e. sampling with direct replacement (Cribari-Neto & Zarkos 1999).

Log transformation

A simple way of addressing the non-normality of the distribution of cost data is to model the log transformation of the dependent variable:

$$ln(y) = \alpha + \beta x + \varepsilon$$

$$\exp(\ln(y)) = \mathrm{e}^{x\widehat{\beta}}$$

Note that this does not necessarily address the problem of heteroscedasticity (Kilian *et al.* 2002).

Two-stage models

A common solution is the application of two-stage models (Mullahy 1998). The first part is a model predicting whether or not service costs were zero, and the second part contains predictors of the costs of care for those with non-zero service costs (here shown in the context of a generalised linear model, see below).

Part 1

$$\Pr(y_i > 0|x_i) = \frac{1}{1 + e^{-B_1 - B_i X_i}}$$

Part 2

$$E(ln(y_i)|x_i > 0, x_i) = X_i\beta_i$$

Generalised linear models

The generalized linear model (GLM) extends the linear model and allows for the specification not just of a linear predictor

$$\eta_i = X_i\beta,$$

the combination vector of independent variables X and the vector of parameters beta to be estimated, but also a probability distribution and a link function that describes how the linear predictor relates to the mean of the distribution function:

$$\mu_i = E(y_i)$$

$$g(\mu_i) = X_i\beta$$

The probability distribution is chosen from a member of the exponential family and characterised by the dispersion parameter τ and the parameter θ. The variance function of the probability distribution specifies the relationship between the mean of the outcome variable and its variance across individuals.

The mean of the distribution is

$$E(y) = \mu = g^{-1}(X\beta)$$

And the variance is a function of the mean:

$$Var(y) = V(\mu) = V\left(g^{-1}(X\beta)\right)$$

The GLM framework accommodates many well-known models. For example, an OLS model can be conceptualised as a GLM with a normal distribution and identity link. In analysis cost data, a common choice is a gamma distribution with a log link, i.e. the link function

$$X\beta = \ln(\mu)$$

The choice of distributional family can be determined using the Park test (Manning & Mullahy 2002) by estimating the OLS model

$$ln(y_i - \hat{y}_i)^2 = \lambda_0 + \lambda_1 ln(\hat{y}_i) + v_i$$

The coefficient on lambda 1 indicates the appropriate distributional family as follows:

=0: Gaussian/normal distribution

= 1 : Poisson distribution

=2 Gamma

=3: inverse normal

MISSING DATA

It has long been recognised that addressing or at least acknowledging missing data and its potential effects is important in any context (Rubin 1976), including health care data (Rubin & Schenker 1991) and economic evaluation of health care interventions (Briggs *et al.* 2003). However, reporting of approaches to missing data is not consistent in the field, and methods often do not reflect the state of the art (Noble *et al.* 2012). This is not just the case in economics, but also in clinical research (Enders 2016), medicine (Hayati Rezvan *et al.* 2015) and epidemiology (Eekhout *et al.* 2012) – disciplines related to health economics.

While the following discussion focusses on the application of missing data methods in the context of cost-effectiveness analysis, i.e. self-reported survey data with baseline and follow-up data collection, the same principles apply generally to all missing data, and to all longitudinal data such as the BCS-70 or ALSPAC (Spratt *et al.* 2010).

MISSING DATA MECHANISMS

There can be different reasons for missing data (Rubin 1976).

With

- Y- Outcome: Y^0 observed, Y^m missing;
- X – baseline covariate;
- W- post-randomisation variable such as hospital stay[1];
- R – missing data indicator (binary).

the following mechanisms can be distinguished.

[1] Note that in the context of non-randomised studies, W could also relate to a post-study entry duration.

Missing completely at random (MCAR)

Missing completely at random is the strongest possible assumption about missing data and states that the reasons for data being missing are independent of both observed and unobserved factors, i.e. unrelated to Y, X and W:

$$P(R|Y, X, W) = P(R)$$

If the assumption is met, it is permissible to ignore missing data. The assumption is implicit in ad-hoc methods to address missing data, such as complete-case analysis, last value carried forward or mean imputation, as otherwise, estimates derived from these methods carry the risk of bias.

Missing at random (MAR)

Similar to MCAR-CD, here the probability of missingness is unrelated to unobserved values, given the observed data:

$$P(R|Y, X, W) = P(R|\ Y0, X, W)$$

This means any systematic differences between missing and observed values can be explained by differences in observer variables, including baseline co-variates, other co-variates and confounders, and the observed outcome. An example might be that participants with lower socio-economic status are less likely to be retained in a cohort study.

Missing not at random (MNAR)

This term describes the situation where missingness is related to unobserved values:

$$P(R|Y, X, W) \text{ not equal } (P(R|\ Y^0, X, W), R \text{ depends on } Y^m$$

For example, participants with lower income may be less likely to stay engaged with a cohort study and therefore are less likely to provide data on their income down the line – and this is not wholly explained by variables that are in the dataset.

This is problematic because if we try to estimate the missing outcome variables based only on observed data, the estimates will be incorrect if they really depend on unobserved variables. The first step in dealing with missing data is therefore to assess whether or not they are missing at random.

MISSING DATA STRATEGIES

Simple methods

If data are MCAR, simple methods such as listwise deletion which deletes a participant from the analysis, or pairwise deletion, which ignores missing values but includes the participant can be employed without the risk of bias – although this still reduces sample size and therefore the power to detect changes in outcomes (Scheffer 2002).

If data are MAR, commonly used methods are to replace missing data with the mean of observed cases, or to impute the missing data using a regression model fit to the non-missing data. Both methods reduce variability in the dataset and therefore lead to smaller standard errors. Inverse probability weighting, where each case is included in the analysis with a weight that is the inverse of the probability of being missing (based on the observed data), can be less efficient because it uses a subset of the available information, and are not suitable for non-monotone missing data patterns that are typical for economic evaluation. If co-variates are missing, this may lead to extreme weights resulting in high variability of the estimates.

Multiple imputation

Multiple imputation (MI) addresses the issues raised by other methods. Instead of a single imputation, as with a regression model, multiple imputations *M* are performed that each create a plausible version of the missing data. Each dataset M_i is analysed separately, and estimates θ are then combined using Rubin's Rules (Bo. *et al.* 2002):

$$\bar{\theta}_M = \sum_{i=1}^{M} \frac{\hat{\theta}_i}{M}$$

The variance of the estimate is made up of the within-imputation variance $\bar{W}_M$:

$$\bar{W}_M = \sum_{i=1}^{M} \frac{W_i}{M}$$

And the between-imputation variance B_M:

$$B_M = \frac{\sum_i^{\mathrm{M}} \left(\hat{\theta}_i - \theta_n\right)^2}{M-1}$$

The total variance T_M is therefore:

$$T_M = \bar{W}_M + B_M + \frac{B_M}{M} = \bar{W}_M + \frac{M+1}{M} B_M$$

Confidence estimates and significance levels can be taken from a t-distribution (Bo. *et al.* 2002)

$$(\theta - \bar{\theta}_M) T_M^{-1/2} \sim t_v$$

With v degrees of freedom:

$$v = (M-1)\left[1 + \frac{1}{M+1} \cdot \frac{\bar{W}_M}{B_M}\right]^2$$

Number of imputations

While (Rubin 1996) showed the relative efficiency (measured in standard deviation units) of an estimate to be approximated by the relationship

$$\left(1 + \frac{\gamma}{m}\right)^{-1}$$

with a rate of missingness γ and a number of imputations *m*, it has been shown in simulation studies that efficiency does not reflect the increase in standard error nor p-value as *m* gets smaller (Graham *et al.* 2007). This 'power falloff' was more pronounced if more than 30% of data were missing. The authors recommend a much larger number of imputations to avoid unacceptable falloff in power, up to 40 or more imputations.

Evaluating MI models

There are two models involved in when using MI procedures: the imputation model and the analysis model. (The imputation model should include all variables that will be part of the analysis model, and any auxiliary variables that are thought to be important in terms of the co-variance matrix. In evaluating whether the model is a 'good model', it is therefore necessary to determine whether

- The imputation model is appropriate and
- Whether the analysis model is appropriate for the data.

However, there are currently no established guidelines for model checking to determine the appropriateness of the imputation model are only emerging, and Nguyen and colleagues (2017) provide an overview of existing approaches that I summarise in what follows.

- Visual inspection of data, e.g. distribution of imputed vs observed data, or comparison of summary statistics between observed and imputed data are suggested. Options for formal testing are proposed:
- Ratio of variances of observed and imputed values not between 0.5 and 2, or absolute difference in means greater than two standard deviations (Stuart *et al.* 2009);
- Kolmogorov-Smirnov test to compare distributions of observed and imputed data, with variables flagged if the p-value was below 0.05 (Abayomi *et al.* 2008), but results were found to be difficult to interpret (Nguyen et al).

These methods focus on differences between observed and imputed data. Nguyen and colleagues note that such differences in themselves are not problematic, since data are assumed to be missing at random. Therefore, the proposed informal methods on their own are of limited use, and the authors suggest using external information to determine whether imputed data are plausible. One example would be where missingness is related to the value

of an imputed variable. The authors use the example of lower socio-economic status being associated with missingness in their panel data, with would lead us to expect those with missing data to have a lower socio-economic status than those without missing data.

This approach is extended to comparing observed and imputed distributions including an estimated propensity for response (i.e. a logistic regression model on the missingness indicator; (Nguyen *et al.* 2017), and visually inspecting the resulting distributions. A further extension proposes grouping individuals based on response probabilities, and performing analysis of variance (ANOVA). The imputation model would be rejected if the ANOVA test is rejected in 2 out of 5 imputed data sets.

Another suggestion is to fit a model to the observed data and refining this model before the imputation procedure (Marchenko & Eddings 2011). Standard model diagnostics can then be applied.

Another option presented by Nguyen (2017) is cross-validation, where one observation is deleted per iteration which is then predicted by the remaining data. The discrepancy between observed and predicted values is then assessed.

Finally, posterior predictive checking is introduced, which compares inference from the complete data to the inference from replication data which is based on the imputation model. Relevant quantities are tested for similarity between estimates from the complete data and the replications, based on the final model to be fitted (He & Zaslavsky 2012) and assessed using posterior predictive p-values that should not be too close to zero or one. As the authors note, this approach focusses on the appropriateness of the analysis model rather than that of the imputation model.

ADDRESSING MISSING DATA IN THIS THESIS

There are two main missing data strategies employed in this thesis. Trial data were analysed on a complete-case basis, after comparing baseline characteristic for those with and without CSRI data. There were no significant differences between the group with data and the full sample, and – due to the efforts of the clinical research team to encourage questionnaire completion – there were few missing data.

For the analyses of ALSPAC and BCS-70 in Chapter 5, missing data were analysed and multiple imputation was performed using chained equations (Azur *et al.* 2011) with the -mi

impute- command (Royston & White 2011) in Stata 14 (StataCorp 2015) for ALSPAC data and Stata 12 (StataCorp. 2011) for BCS-70 data. Following the recommendations by (Graham *et al.* 2007), M=40 sets were imputed for the ALSPAC data, and M=20 sets were imputed in the BCS-70 data, where a smaller overall proportion of data were missing.

As of yet, there is no consensus on the recommended procedure for ensuring a 'good' performance of the imputation model, and options provided as part of commonly used statistical packages are very limited, the choice regarding methods applied in this thesis was made with a view to practicality, and to choosing methods that do not simply rely on inspecting differences between imputed and observed data. Therefore, models were fit on the imputed data and adjusted r-squared – available as part of the STATA command -mibeta- generated. Following imputation, visual inspection of residuals was performed on a sub-set of imputed datasets to asses fit.

DISEASE MODELLING

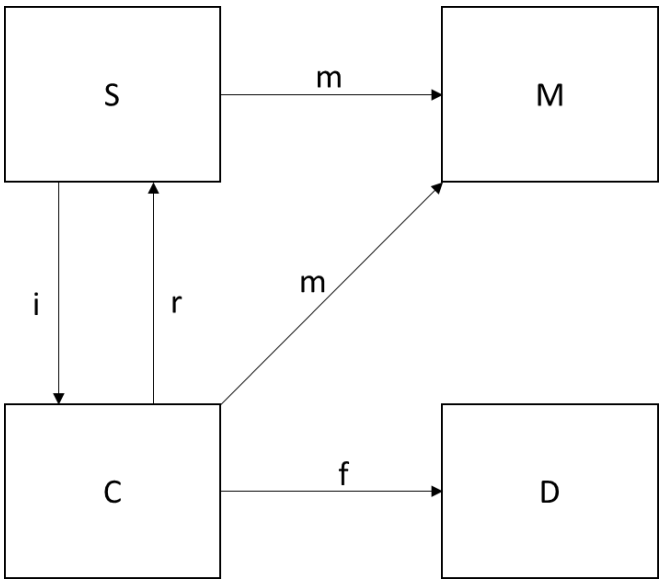
INCIDENCE AND PREVALENCE

Some of the ad-hoc calculations for the CoI estimate (see below, and Chapter 8) required an estimate of prevalence. As the literature review showed, there is no prevalence estimate for AN for the general population in England.

The DISMOD-II disease modelling software (Barendregt *et al.* 2003) is freely available through the World Health Organisation. The software contains a simple disease model with three disease-specific states (see Figure 3-1) and general mortality (M):

- S: Healthy
- C: With disease
- D: Disease mortality

Figure 3-1: The DISMOD-II disease model from Barendregt et al (2003, p. 3)



In addition, there are three disease-specific transition hazards:

- i: incidence
- r: remission
- f: case fatality

Fatality from other causes is represented by M (state) and m (transition hazard). Two disease-specific parameters are required to calculate the third.

In addition to the states above, where the probability of being in each state is determined by a set of equations which are detailed by Barendregt and colleagues (2003), it is possible to enter information on

- Incidence as a population rate;
- Prevalence;
- Duration;
- Mortality.

For these inputs, the model is solved using a downhill simplex method, a multi-dimensional optimisation method. This optimisation method is also employed where the three transition hazards are not consistent with each other, which may be the case where information is

taken from different sources – a common occurrence in any kind of modelling. Similarly, the procedure will be applied where the model is overidentified, i.e. all three disease-specific parameters are available. The procedure then adjusts the values of the input variables to ensure internal consistency.

In the case of AN in England, information on incidence as a population rate, remission and disease-specific mortality are available. The objective is to calculate prevalence and (for convenience) incident cases by age group for modelling Years of Potential Life Lost (YPLL, see Chapter 7).

LIFE EXPECTANCY

An estimate of life expectancy for women with AN was required to calculate YPLL. This was derived using data from the National Life Tables for England for 2010-2012 (Office for National Statistics 2015), and adopting the underlying methods as follows.

The life tables are constructed in multiple steps. Assuming initially, data on the number of people eat each age and the number of people dying in each period are available, mortality (m_x) is calculated by dividing the sum of deaths by the sum of the mid-year population.

The mortality rate between age x and age x+1 (q_x) is calculated as

$$q_x = \frac{2m_x}{2 + m_x}$$

The number dying in each period is

$$d_x = q_x \times l_x,$$

where l_x is the number of survivors in the period.

Accordingly, the number surviving to the next period is

$$l_{x+1} = l_x - d_x .$$

The next calculation is 'years alive' at each age, the average of survivors at ages x and x+1:

$$L_x = \frac{l_x + l_{x+1}}{2} .$$

Summing this number for year x to the final year (100) yields T_x, the total number of years lived:

$$T_x = \sum_{100}^{i=x} L_i$$

Finally, life expectancy at age x is calculated by dividing this by the number of people at age x:

$$e_x = \frac{T_x}{l_x}$$

To calculate life expectancy for AN, d_x was multiplied by the standard mortality rate (SMR) for AN of 5.86 (Arcelus *et al.* 2011). The reduction in life expectancy for AN was calculated by subtracting the life expectancy for AN at each age from the life expectancy from all-cause mortality as provided by the ONS data.

YEARS OF POTENTIAL LIFE LOST AND YEARS LIVED WITH DISABILITY

Years of Potential Life Lost (YPLL; life years lost due to premature death from AN) and Years Lived with Disability (YLD; number of years lived with AN) were calculated to estimate the loss to society from AN in terms of excess mortality, the intangible cost of AN.

YPLL were calculated for the age of onset within each five-year age group for ages 10-49 by first determining whether a person with age of onset at age x was alive or not alive at a given future age up to 82, based on life expectancy at age x. This indicated whether a year of life was lost to AN or not. Similarly, YLD were calculated based on the duration of illness of AN. Future YPLL and YLD were discounted to present value at age of onset, using a discount rate of 3.5%.

To place a monetary value on the resulting YPLL and YLD estimates, a valuation for a life year is required. As discussed above, there are several approaches available to place a monetary value on life and none of them are without flaws. YPLL are distinct from QALYs. While both one year of life lost and one full QALY (one year lived at full health) cover a one-year period, YPLL measures only duration of life without adjusting for quality. For the purpose of this CoI estimate, I use the NICE cost-effectiveness threshold to value a YPLL at full health. To reflect the discussion around the 'true' or appropriate value of the CE threshold, I use values of £15,000, £20,000 and £30,000, Since it is unlikely that these additional years would have been lived at full health, I employ a disability weight to reflect this reduction in QoL. In the absence of an estimate for AN, the disability weight for depression (46% reduction, Kruijshaar *et al.* 2005) was applied to the final figure.

COST-OF-ILLNESS ESTIMATE

There is no single data source that would allow the calculation of a cost-of-illness for AN. In particular, there is a paucity of data on the short and longer-term patterns of service use and associated costs. It is common in economic analysis – especially in cost-effectiveness analysis – to make use of modelling techniques to synthesise and analyse in a single overarching model evidence from various different sources (Philips *et al.* 2004)..

Barton and colleagues (2004, p. 110) provide a useful overview of the reasons justifying the use of modelling techniques:

- Absence of 'hard data', where modelling can be used to provide a best estimate to inform policy;
- Need for 'temporal extrapolation' beyond the observed data, such as short-term data observed in a clinical trial that is used to predict costs or outcomes over a longer period of time;

- Need for 'contextual extrapolation', where data collected in one setting are applied in another;
- Linking of intermediate and final outcomes, such as clinical outcome measures and associated health outcomes;
- Comparisons of interventions where a direct comparison has not been made in a clinical trial (relative effectiveness or cost-effectiveness).

The goal of the modelling process here is to obtain a CoI estimate. CoI studies have been conducted at least since the 1950s for a range of conditions, for example for depression (Berto *et al.* 2000; Hodgson & Meiners 1982; Malzberg 1950). Best-practice guidelines have been established for their construction and use (Philips *et al.* 2004). The costs included in the model should be estimated using the principles of economic costing described above, but in practice the approach taken varies and often depends on data availability (see for example, Clabaugh & Ward 2008).

Use of modelling techniques allows for evidence to be synthesised so that CoI studies are possible even for conditions with low prevalence because gaps in the evidence and uncertainties arising from small sample sizes can be addressed by the use of sensitivity analysis. Examples of the successful use of this approach are estimates of the economic cost of autism (Knapp *et al.* 2009), acquired brain injury (Beecham *et al.* 2009) and conduct problems (Bonin *et al.* 2011) in the UK.

Two main approaches are commonly used in economic modelling; both originate in decision analysis (Barton *et al.* 2004):

- Decision trees illustrate the consequences of decisions (represented by 'decision nodes') and the associated probabilities that each (mutually exclusive) event or outcome will occur. In economic analysis, it is common to associate a cost with each outcome. The expected value of a decision is then calculated by calculating the probability-weighted cost associated with the decision. Decision trees are advantageous for simple models as they require few assumptions but can become quite extensive when there are many decision points.
- Alternatively, a Markov model can be constructed where repeating outcomes can be summarised into discrete 'states' and 'transitions' between states happen on

cycles of equal length ('Markov periods'), e.g. one year. This approach requires more data, including transition probabilities for each cycle.

Both approaches are cohort simulations, where the costs associated with all possible outcomes are added, weighted by the probability of an outcome occurring. A Markov model additionally takes into account the time spent in each state.

Beyond these two relatively simple forms, some extensions are possible (Briggs *et al.* 2006). Decision trees and Markov models can be combined, either where state transitions take the form of a tree ('Markov trees'), or where different interventions or strategies are evaluated as part of a decision tree leading to an event/outcome, with a Markov model extrapolating beyond the event. Another extension is the possibility of building time dependencies into Markov models, for example, a change in transition probabilities as the cohort 'ages' (e.g. differential mortality rates over time), or a varying transition probability, such as the mortality rate, depending on how long a patient has spent in a disease state.

In contrast to the cohort models described above, patient-level simulation models focus on individual data and track each patient through the model. This is usually achieved by employing Monte Carlo simulation, where a model is run many times on a sample of the population. While these models offer more flexibility, e.g. they do not require a fixed cycle length, they often require more data to model the future path through the model based on patient factors, which is what drives the variation that results from the sampling approach (Barton *et al.* 2004; Briggs *et al.* 2006).

While some patient-level models are similar in structure to cohort models in that the simulation continuously tracks individuals over time, discrete event simulations focus on time in state as an individual moves through a list of well-defined events. An example of such discrete events may be admission to inpatient treatment (with an associated time in state, the duration of the admission), followed by discharge (Allen *et al.* 2015). These models offer great flexibility in defining rules that can be used to model complex systems.

System dynamics have a place in modelling where individuals beyond the patient are affected. This is usually the case in modelling infectious diseases, or where treatment provided to one patient affects the treatment of another (Barton *et al.* 2004).

Given the limited data available to construct a CoI for AN, most calculations in Chapter 8 use decision trees with one or two sequential decision nodes. A Markov model underpins the DISMOD-II disease model, and is used in this thesis to calculate life expectancy and YPLL.

CHAPTER SUMMARY

In this chapter, I discussed the methods and data available to answer the research questions and to meet the aim of this thesis – to estimate the annual societal costs of AN in England, and to explore why costs may vary. Given that such a CoI model requires a wide range of information, and no one source is available to derive the estimate, a range of methods and data will be used in the empirical chapters that follow.

This includes:

- Applying the principles of economic costing to information on resources needed to provide treatments for AN in outpatient settings;
- Using econometric techniques to explore cost variations, accounting for the typical characteristics of cost data outlined above;
- Using econometric modelling techniques to investigate the impact of AN on education attainment, employment, income and related outcomes;
- Using disease modelling software to estimate the prevalence of AN for different age groups, given known incidence rates;
- Applying a simple Markov model to life table data to calculate life expectancy for people with AN and determining Years of Potential Life Lost from AN;
- Using the principles of decision analysis to combine information from a variety of sources into a cost of illness estimate for AN;
- Employing appropriate missing data strategies.

Chapters 4-8 present the empirical findings, followed by a discussion of results and concluding thoughts in Chapter 9.

CHAPTER 4

Direct costs: Unit costs of outpatient treatments for Anorexia nervosa

CHAPTER INTRODUCTION

This first empirical chapter focusses on the direct costs associated with AN and on answering RQ1: "What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?"

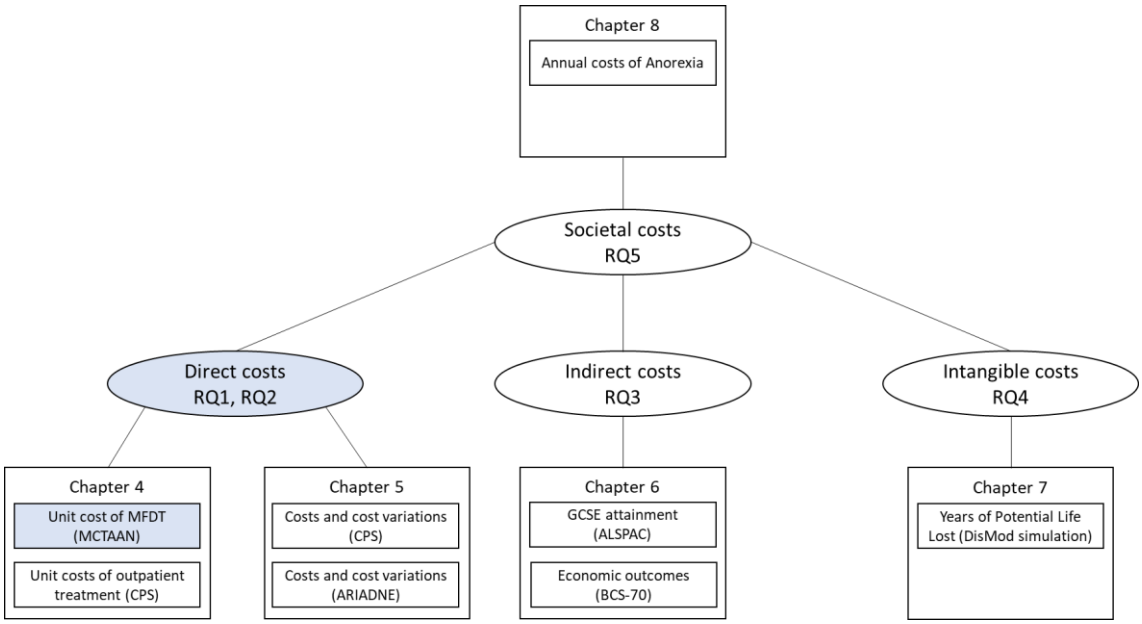
While this chapter is concerned with unit costs (cost per session or treatment unit) and therefore takes a service-level perspective, Chapter 5 will look at service costs and variation in service costs at the patient level.

Mapping studies have found specialist ED services to be concentrated in the South East of England (O'Herlihy *et al.* 2003b; Tulloch *et al.* 2008), and 25% of the population live in areas without specialist provision (Royal College of Psychiatrists 2000) while referral from primary care to specialists services may depend on availability of such services within the area (Currin *et al.* 2006). Consequently, setting up outpatient services may facilitate more equitable access to treatment.

But while the Hospital Episode Statistics provide some insight into inpatient treatment provided for AN, little is known about the full spectrum of service use and costs associated with outpatient treatment of AN. Given the paucity of evidence on cost-effective treatments, there is a need for information on the costs of treatment provided in outpatient services for AN as a first step towards developing the cost-effectiveness argument.

In this chapter, I collate information from two different studies, focussing on the unit costs of different types of outpatient treatments for people with AN. In Part 1, I present the unit costs (cost per day and cost per family per day) of Multi-Family Day Treatment (MFDT), calculated based on information obtained alongside the MCTAAN trial. In Part 2, I detail the unit costs of other treatments provided in outpatient settings, which is based on information from the Care Pathways Study. I also analyse why these costs vary between services with different degrees of specialisation with regard to ED treatment.

PART 1: UNIT COST OF MULTI-FAMILY DAY TREATMENT



INTRODUCTION

Here I present the unit costs of Multifamily Day Therapy (MFDT) estimated alongside a pragmatic multi-centre RCT comparing MFDT to single family therapy (SFT; Eisler *et al.* 2016). This was the first trial of MFDT, and the work presented here is the first time the costs of this promising form of outpatient treatment for AN have been detailed, using a rigorous economic method. Unit costs for SFT and individual therapy (IT) – the control treatment and supplementary treatments to MFDT – are also presented. The economic analyses conducted for this study are published elsewhere (Bonin *et al.* 2013)

While family therapy for AN has a longstanding history (e.g. Russell et al., 1987, but note that there are earlier studies), and a growing body of evidence existed that indicated family therapy is a promising approach to treating AN in adolescents and can potentially provide an alternative to inpatient treatment (Eisler 2005), trials were often underpowered and issues of potential bias were identified (Fisher *et al.* 2010).

MFDT is a form of the 'Maudsley method' of family-based treatment (Rienecke 2017), a manualised treatment that is considered suitable for patients who are medically stable and which consists of three phases:

Phase 1: Restoration of physical health, with a focus on avoiding inpatient admissions by giving parents responsibility for decisions about eating.

Phase 2: Once a steady weight gain is achieved, responsibility for decisions about eating is gradually transferred back to the patient.

Phase 3: Review of patient development, identification of future challenges and strategies for helping the young person to cope without reverting to the ED behaviours.

Throughout, MFDT focusses on parental and family input, supported by the therapist. This links back to the model of maintenance factors in AN discussed in Chapter 3, which highlight the role of carers in AN. Similarly, 'transdiagnostic' theories of family therapy have been put forward (Loeb *et al.* 2012).

MFDT is an intensive form of family therapy. It consists of a one-week intensive programme of day-long sessions for up to six families. This is followed by four or five additional day-long meetings at 4-8 week intervals, although single-family therapy sessions

(SFT) and individual therapy (IT) can be scheduled between group meetings as needed. Shared families' experiences and the group dynamics are key components of the treatment. The overall length of the MFDT programme is 12 months.

A total of 169 moderately ill adolescents with a DSM-IV diagnosis of AN or AN-type EDNOS (restricting) were randomised to MFDT or SFT (Eisler *et al.* 2016). In the SFT group, around 60% achieved a good or intermediate outcome as measured on the Morgan-Russel scale, compared to 75% in the MFDT group – a significantly better improvement (Eisler *et al.* 2016). A qualitative study with five adolescents and 10 parents who participated in MFDT found that participants experienced the therapy as positive, and that shared experiences and mutual learning and support facilitated change (Voriadaki *et al.* 2015).I first detail the methods used to obtain a description of the MFDT intervention and how resources needed to provide the intervention were costed. The data were then analysed following the four-stage process proposed by Beecham (2000), I then describe the different elements of the intervention, quantify the required resources and associated costs and finally present the unit costs of MFDT. Descriptive results are reported and I briefly discuss variations in costs across the four intervention sites. Given that the sample consisted of only services (services A, B, C and D), no statistical analyses were undertaken.

This piece of work is an example of costing a complex intervention where an economic evaluation was added after the RCT design and implementation was completed, and illustrates some of the challenges arising from the need to collect retrospective data. However, resources required to provide specific interventions within a service are not routinely recorded within CAMHS, and this intervention took place prior to the implementation of electronic health records Therefore, this type of retrospective costing exercise is the only way of estimating robust intervention costs that adhere to the principles of economic costing.

METHODS

COLLECTING INFORMATION ON INTERVENTION ELEMENTS AND RESOURCES

To calculate the unit costs of MFDT, a Service Information Schedule (SIS) was developed to capture all resource inputs related to the intervention so that economic costs could be calculated. In accordance with the principles of economic costing detailed in Chapter 1, a preliminary SIS was designed to guide an initial interview with Prof. Ivan Eisler to gain a better understanding of the intervention and to identify the elements of the MFDT intervention. The SIS (attached as Appendix 1) was developed based on this interview.

Resources needed to provide interventions can generally be broken down into staff time and associated salaries, salary on-costs (national insurance, pensions), overheads and other resources such as materials and catering, and these elements are reflected in the design of the SIS.

The principles of economic costing prescribe that not just time spent directly on providing the intervention, but also 'indirect' time spent on related activities needs to be included (see also, Barrett & Byford 2008). It is therefore necessary to capture information on all activities related to the intervention. Based on the description of the MFDT intervention obtained from Prof. Eisler, the final SIS was designed to record information on staff time for the following activities:

- Designing the intervention;
- Providing an information evening;
- Training and supervision;
- Preparation and feedback;
- Administration;
- Travel time;
- Providing the intervention.

Information on non-staff elements such as room hire and catering were collected for all intervention activities combined.

The resulting SIS was used to structure interviews with clinicians at the four sites where the MFDT intervention was provided to participants in the MCTAAN trial. I travelled to the

four intervention sites (Services A-D, located in London and surrounding areas) and conducted interviews of 30-60 minutes with clinicians to complete the SIS for each service.

COSTING INTERVENTION RESOURCES

Once the information had been collected via interview, resources were costed in the following way.

- Staff time: Information was collected on profession, salary grade (where applicable) and number of hours spent by each member of staff on each of the activities listed above. Based on this information, an appropriate unit cost (cost per hour) for each member of staff was drawn from the PSSRU Unit Costs of Health and Social Care publication (Curtis 2011). These costs include salaries, employer on-costs and capital and non-capital overheads. One site, service C only the provided total clinician and administrator time, so that a breakdown into different intervention activities was not possible.
- Rooms: To ensure consistency in the cost estimates and to reflect the integration of the intervention into existing service provision within the hospitals, the capital overhead charges presented in the PSSRU unit cost volume (Curtis 2011) were used.
- Travel: Any staff travel to a location other than their usual place of work that is related to the normal provision of the intervention (as opposed to being related to the requirements of the research design) were included at the rates of reimbursement detailed in the NHS Terms and Conditions of Service Handbook in force in 2009[2]. Trial participants were asked to provide information on travel time and travel expenses relating to their participation in the intervention. Clinicians were asked to judge whether or not participant travel costs were related to the requirements of the RCT.
- Other resources: Expenditure on non-staff resources was recorded in currency amounts and no separate costing step was required.

[2] http://www.nhsemployers.org/your-workforce/pay-and-reward/agenda-for-change/nhs-terms-and-conditions-of-service-handbook/archive---nhs-terms-and-conditions-of-service-handbook

ASSUMPTIONS USED TO ADDRESS MISSING INFORMATION

Where information on the time spent on an activity was missing, the cost was estimated based on information provided by another service. As Service A was where most MFDT groups were held and the manualised treatment was considered to be most embedded, figures from Service A were used to fill missing information where possible, unless a more conservative estimate was available from another service. Given that Service C was unable to break down staff time by intervention activity, it was not possible to use data provided by this service to replace missing data. Missing information was therefore handled as follows:

- The costs of the information evening for participants from Service B and Service D were calculated based on information provided by Service A;
- Preparation time at Services A and B were calculated based on information provided by Service D;
- The costs of snacks for Service D were assumed to be the same as in Service B, which had the lowest cost for this item.

ASSUMPTIONS ABOUT ATTENDANCE

Between five and seven families – but typically six – form an MFDT group. Attendance was reported to be generally good with full attendance during the intensive phase of the intervention and families only occasionally missed sessions during the follow-up phase (Eisler *et al.* 2016). Barrett and Byford (2008) point out that costs of group therapy can be estimated either based on the number of sessions allocated to each participant, or the number of sessions actually attended, and that the former should be used unless there is perfect replacement of those who do not attend, as resources will have been committed even if they miss a session.

While Bonin and Beecham (2012) show that the choice of approach can affect the conclusions drawn with regard to cost-effectiveness, in this instance the apparent low level of absenteeism justifies the calculation of a cost per session based on allocation, as it will be very similar to an estimate based on attendance, and no attendance records were available.

CALCULATING UNIT COSTS

The costs of the multi-family groups were calculated for each service. The costs of staff and non-staff resources were added to arrive at the total cost for one iteration of the MFDT treatment for each service. This total was divided by the number of families participating in the groups to calculate the cost per family. Finally, the cost per family was divided by the number of days of MFDT, based on 11 days of treatment, which respondents considered to be typical and consisted of five days in the intensive phase and six follow-up days.

RESULTS

DESCRIPTION OF INTERVENTION COMPONENTS AND RESOURCES

This section describes the intervention components and resources (staff and non-staff) required to provide it.

Designing the intervention

The intervention is based on an existing manual and it has not been possible to determine what resources went into designing it originally. No adaptation was necessary for the MCTAAN study as it was designed specifically for the patient group. Therefore, staff time and other resources required for this intervention-related activity were zero.

Training and supervision

Three two-hour training workshops on MFDT were held at Service A before the trial started, and more were run later in the trial period. Service A plays an important role in training new staff; most of the MCTAAN workshops were run there and it appears to be the largest provider of MFDT more generally. Staff members from other centres were sent to Service A for MFDT training at the workshops. One centre, for example, sends one person each year to Service A for training; no charge is made for this. Apart from the workshops, which were not attended by every staff member providing the MFDT intervention, staff received a few hours' introduction, but their training mainly consisted of helping to run the programme and background reading.

Trainee family therapists also receive supervision. The arrangements vary between centres. In one, supervision takes place approximately once per month. In another, it consists of

pre- and post-session discussions. These sessions also vary in length. To add another layer of complexity, trainees' supervision is usually related to the entire course of study in family therapy, not just the MFDT. Therefore, only the time trainees spend providing MFDT is known and lack of data means that it is not possible to include MFDT-specific supervision.

Information evenings

Information evenings for prospective participants were held in at least three services, with no information available on Service C. At Service A, this session lasted 2.5 hours. Two staff members led the evening supported by four volunteers, and a junior doctor gave a talk lasting about an hour.

Preparation and feedback

Arrangements for preparation and feedback also vary between sites, and supervision may be integrated into these sessions. In one centre, staff members meet for one hour before and 1.5 hours after each day's group session.

Rooms

Generally, the intervention takes place within hospital buildings and the type of room used depends on availability. If several rooms are available, the groups may split up with the young people in one room and the parents in another. If only one room is available, partitions may be used to separate the space. One centre which did not have a large enough room rented a hall at the local YMCA at a charge of £1,000 for one iteration of the MFDT intervention.

Materials and refreshments

A variety of materials were used, mostly for arts and crafts such as colouring/drawing, collaging and making posters. Estimated costs ranged from approximately £12 to £75 per group. The costs of refreshments ranged from £12 to £42 per day.

Travel

As the intervention commonly took place at the staff members usual place of work, no additional staff travel costs were incurred, unless staff members were acting as key workers.

Information about participants' travel to the MFDT intervention for the intensive phase (over the three months following the baseline assessment) is available for 45 young people. Most (n=43) travelled with their parents, commonly by car (n=26) or public transport (n=17), although some used more than one mode of transport. Average travel time was almost an hour but ranged from eight minutes to six hours (n=37), and the average distance travelled was 26 miles (range 0.3 miles to 250 miles, n=26). The average public transport fare was around £25 but ranged from £0.40 to £200 (n=19). These figures are not included in the unit cost of MFDT presented below because they were deemed to be a research cost associated with conducting the RCT, rather than the treatment itself, as participants had to travel to specific services involved in the trial rather than receiving the intervention at a service local to them.

UNIT COSTS OF MFDT

Table 4-1 shows the staffing inputs into the intervention provided by each service and applies unit costs per hour to these staff hours, as well as other, non-staff costs. Total costs for each of the four services are also shown. Then, the following unit costs for the MFDT intervention are calculated:

- Costs per MFDT group, i.e. running one iteration of the group-based intervention, including the intensive phase and follow-up sessions over a 12-month period;
- Costs per participating family over the 12-month period;
- Costs per family per day of MFDT.

Table 4-1: The cost of the MFDT intervention, by treatment centre (2008/09 cost)

	Service A		**Service B**		**Service C**		**Service D**	
	Hrs	***Cost***	***Hrs***	***Cost***	***Hrs***	***Cost***	***Hrs***	***Cost***
Information evening								
Family therapist	5	£220	5	£220	-	-	5	£220
Junior/ward doctor	1	£28	1	£28	-	-	1	£28
Volunteers/trainees	10	£310	10	£310	10	£310	10	£310
MFDT group								
Family therapist	77	£3,388	69	£3,049	-	-	92	£4,066
Psychologist	39	£1,425	77	£3,388	-	-	-	-
Consultant	39	£4,212	-	-	-	-	77	£8,316
Junior/ward doctor	39	£1,078	77	£5,313	-	-	-	-

	Service A		Service B		Service C		Service D	
	Hrs	***Cost***	***Hrs***	***Cost***	***Hrs***	***Cost***	***Hrs***	***Cost***
Occupational therapist	-	-	69	£1,802	-	-	-	-
Clinical nurse specialist	-	-	-	-	-	-	77	£1,925
Volunteers/trainees	159	£4,937	62	£1,910	116	£3,581	15	£477
Preparation & feedback								
Family therapist	28	£1,210	25	£1,089	-	-	21	£924
Psychologist	14	£509	28	£1,210	-	-	-	-
Consultant	14	£1,504	-	-	-	-	18	£1,890
Junior/ward doctor	14	£385	28	£1,898	-	-	-	-
Occupational therapist	-	-	25	£644	-	-	-	-
Clinical nurse specialist	-	-	-	-	-	-	18	£438
Volunteers/trainees	57	£1,763	22	£682	41	£1,279	4	£109
Total staff costs								
Clinician	-	-	-	-	187	£9,537	-	-
Administrator	-	-	-	-	39	£982	-	-
Total	£20,969		£21,543		£15,689		£18,703	
Other costs								
Materials	-	£36	-	£75	-	£13	-	£20
Refreshments	-	£462	-	£138	-	£220	-	£138
Unit costs								
Total cost per group	£21,466		£21,754		£15,921		£18,860	
Total cost per family	£3,578		£3,626		£2,653		£3,143	
Total cost per family per day	£325		£330		£241		£286	

The cost of the MFDT intervention was calculated at £325 per day for Service A, where most sessions for this patient group took place. Across the four services, estimates ranged from £241 to £330.

COST VARIATIONS

Given that MFDT is a manualised intervention, variations in costs between services were expected to be small. As can be seen from the results above, Services A and B have roughly similar unit costs. Tentatively, cost variations between Services A, B and D seem to result from differences in staff providing the intervention. Notably, costs per family per day for Service C were lowest by a large margin. This was the service that only provided totals for

staff costs and administrator costs, rather than information needed for micro-costing based on the principles of economic costing. It is therefore possible that the difference is due to different underlying assumptions or inclusion and omission of cost categories, for example about the level of overheads or their inclusion in the cost data provided by the service.

DISCUSSION

This is the first study of the costs of MFDT. Data were collected and costs calculated following best practice in economic evaluation, giving a high level of confidence in the unit costs for those services that were able to provide data in line with the request (Services A, B and D).

The main limitation of this study is the fact that data were collected after the trial had been completed, rather than alongside the study which would have allowed staff time use data to be collected using diaries, time sheets or other means of real-time recording. One problem was that in those services providing the intervention on a 'routine' basis it was difficult for interviewees to recall at interview which resources had been used specifically for the groups run as part of the RCT. This is likely to have biased the information, and it is unclear whether this would have increased or decreased the resulting unit costs. However, if the interest in the unit cost of MFDT is with a view to rolling out the intervention more widely, costs estimated after a 'bedding down' phase will be a more useful estimate of costs in the longer term, as any set-up issues will have been ironed out.

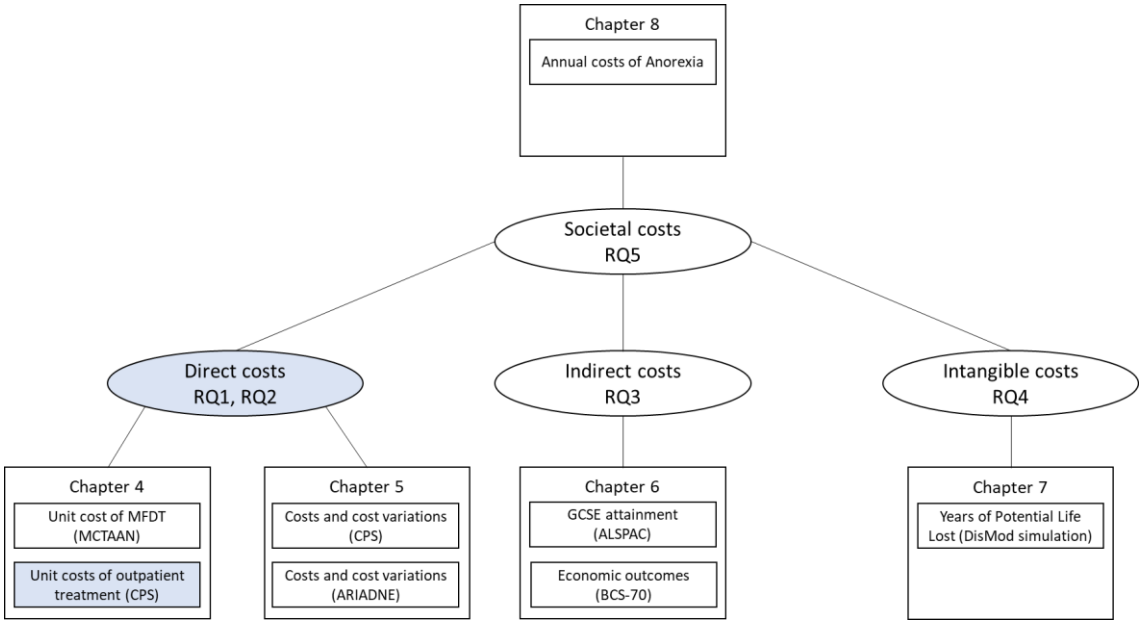
Information was missing from some services, and assumptions had to be made to fill those gaps. However, the methods used to obtain data and to calculate unit costs follow best practice, and any assumptions are clearly stated in the methods section.

The fact that the estimates for three of the services (A, B and D) are close to each other gives confidence that they are reasonably accurate. The unit cost for Service C, which only provided data recorded for administrative purposes, is much lower than for other services where more detailed information could be obtained. This may be due to a different underlying model of calculation, as often services calculate costs not based on long-run marginal costs, but on short-term marginal costs, i.e. omitting overheads, or using only a partial overhead figure. Given that no authoritative source for these intervention costs exists, it is not possible to validate the data collected for this study, and the unit costs presented here are the only available estimate for MFDT.

The cost of one MFDT session for one family was equivalent to around two sessions of SFT calculated for the same trial, but less than half the cost per hour. At the same time, MFDT treatment costs compare favourably to the cost of one day of inpatient treatment

for ED - £330 or less compared to a minimum of £482 per day (Department of Health 2010).

PART 2: UNIT COSTS OF OUTPATIENT TREATMENTS (CARE PATHWAYS STUDY)



INTRODUCTION

This second part of Chapter 4 again focusses on the direct costs associated with AN. Again, this section takes a service-level approach, but here I attempt to 'unpack' the treatment components of outpatient services for AN.

In this study, I analyse data from the Care Pathways Study (CPS) to determine

- What types of treatment are provided for AN in outpatient ED services,
- Which staff provide them, and
- Why costs may vary.

In particular, I focus on different levels of services specialisation with regard to eating disorders:

- Specialist ED services: NHS child and adolescent ED services (CAEDs) and adult ED services;
- Specialist CAMHS: General CAMHS with ED specialisation;
- Non-specialist CAMHS: General CAMHS without ED specialisation.

In addition to being the first study to look at the costs and variations in costs of outpatient treatments for AN in England, this study contributes an economic argument to the debate on service specialisation, which tries to determine whether specialist services provide more effective care for ED than general CAMHS services in terms of treatment outcome.

While the private sector provided over 80% of inpatient units in 1998 (Brown 1997; O'Herlihy *et al.* 2003b; Palmer & Treasure 1999), there has been a recent effort to increase the availability of outpatient services through the NHS. This is considered to be a less costly, and potentially cost-effective, mode of treatment compared to inpatient care. However, little is known about treatments provided in outpatient settings (Royal College of Psychiatrists 2000), and about costs associated with different treatment options.

To help address the evidence gap with regard to outpatient treatment for AN, the Care Pathways Study (House *et al.* 2012; House 2011) examined different care pathways for adolescents aged 13-18 with AN across 4 PCTs in the Greater London Area. Data on service contacts and treatment received were collected by House and colleagues from case notes and treatment pathways were tracked over 12 months. In addition, data were collected

on the types of treatment provided for AN within outpatient services, and the staff involved in providing these treatments. These data service-level data are used in the analyses presented here.

METHODS

DATA COLLECTION

As part of the main CPS, a service-level questionnaire was given to clinicians to complete (see Appendix 3), with the main aim of collecting data for the mapping and analysis of care pathways. This questionnaire asked about treatments for AN provided within the service. A separate questionnaire for service managers was designed by Jennifer Beecham, Jennifer House and myself to address the particular data needs of the economic evaluation (see Appendix 2), asking in more detail about the grades and salaries of staff providing ED treatments.

Service managers or other relevant contacts were identified with the research team and through internet searches. I then contacted them by e-mail. The request included a letter outlining the CPS and the aims of the economic analysis as well as the service questionnaire. This initial e-mail was followed-up by one or two telephone calls, either by myself or Annette Bauer, another researcher at the PSSRU. This approach proved unsuccessful so a follow-up letter was sent to each service, including the questionnaire, a pen and a franked return envelope. Despite these efforts, only one completed questionnaire was returned, and this had been completed for the wrong period.

Given this disappointing outcome, the data collected via the service-level questionnaire for clinicians for the main study were used to estimate the unit costs presented here.

From the available data, I created a dataset containing the relevant information. This included:

- Level of service specialisation with regard to ED
- Service location (hospital or community)
- Details on ED assessment
- Typical length of assessment
- Staff typically involved in assessment

- Whether outpatient treatment is provided for AN
- Type of treatments available
- Typical length of session
- Typical number of sessions
- Staff typically providing the session
- Details on other treatments provided, e.g. inpatient, day patient

Data were available for 26 services, with n=5 categorised as specialist ED services, n=6 as CAMHS with ED specialisation and n=15 as CAMHS without ED specialisation.

COSTING SERVICES AND TREATMENTS

The cost of treatment provided within each service and an average for each group of services by level of ED specialisation were calculated using a long-run marginal opportunity cost approach (Beecham 2000). For each type of staff member, a unit cost was calculated based on relevant schemas in the PSSRU volume Unit Costs of Health and Social Care (Curtis 2011), taking into account the likely Agenda for Change pay grade, working hours, ratio of client contact to other tasks and overheads based on service location. Unit costs used in the calculations are shown in Table 4-2. All costs are presented in 2010/11 prices.

Table 4-2: Unit costs

	£ per hour	**Sources of information**
Doctors		
Associate specialist	166	Curtis (2011), p. 202. Time ratio as per consultant (medical) from Curtis (2009), p. 170.
Consultant (assume medical)	202	Curtis (2011), p. 203. Time ratio as per consultant (medical) from Curtis (2009), p. 170.
GP (hospital)	229	Curtis (2011), p. 148.
GP (community)	138	Curtis (2011), p. 148.
Paediatrician (hospital)	202	As consultant (medical). Curtis (2011), p. 203.
Paediatrician (community)	138	As GP, Curtis (2011), p. 156.
Senior house officer	61	As foundation house officer year 2. Curtis (2011), p. 199. Time ratio as per consultant (medical) from Curtis (2009), p. 170.
Specialist registrar	89	Curtis (2011), p. 201. Time ratio as per consultant (medical) from Curtis (2009), p. 170.
Staff doctor/ward doctor	117	Based on consultant (medical), Curtis (2011), p. 203. Time ratio as per consultant (medical) from Curtis (2009), p. 170.

	£per hour	Sources of information
Nurses		
CAMHS nurse	75	Based on CAMHS member with band 5 median salary. Curtis (2011), p. 173.
CNS	73	As community mental health nurse, Curtis (2011), p. 142.
Key nurse	120	Curtis (2011), p. 192.
Nurse (hospital)	104	Curtis (2011), p. 193.
Nurse (community)	71	Curtis (2011), p. 141.
Psychology nurse	104	As specialist nurse. Curtis (2011), p. 193.
Senior staff nurse	120	Curtis (2011), p. 192.
Specialist nurse	104	Curtis (2011), p. 193.
Specialist nurse (community)	89	Based on nurse specialist Curtis (2011), p. 144.
Psychologists and psychiatrists		
Child & adolescent psychiatrist	295	As consultant (psychiatric). Curtis (2011), p. 205.
Child psychiatrist	295	As consultant (psychiatric). Curtis (2011), p. 205.
Child psychiatrist (community)	293	As consultant (psychiatric). Curtis (2011), p. 205, with overheads from CAMHS team (Curtis (2011), p. 173).
Child psychologist (hospital)	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Child psychologist (community)	152	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137.
Clinical psychologist (hospital)	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Clinical psychologist (community)	152	Clinical psychologist, face-to-face contact. Curtis (2011), p. 137.
Consultant psychiatrist (hospital	295	Patient-related hour. Curtis (2011), p. 205.
Psychiatrist (community)	293	As consultant (psychiatric). Curtis (2011), p. 205, with overheads from CAMHS team (Curtis (2011), p. 173).
Psychologist (hospital	156	As clinical psychologist, overheads as consultant (psychiatric). Curtis (2011), p. 205.
Psychologist (community)	152	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137.
psychology assistant	123	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137. Median salary grade 6.
Therapists		
Art therapist (hospital)	139	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137. Median salary grade 7.
Art therapist (community)	136	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137. Median salary grade 7.

	£per hour	Sources of information
Child psychotherapist	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Cognitive analytical therapist	139	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137. Median salary grade 7.
Counselling psychotherapist	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Drama therapist	139	as art therapist
Family therapist (community)	183	As clinical psychologist, face-to-face contact. Curtis (2011), p. 137. Median salary grade 8b.
Family therapist (hospital)	186	Clinical psychologist, face-to-face contact. Curtis (2011), p. 137, using overheads for hospital-based health care staff (pp. 181-187)
Psychotherapist (hospital)	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Psychotherapist (community)	152	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137.
Systemic psychotherapist	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Therapist	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
Dieticians		
Dietician (hospital)	36	Curtis (2011), p. 184.
Dietician (community)	34	Dietician (hospital). Curtis (2011), p. 184, capital overheads from CAMHS teams (pp. 172-175).
Paediatric dietician	47	Curtis (2011), p. 184, using median salary band 6.
Specialist dietician	47	Curtis (2011), p. 184, using median salary band 6.
Other		
Behaviourist	156	As clinical psychologist, face-to-face contact, Curtis (2011), p. 137. Overheads as consultant (psychiatric). Curtis (2011), p. 205.
CAMHS professional (hospital)	101	Targeted CAMHS team member. Curtis (2011), p. 175, using overheads for hospital-based health care staff (pp. 181-187).
CAMHS professional (community)	98	Targeted CAMHS team member. Curtis (2011), p. 175.
Occupational therapist (community)	35	Curtis (2011), p. 134. No time ratio applied.
Occupational therapist (hospital)	36	Curtis (2011), p. 182. No time ratio applied.
Occupational therapist assistant	31	Based on Occupational Therapist. Curtis (2011), p. 182. Median salary grade 4 (assistant practitioner). No time ratio applied.
Physiotherapist (community)	35	Curtis (2011), p. 133. No time ratio applied.
Physiotherapist (hospital)	37	Curtis (2011), p. 181. No time ratio applied.

	£per hour	Sources of information
Social worker (child)	146	Curtis (2011), p. 157. No time ratio applied.
Therapeutic carer	104	Curtis (2011), p. 193.

ASSUMPTIONS REGARDING MISSING OR INCONSISTENT INFORMATION

Given that the information used to generate the dataset for these analyses was not collected explicitly with an economic analysis in mind, assumptions needed to be applied where required data were not available. The approximate cost of each type of treatment session was calculated by applying of the following assumptions:

- The unit costs for all staff members' time listed as involved in providing a treatment were added together;
- Where the questionnaire stated that one or another type of staff member provided the treatment (e.g. "psychiatrist or psychologist"), an average unit cost was applied;
- For group treatments, a group size of 6 patients or families was assumed.

There were some potential inconsistencies where the number of staff members involved in a treatment session appeared to be too high to justify the assumption that they were all present at the same time. It may be that the question was interpreted as asking for the total number of staff who potentially provide the treatment within the service, rather than how many people are involved in any one particular treatment session. For example, if it was stated on the questionnaire that three psychologists proved individual family therapy, it seems unlikely that they all provide the treatment together. Rather, it seems plausible that there are three psychologists within the service who can provide family therapy. In these cases, it was assumed that one staff member provides a treatment session.

Calculating the cost of an assessment presented additional difficulties because there were often many members of staff involved and it is not clear from the available information how much time each staff member spends on the assessment. To explore the range of possible cost of an assessment, three estimates were calculated:

- An 'average' unit cost, calculated based on the assumption that each staff member spent an equal amount of time with the patient;

- A low estimate, assuming the lowest-cost staff member provided the entire assessment;
- A high estimate, assuming the highest-cost staff member provided the entire assessment.

There were four services where the duration of the assessment was given as several months (possibly implying ongoing monitoring rather than a formal assessment session) or as "variable". These were treated as missing. After presenting the three estimates described above, the base case estimate is used for all further analysis.

The work presented in this chapter also links with Chapter 5, where the perspective shifts from service-level costs and variations in costs to the individual level. The types of outpatient treatment reported in the individual-level data are not as fine-grained as those available from the service-level analysis presented in this section. To arrive at a unit cost for each type of outpatient treatment that could be applied to the individual-level data, a weighted average was calculated by applying the proportion of services providing each type of treatment as a weight. For example, if 80% of services provide cognitive behaviour therapy (CBT) and 12% provide psychodynamic psychotherapy (PDT), the weighted average cost of individual treatment (IT) for the service in question is (0.8*(cost CBT) + 0.12*(cost PDT))/(0.8+0.12).

In addition to calculating these unit costs for each service, the average unit cost for each level of service specialisation was calculated. This average was used to estimate unit costs for services where patients received treatment that were not part of the study or that had not provided sufficient data to estimate those unit costs.

ANALYSES

In presenting the results regarding outpatient treatments and their costs, staff members providing the treatment and the unit costs of treatment, outpatient services were grouped according to their level of ED specialisation:

- Specialist ED services: NHS CAEDs and adult ED services;
- Specialist CAMHS: General CAMHS with ED specialisation;
- Non-specialist CAMHS: General CAMHS without ED specialisation.

The number and percent of services within each service category providing each type of treatment and the type of staff involved in the most commonly provided treatments are presented. From these data, the costs of different types of treatments were calculated at the service level. Differences in the odds that a treatment was provided or a professional provided a treatment were tested for statistical significance using univariate logistic regression models. Differences in the number of treatments were tested using simple regression models (equivalent to a t-test where there are only two predictor categories, and extendable to accommodate more than two categories), and the p-value associated with the F-test for significance of the overall model is presented. Differences in the mean cost of treatments between services were investigated using regression models with 10,000 bootstrap replications. This model was chosen because the Park test indicated that there was no benefit from fitting, for example, a generalised linear model with a log link or a non-normal distribution, as can be the case for skewed cost data. A 95% significance level was used unless indicated otherwise. The analyses use complete data and the number of services providing information is presented alongside the results.

RESULTS

TREATMENTS PROVIDED

Table 4-3 shows the number of services that provided treatments for AN on an outpatient basis[3] and identifies average costs for each treatment, by level of ED specialisation. Across all levels of specialisation, cognitive behavioural therapy (CBT), single family therapy (SFT) and dietary advice are the most commonly provided treatments.

I investigated whether level of service specialisation was associated with the number of different treatments offered. As Table 4-3 shows, most treatments provided were individual treatments (treatments provided one-to-one, as opposed to treatments provided in a group setting or to a family). Table 4-4 shows the number of individual treatments provided, the total number of treatments offered (including both individual and group or family treatments), and number of sessions and length of sessions for the two most commonly provided treatments, CBT and SFT. Specialist ED services offered on average 2.6 types of

[3] Note that the cost of MFDT shown is based on a re-costing of the MCTAAN data presented in Chapter 4, Part 1 as I have inflated the costs to 2010/11 prices.

individual treatments, while specialist CAMHS offered 2.0, and non-specialist CAMHS offered 1.6 ($p > 0.01$). The total number of treatments offered differed significantly between service types.

Specialist ED services offered more than eight different psychological or psychiatric treatments in total, while in specialist CAMHS it was 7.0 and in non-specialist CAMHS it was 5.2 ($p > 0.01$). A (non-significant) trend seems to be that a higher degree of service specialisation appears to be related to the likelihood of providing treatments beyond CBT, SFT and dietary advice, although there do not appear to be large differences between specialist ED services and specialist CAMHS.

There are no significant differences in the number of sessions or duration of CBT and SFT by level of service specialisation, but the data show a large variation within each specialisation category.

Table 4-3: Number of services providing outpatient treatments for AN, by service specialisation

	Specialist ED services (n = 5)			**Specialist CAMHS (n = 6)**			**Non-specialist CAMHS (n = 15)**		
	Number providing (%)	***Mean £(SD)***	***Valid n (cost)***	***Number providing (%)***	***Mean £(SD)***	***Valid n (cost)***	***Number providing (%)***	***Mean £(SD)***	***Valid n (cost)***
Assessment	5 (100%)	152.79 (49.53)	5	6 (100%)	208.75 (51.86)	6	15 (100%)	152.48 (67.99)	13
CBT	5 (100%)	135.52 (20.84)	5	6 (100%)	170.72 (26.46)	6	10 (67%)	163.85 (42.28)	9
PDT[a]	3 (60%)	123.91 (10.24)	3	3 (50%)	129.82 (n/a)	3	5 (33%)	137.12 (13.91)	5
Nurse Counselling	3 (60%)	90.60 (n/a)	2	1 (17%)	71.27 (n/a)	1	3 (20%)	82.09 (n/a)	2
Other indiv. therapy	2 (40%)	129.82 (n/a)	1	2 (33%)	186.17 (n/a)	1	5 (33%)	120.82 (n/a)	1
Group w/o parents	2 (40%)	40.31 (11.69)	2	0 (0%)	n/a	0	0 (0%)	n/a	0
Other group therapy	1 (20%)	n/a	0	0 (0%)	n/a	0	0 (0%)	n/a	0
SFT[b]	5 (100%)	204.67 (37.63)	4	6 (100%)	242.26 (86.03)	6	12 (80%)	246.05 (99.51)	8
MFT[c]	1 (20%)	547 (n/a)	1	2 (33%)	547 (n/a)	1	2 (13%)	547 (n/a)	1
Other FT[d]	1 (20%)	n/a	0	1 (17%)	21.55 (n/a)	1	2 (13%)	129.54 (n/a)	2
Refeeding	2 (40%)	n/a	0	2 (33%)	n/a	0	3 (20%)	n/a	0
Dietary	5 (100%)	40.55 (18.55)	4	5 (83%)	38.95 (10.78)	3	8 (53%)	108.68 (n/a)	2
(Medical monitoring)	5 (100%)	121.56 (89.19)	2	5 (83%)	73.85 (n/a)	1	10 (67%)	177.91 (77.60)	5

	Specialist ED services (n = 5)			Specialist CAMHS (n = 6)			Non-specialist CAMHS (n = 15)		
	Number providing (%)	***Mean £(SD)***	***Valid n (cost)***	***Number providing (%)***	***Mean £(SD)***	***Valid n (cost)***	***Number providing (%)***	***Mean £(SD)***	***Valid n (cost)***
Other	1 (20%)	n/a	0	3 (50%)	115.79 (n/a)	1	0 (0%)	n/a	0

a Difference between Specialist ED services and Non-specialist CAMHS statistically significant at the 95% level
b Difference between Specialist ED services and Specialist CAMHS statistically significant at the 95% level
c Difference between Specialist ED services and Non-specialist CAMHS statistically significant at the 90% level

Table 4-4: Differences in treatment intensity, by service specialisation

	Specialist ED services			Specialist CAMHS			Non-specialist CAMHS			
	Mean	***SD***	***Range***	***Mean***	***SD***	***Range***	***Mean***	***SD***	***Range***	***p-value (F-test)***
Individual treatments offered	2.60	1.14	1-4	2.00	0.89	1-3	1.64	0.93	0-3	0.182
Total treatments offered	8.40	1.52	6-10	7.00	2.19	4-10	5.23	1.86	1-8	0.011
CBT sessions number	17.50	9.85	6-30	12.00	2.83	9-15	17.00	13.06	9-40	0.630
CBT session length (minutes)	55.00	5.00	50-60	53.33	7.53	45-60	56.5	5.80	45-60	0.616
SFT sessions number	23.00	13.71	4-40	17.50	8.66	10-30	9.25	4.27	6-15	0.180
SFT session length (minutes)	56.00	5.48	50-60	67.50	12.55	60-90	67.17	12.68	50-90	0.180

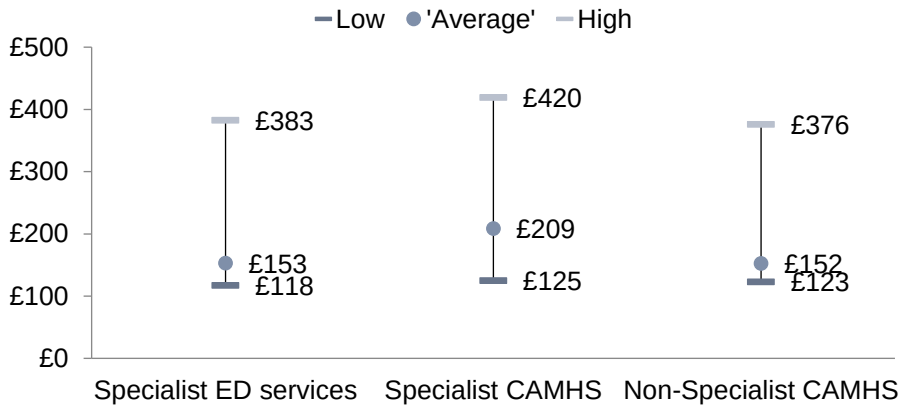
a Difference between Specialist ED services and Non-specialist CAMHS statistically significant at the 95% level
b Difference between Specialist ED services and Specialist CAMHS statistically significant at the 95% level
c Difference between Specialist ED services and Non-specialist CAMHS statistically significant at the 90% level

VARIATIONS IN COST

Assessment

Figure 4-1 shows the average of the three estimates of assessment costs, based on the scenarios ('average', low and high cost) described above. Data were available for all specialist ED services and specialist CAMHS, and 13 of the 15 non-specialist CAMHS services. There is a wide variation in the different estimates, resulting in uncertainty. Given that it is not possible to determine which estimate is the most appropriate for each service, the average cost will be used in the analysis of individual-level data in Chapter 5.

Figure 4-1: Assessment costs: Averages of three estimates, by service specialisation



CBT and SFT

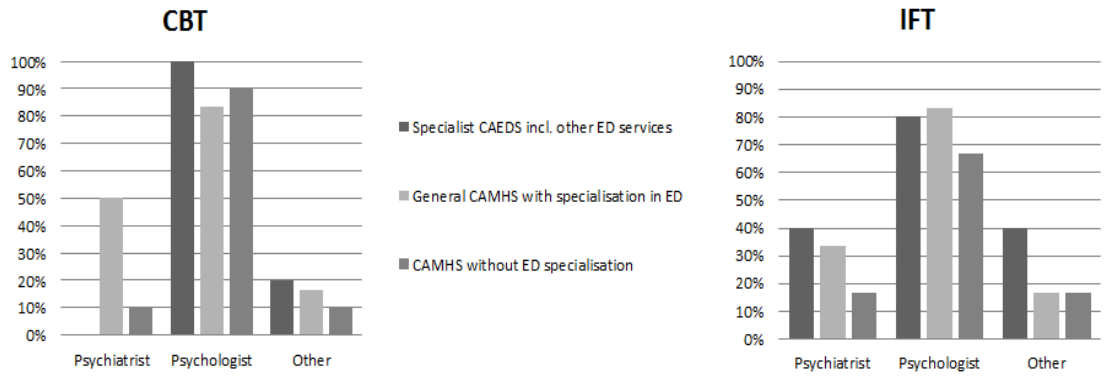
Looking more closely at the most commonly provided treatments, CBT and SFT, there are differences in average cost per CBT session between service types significant at the 90% level (p=0.096), but not in the cost of an SFT session (p=0.667).

The profession and grade of staff delivering the treatment influences the per session cost of that treatment. The percentage of services (by degree of ED specialisation) where specific staff members are involved in providing assessment, CBT and SFT are shown in Figure 4-2. The 'other professionals' category includes staff such as occupational therapists, CAMHS team members and unspecified staff.

There are no statistically significant differences in terms of delivery of SFT, but psychiatrists are more likely to be involved in CBT in services that are specialist CAMHS compared to

non-specialist CAMHS ($p < 0.001$). No specialist ED service reported that psychiatrists delivered CBT.

Figure 4-2: Staff members involved in assessment and treatment, by service specialisation



Average unit costs of outpatient treatment

The unit costs for the types of outpatient treatment, summarised by service type to match the types of outpatient sessions recorded in the individual-level data set (see Chapter 5 part 1), are shown in Table 4-5. These averages were used to estimate the cost of treatment for patients who were in contact with services not taking part in the study, based on service type.

Table 4-5: Average unit costs of AN outpatient treatment, by level of specialisation for ED

	Specialist ED services		Specialist CAMHS		Non-specialist CAMHS	
	Valid n	*Mean £*	*Valid n*	*Mean £*	*Valid n*	*Mean £*
Individual	3	£135	6	£163	11	£163
Group session	1	£32	0	-	0	-
SFT	3	£187	5	£235	8	£246
MFT day/session	1	£547	1	£547	1	£114
Parent session	1	£101	1	£22	1	£98
Dietic session	3	£33	3	£39	2	£109
Occupational therapy	0	-	0	-	0	-
Physiotherapy	0	-	0	-	0	-

DISCUSSION

In this study, I identified the different types of outpatient treatments provided by specialist ED services, specialist CAMHS and non-specialist CAMHS in four Greater London PCTs. I generated a dataset that allowed me to calculate unit costs for these treatments. I then explored variation in costs by degree of service specialisation with regard to ED. While service provision in outpatient services has previously been mapped by the Royal College of Psychiatrists (Royal College of Psychiatrists 2012), the Care Pathways Study allowed this to be broken down by type of eating disorder, and this is the first study reporting in detail the costs of these treatments.

The research identified treatments delivered to a cohort of patients from case notes, rather than solely relying on reports from services about what they could provide. Cognitive behaviour therapy and single-family therapy were the most common treatments. Mean per session unit costs for treatment varied considerably. Average unit costs were lowest in the specialist ED services (£136 for CBT and £205 for SFT) with SFT unit costs similar for the specialist CAMHS and non-specialist CAMHS services (approx. £245).

Unit costs are sensitive to the number and profession of staff delivering the intervention, as well duration of the session and whether the intervention is provided in a group or individual setting. While the small number of services involved poses a challenge to statistical analysis, it is reasonable to conclude that differences in unit costs are due to variations in staff profession (driven by salary) and staff time. In the case of multi-family therapy, specialist services delivered this as whole-day sessions, while in the non-specialist CAMHS the sessions lasted only 60-90 minutes (see Table 4-4). The high cost of dietetic sessions in non-specialist CAMHS arises because psychiatrists provide dietary advice, while in other types of services it is more likely to be provided by dieticians or nurses who receive lower salaries. In the case of parent sessions, the variation in unit costs is mainly due to group provision of sessions for parents in some services (so staff costs per session are shared between several families).

While there were few differences in the type of professionals providing CBT and SFT, the probability that a psychiatrist is involved in providing CBT was significantly higher in general CAMHS with ED specialisation than in other service types. In part this may be because generic CAMHS teams tend not to include psychiatrists (see Curtis 2011, pp. 172-174).

Specialist skills may also be important. Specialist ED services are likely to include more staff with expertise specific to ED, so that staff on lower pay bands (nurses, perhaps) can provide treatments that in specialist CAMHS are more likely to be provided by a psychiatrist. The belief that specialisation facilitates experience and confidence in treating ED is prominent in the literature (Gowers & Bryant-Waugh 2004). Also, as House (House *et al.* 2012) remarks, ED specialisation in general CAMHS is often due to a consultant taking a special interest. Part of the explanation for the low number of non-specialist services where psychiatrists treat AN may again be that generic CAMHS teams tend not to include psychiatrists.

The analysis of treatment provision indicates that a higher degree of specialisation may be associated with offering a wider variety of treatments, and specialist services appear to be more likely to provide a specific treatment beyond CBT, SFT and dietary advice. But given the small number of services, differences are unlikely to be detected. However, the findings regarding the most commonly provided treatments are broadly in line with the results of a survey of ED services by the Royal College of Psychiatrists (Royal College of Psychiatrists 2012).

Limitations of the study arise from the design and conduct of the Care Pathways Study, which are discussed by House (2011, pp. 81-83). The study design in turn reflects the difficulties encountered in researching complex and rare conditions generally, and research involving CAMHS data in particular (see Batty *et al.* 2013 for a discussion of measurement of routine outcome measures in CAMHS). While a high proportion of eligible services (84%) provided data, some key CAMHS services did not agree to participate or agreed but failed to provided data. While this is likely to have a greater impact on the individual-level data analysis (see Chapter 5, part 2) due to participants not being recruited, it also means these services are not represented in the service-level cost data. The focus on Greater London, which differs from much of the rest of the UK due to higher concentration of specialist NHS and of private ED services, limits generalisability. House stipulates that the presence of specialist services may lead to a de-skilling of CAMHS with regard to ED treatment. At the same time, those PCTs that are likely to be more comparable to the rest of the UK, i.e. those without specialist ED provision, were underrepresented in the study.

Further limitations arise from the difficulties in collecting data specifically for the economic analysis, so that less detailed data had to be used, alongside a set of assumptions (detailed

above). The resulting need to use national unit costs means that any variation in salary levels and overheads between services is not captured.

While the small number of specialist services involved in the study means it is difficult to draw firm conclusions, this exploratory analysis generates questions that can be addressed by future research.

CHAPTER SUMMARY

The literature review highlighted significant gaps in the data on outpatient treatment for AN as reflected in the lack of data in previous estimates of the CoI of AN. The review further revealed a lack of data on the types of treatments provided and their unit costs. This information is required to meet the overall aim of this thesis – to present a comprehensive CoI estimate for AN – but also useful to service planners and clinicians alike. This chapter therefore explored the types of treatment for AN provided in outpatient settings, their unit costs and variations in these costs. The main findings can be summarised as follows:

- The unit cost of MFDT was estimated at £241-£330 per session (in 2009 prices), with £325 in the service providing the largest number of sessions within the RCT.
- Within Greater London outpatient services, the most commonly provided treatments for AN regardless of level of service specialisation were CBT, SFT and dietary advice.
- The average cost of CBT was £136 in specialist ED services, £209 in specialist CAMHS and £153 in non-specialist CAMHS.
- The average cost of SFT was £205 in specialist ED services, £242 in specialist CAMHS and £246 in non-specialist CAMHS.
- The usual duration of CBT and SFT sessions and total number of sessions provided were similar across levels of service specialisation.
- The average cost per CBT session was significantly lower when provided by specialist ED services.

No specialist ED service reported that CBT was provided by psychiatrists, indicating that the cost difference stems from differences in the type of staff providing the treatment.

In conclusion, despite the small sample size and within-group variations, there were some significant variations in unit costs that point towards an advantage of service specialisation for ED in terms of the costs of treatment, and therefore contributes towards an economic argument in the debate around specialist vs non-specialist services for the treatment of AN and ED – although this finding deserves further scrutiny. The unit costs calculated here will be applied to the analysis of individual-level data from the CPS in Chapter 5.

CHAPTER 5

Direct costs: Variations in individual-level costs associated with service use by patients with Anorexia nervosa

CHAPTER INTRODUCTION

This chapter contributes to the aims of the thesis – presenting an estimate of the societal costs of AN – by addressing RQ1: "What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?"

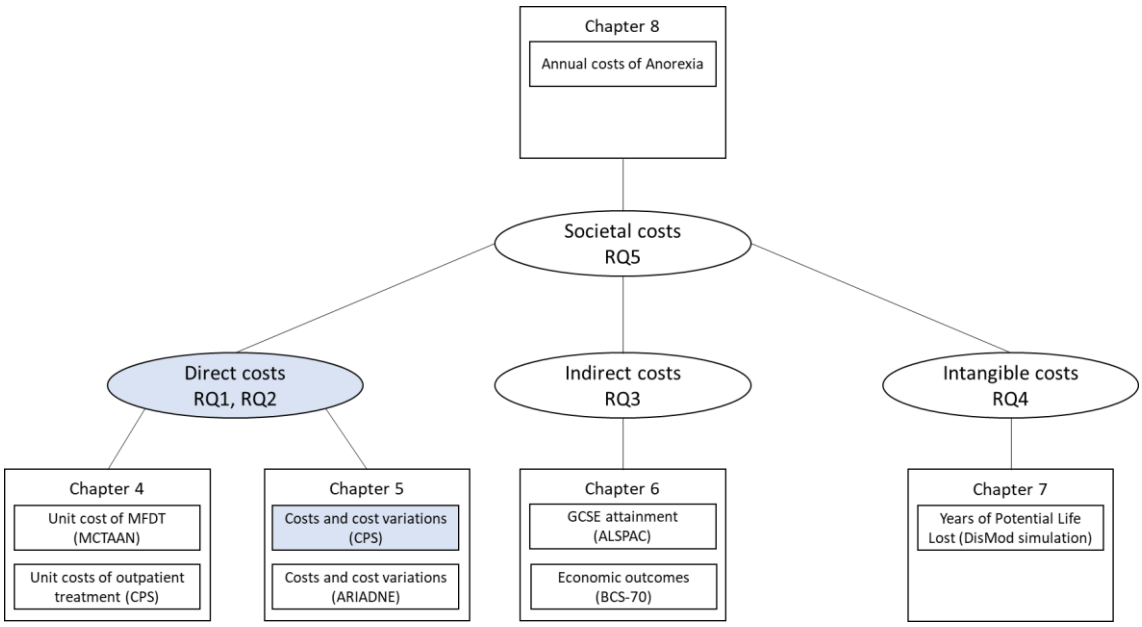
In particular, I explore variations in costs associated with outpatient treatment, where my literature review identified a considerable gap in the knowledge.

Several authors have argued that CoI estimates on their own are of limited use, but that looking at variations in costs is a step towards cost-effectiveness analysis and therefore economic evaluation. Further, exploring variations in individual-level cost is motivated by the production of welfare approach: Are resources directed based on health care need or impairment, or do costs vary by demographic features – potentially pointing to issues in equity in terms of access or provision of treatment?

While several studies have looked at resource use in AN in terms of length of inpatient stay or number of outpatient contacts both internationally (Krauth *et al.* 2002; Striegel-Moore *et al.* 2000; Toulany *et al.* 2015) and in England (Jacobs *et al.* 2004; ProBono Economics 2012; Tulloch *et al.* 2008), little information is available about the types of treatment received in outpatient settings. To my knowledge, to date there is only one RCT in England that reports on wider service use and associated costs (Byford *et al.* 2007a).

This chapter looks at the service use of individuals with AN, the associated costs and variation in costs. I present data from two different studies. First, I show the service use and associated costs for a cohort of young people with AN who were in contact with ED services in the Greater London Area, over a one-year time period. As Chapter 4, Part 2, this again uses data from the Care Pathways Study. Then, I show the service use and costs for participants in three clinical trials (part of the ARIADNE programme: MOSAIC (Schmidt *et al.* 2013), CASIS (Goddard *et al.* 2013b), iMANTRA (Schmidt *et al.* 2017) prior to commencing their allocated treatment in the RCTs. I explore variations in costs due to individual characteristics for the Care Pathways cohort, and two of the RCTs.

PART 1: INDIVIDUAL-LEVEL COST VARIATIONS AND SERVICE SPECIALISATION – EVIDENCE FROM THE CARE PATHWAYS STUDY



INTRODUCTION

This first part of Chapter 5 uses data from the Care Pathways Study (CPS; House 2011) to investigate the service consumption and associated costs of a cohort of adolescents with AN or EDNOS-AN entering ED services in four Greater London PCTSs. I then explore variations in costs based on individual characteristics and by care pathway.

The objective is to illuminate what treatments patients receive within outpatient settings, and whether variations in costs are associated with clinical or socio-demographic variables.

This is part of the effort to contribute to knowledge about costs of treatment in outpatient services, where there is currently a major gap. It is also an important contribution to the CoI model presented in Chapter 8.

I describe service use by care pathway, calculate total costs and fit univariate regression models to explore variations in costs for this cohort of adolescents.

METHODS

DATA

In this chapter, I use data from the cohort element of the Care Pathways Study (CPS) Patients identified through services participating in the health services research study were eligible for inclusion if they

Had an initial contact or re-contact after a treatment break of at least 6 months with a participating service between 01/12/2006 and 30/11/2008

- Were adolescents (age 13-17)
- Had a primary diagnosis an eating disorder (ED)
- Were registered with a GP from a Greater London PCT

378 unique cases meeting all inclusion criteria were identified and 93 with a known diagnosis of AN or EDNOS-AN consented to be part of the study. Care pathways data were available for 90 patients.

The main CPS collected patient-level data on a cohort of adolescents from participating services.

The patient-level data provides the following information relevant to the economic analysis:

- Patient socio-demographic characteristics
- Patient clinical data (weight and height)
- Treatment received within each outpatient service along the care pathway over a 12-month period:
- Number of assessments
- Number of individual or family sessions
- Number of group, dietic and medical outpatient sessions
- Number and type of outpatient appointments for physical tests
- Number of telephone calls
- Number of psychiatric reviews
- Number of inpatient days for ED or other reasons

The data were re-entered to better suit the needs of the economic analysis, showing the total number of service contacts for each individual within each service along their care pathway.

The analysis of service use and costs compared three care pathways identified in the main study:

- Specialist to specialist (S-S): Initial contact with ED services is through a specialist service, and onward referral is also to a specialist service.
- Non-specialist to specialist (NS-S): Initial contact is through a non-specialist service, with onward referral to a specialist service.
- Non-specialist to non-specialist (NS-NS): Initial contact and onward referral are both with a non-specialist service.

The 'private' pathway was omitted from the economic analysis presented here because costs could not be estimated reliably, as the components required for cost estimation (in particular salaries and overheads) were not publicly available. Data for this analysis were available for 84 out of 90 participants.

SERVICE USE AND COSTS

Service use for the cohort was described for the full sample and by care pathway. The costs associated with service use were calculated by multiplying instances of services use by the unit costs calculated from service-level information and presented in Chapter 4 to arrive at individual treatment costs over the one-year period, which are described by repenting means, standard deviations and ranges. The unit costs of different outpatient treatments were summarised by service type to match the types of outpatient sessions recorded in the individual-level data set. These averages were used to estimate the cost of treatment for patients who were in contact with services that were not taking part in the study, based on degree of service specialisation. In addition to the unit costs estimated from the Care Pathways data, unit costs for several other treatments were drawn from publicly available sources (Curtis 2011; Department of Health 2011),. Average costs and measures of dispersion are shown by care pathway, for each type of treatment and for total costs. The contribution of component costs to total costs is also shown.

Table 5-1: Additional unit costs for the analysis of care pathways costs

Treatment	Cost	Source
Psychiatric review	£645 for community-based services	ED service ID 1: Duration 60-90 minutes, all treating and consulting staff members participate.
	£694 for hospital-based services	Costed as 75 mins, 1 psychiatrist, 1 psychologist, 1 nurse.
Telephone call	£17.9 for community-based services	7.1 minutes as per GP (Curtis 2011, p. 49), with clinical psychologist
	£18.5 for hospital-based services	
Outpatient medical	£775	Weighted average for all paediatric outpatient contacts (Curtis 2011, p. 73)
Day patient day	£552	NHS day cases HERG (Department of Health 2011)
MFDT	£557	Inflating of MCTAAN unit cost (see Chapter 4)
Medical inpatient admission	£593 per day	NHS mental health inpatients, children (Department of Health 2011)
ED inpatient admission	£492 per day	NHS mental health inpatients, ED children (Department of Health 2011)

STATISTICAL ANALYSES

An exploratory analysis of predictors of treatment costs was performed by fitting univariate models with total service costs as the dependent variable and patient characteristics and measures of clinical severity as explanatory variables. To account for the skewed distribution of cost data, after the Park test suggested that different distributional assumptions and link functions did not provide a benefit over a linear model, regression analysis was performed with 10,000 bootstrap replications.

RESULTS

PARTICIPANT CHARACTERISTICS

Patient-level data are available for 84 young people. There were no significant differences in characteristics between consenters and non-consenters except in the proportion of consenters by level of service specialisation: Those on the S-S pathway were more likely to consent (55%) than those on the S-NS pathway (26%) and on the NS-NS pathway (23%) (see House *et al.* 2012 for details).

The main study found that 53 of them were assessed in specialist ED services and remained in specialist ED services for treatment (specialist – specialist pathway; S-S). Another 16 were assessed in non-specialist CAMHS and referred to specialist services for treatment (non-specialist – specialist pathway; NS-S), while 15 were assessed in non-specialist CAMHS and remained there for treatment or were directly admitted as inpatients (non-specialist – non-specialist pathway; NS-NS).

Table 5-2 shows patient demographics, baseline diagnosis, clinical characteristics and distribution between care pathways for the entire cohort. Categories with at least five participants in the cell were considered in the analysis of cost variations.

Table 5-2: Patient characteristics (full sample)

	Variable	**n (of N)**	**%**
Demographics	Female vs male	81 (84)	96%
	White British vs other	58 (80)	69%
Parental social class	Class I or II	56 (70)	80%
	Class III or IV	10 (70)	14%
	Unemployed or inactive	4 (70)	6%
Parents marital status	Married or cohabiting vs other	64 (84)	76%
Living situation	Living with two parents vs other	64 (84)	76%
Baseline diagnosis and ED behaviours	Anorexia vs EDNOS-AN	36 (84)	43%
	Dietary restriction	30 (84)	36%
	Bingeing	6 (84)	7%
	Vomiting	19 (84)	23%
	Laxative use	6 (83)	7%
	Exercise	40 (83)	49%

	Variable	n (of N)	%
Clinical characteristics (baseline)	Other medical condition	11 (84)	13%
	Any co-morbid psychiatric condition	24 (84)	29%
	Co-morbid depression	17 (84)	20%
	Co-morbid OCD	1 (84)	1%
	Co-morbid anxiety	5 (84)	6%
	Self-harm	6 (84)	7%
	Other psychiatric condition	7 (84)	8%
	Taking psychiatric medication	5 (79)	6%
	Previous outpatient treatment for ED	4 (84)	5%
	Previous inpatient treatment for ED	1 (84)	1%
Care Pathway	Specialist-specialist	53 (84)	59%
	Non-specialist-specialist	16 (84)	18%
	Non-specialist-non-specialist	15 (84)	17%
		Mean (SD)	Range
Age (years), n = 84		15.0 (1.21)	12-17
Duration of illness (months), n = 82		7.7 (7.48)	0-36
Baseline weight/height, n = 83		83.3 (10.29)	63-132
Number of psychiatric co-morbidities, n=84		0.43 (0.80)	0-3

Most participants were female and white British. Given the young age, most were living with parents. The diagnostic split between AN and EDNOS-AN was 44% vs 56%. About a third had a co-morbid psychiatric condition, most commonly depression. Restriction was present in about a third, with bingeing and purging in 10% and 23%, respectively. The average weight for height percentile was 82.8. Average duration of illness was relatively short at just over 8 months, but ranged up to three years. Most participants (59%) were in the S-S pathway, with just under 20% each in the NS-S and NS-NS pathways.

TREATMENT RECEIVED

The number and percentage of participants receiving each type of treatment as well as the mean number of contacts for the full sample and by care pathways are shown in Table 5-3 and Table 5-3, respectively.

Table 5-3: Participants receiving outpatient treatments and number of service contacts, full sample

	Full sample (n = 84)					
Type of treatment	***n***	***(%)***	***Mean contacts (SD)***		***Range***	
Assessment	84	100%	-	-	-	-
Individual OP	68	81%	8.3	8.3	0	35
Family OP	82	98%	13.8	9.7	0	43
Multi-family OP	13	15%	0.8	2.1	0	8
Parent only OP	37	44%	1.5	2.9	0	15
Dietic OP	40	48%	2.0	4.6	0	24
Medical OP	52	62%	4.2	7.0	0	35
Telephone calls	52	62%	2.4	3.4	0	17
Psychiatric review	34	40%	1.7	3.5	0	19
Day patient	2	2%	0.5	3.9	0	34
Inpatient (medical)	15	18%	3.0	10.9	0	75
Inpatient (ED)	17	20%	24.9	59.6	0	280

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Table 5-4: Participants receiving outpatient treatments and number of service contacts, by care pathway

	Specialist - specialist (n = 53)						**Non-specialist - specialist (n = 16)**						**Non-specialist - non-specialist (n = 15)**					
Type of treatment	***n***	***%***	***Mean contacts (SD)***		***Range***		***n***	***%***	***Mean contacts (SD)***		***Range***		***n***	***%***	***Mean contacts (SD)***		***Range***	
Assessment	53	100%					16	100%					15	100%				
Individual OP	45	85%	9.0	8.3	0	35	9	56%	6.4	8.4	0	24	14	93%	8.1	8.5	0	29
Family OP	51	96%	14.6	10.3	0	43	16	100%	12.8	9.6	2	37	15	100%	12.0	7.1	2	25
Multi-family OP	8	15%	0.8	2.0	0	7	2	13%	0.9	2.4	0	8	3	20%	0.9	2.1	0	6
Parent only OP	23	43%	2.0	3.5	0	15	9	56%	0.9	1.2	0	4	5	33%	0.7	1.5	0	6
Dietic OP	26	49%	2.8	5.7	0	24	6	38%	0.6	1.1	0	4	8	53%	0.8	1.1	0	4
Medical OP	32	60%	3.9	6.8	0	35	11	69%	6.3	9.0	0	28	9	60%	3.3	5.2	0	18
Telephone calls	31	58%	2.4	3.7	0	17	11	69%	2.9	3.6	0	13	10	67%	1.7	1.9	0	6
Psychiatric review	22	42%	2.0	4.1	0	19	6	38%	1.2	2.1	0	8	6	40%	0.9	1.8	0	7
Day patient	0	0%	0.0	0.0	0	0	0	0%	0.0	0.0	0	0	2	13%	2.9	9.0	0	34
Inpatient (medical)	5	9%	1.4	6.1	0	32	6	38%	9.6	21.6	0	75	4	27%	1.3	2.6	0	8
Inpatient (ED)	8	15%	13.1	36.7	0	149	3	19%	29.5	74.8	0	280	6	40%	61.5	89.8	0	272

* Medical outpatient appointments include blood tests, bone density scans, pelvic ultrasounds, electrocardiograms and other physical tests.

Across all care pathways, outpatient single family therapy was the most commonly used form of treatment. In the S-S and NS-NS pathways, this was followed by individual outpatient therapy and medical outpatient appointments. In the NS-S pathway, the order of individual therapy and medical appointments was reversed.

About one in three in both pathways with assessment in non-specialist services had a medical inpatient admission. Those on the NS-NS pathway had the highest proportion of inpatient admissions related to their ED. The proportion of people with ED-related inpatient admissions was similar for people treated in specialist services regardless of where they were initially assessed (15% vs 19%). The average number of inpatient days for ED was highest in the NS-NS pathway, and was more than four times as high as in the S-S pathway. The analysis of differences in the likelihood of admission and in length of stay can be found by House (2011), who found that the NS-NS pathway was associated with a significantly higher rate of admission compared to the other pathways.

TREATMENT COSTS

Table 5-5 shows the total costs over a one-year period for each pathway (bottom row). Mean costs were lowest for the S-S pathway, and highest for the NS-NS pathway. However, in each case the SD is larger than the mean suggesting a wide variation in the total cost of treatment for the participants who followed each pathway.

The average costs of individual and family outpatient therapy are roughly similar across all pathways, although the average cost of individual outpatient therapy is slightly lower in the NS-S group and the cost of family outpatient therapy is slightly higher in the S-S pathway. The combined average cost of family treatments (single- and multi-family outpatient therapy, outpatient sessions for parents) is highest in the S-S group. Even though dietary advice is a treatment reported to be commonly provided, the cost of dietic outpatient sessions for this group of young people is actually very low compared to other cost categories. The cost of medical outpatient appointments and inpatient admissions for medical reasons appears to be higher for patients following the NS-S pathway, possibly indicating a higher level of medical complications.

Table 5-5: Costs of outpatient treatment, by care pathway

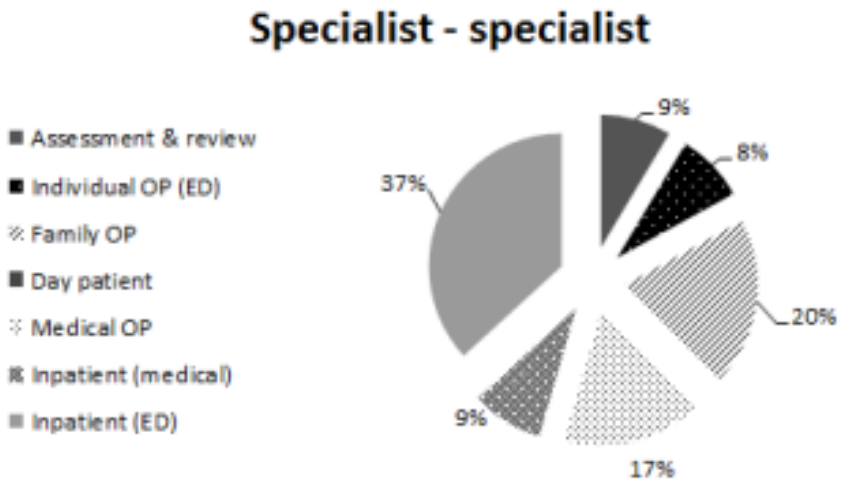
	Specialist – specialist (n = 53)		Non-specialist – specialist (n = 16)		Non-specialist - non-specialist (n = 15)	
Type of treatment	*Mean £(SD)*	*Range*	*Mean £(SD)*	*Range*	*Mean £(SD)*	*Range*
Assessment	170 (36)	112 - 293	151 (43)	98 - 209	152 (40)	98 - 230
Individual outpatient (OP)	1,341 (1,195)	0 - 4,206	955 (1,229)	0 - 3,923	1,933 (1,228)	0-4,414
Family OP	2,976 (2,078)	0 - 8,005	2,998 (2,944)	457-11,786	2,909 (1,135)	965-5,099
Multi-family OP	443 (1,080)	0 – 3,829	479 (1,323)	0 – 4,376	474 (1,149)	0-3,282
Parent only OP	174 317)	0 – 1,509	15 (172)	0 – 591	61 (151)	0-585
Dietic OP	90 (188)	0 – 847	15 (23)	0 – 71	78 (105)	0-382
Medical OP*	2,998 (5,296)	0 - 27,125	4,892 (6,993)	0 - 21,700	2,583 (4,023)	0 – 13,950
Telephone calls	43 (68)	0 – 314	53 (67)	0 – 240	37 (38)	0 - 108
Psychiatric review	1,337 (2,644)	0 - 12,255	784 (1,389)	0 - 5,160	562 (1,166)	0 - 4,515
Day patient	-	-	-	-	1,619 (4,952)	0 – 18,768
Inpatient (medical)	1,529 (6,520)	0 – 34,112	10,260 (22,998)	0 – 79,950	1,421 (2,752)	0 – 8,528
Inpatient (ED)	6,452 (18,073)	0 - 73,308	14,514 (36,791)	0 – 137,760	30,242 (44,199)	0 – 133,824
Total costs	17,544 (28,738)	1,323 - 149,406	35,215 (53,575)	694 -165,656	42,072 (48,277)	3,649 - 168,941

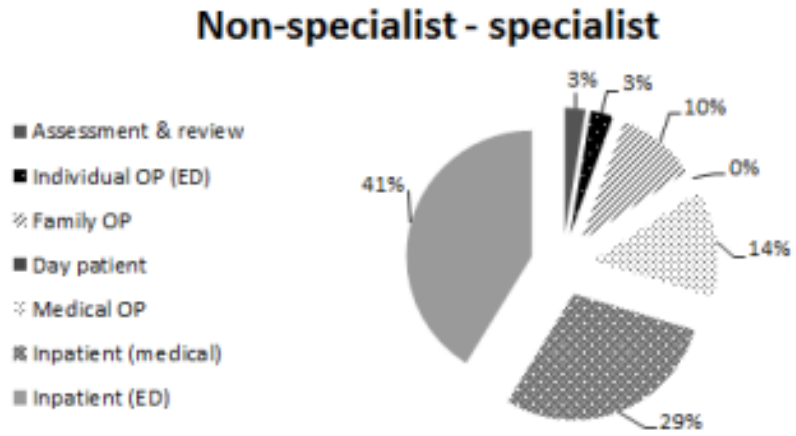
* Medical outpatient appointments

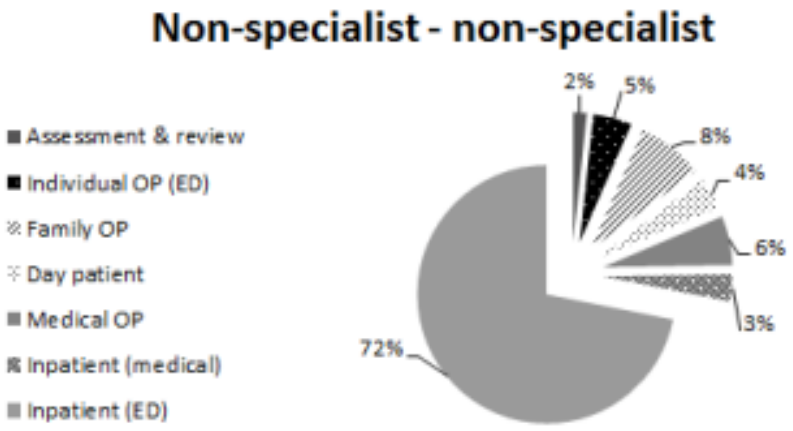
While these data capture outpatient treatment and inpatient treatment, there are no records of contacts with accident and emergency departments available, which may have played a role in, for example, emergency admissions for medical complications. If this was a common occurrence in this cohort, there is a potential for under-estimating total costs. Please note that the aim of the study was not to consider use of lower-tier health services such as primary care.

Figure 5-1 the distribution of service costs by care pathway. The largest contributor to total costs for all care pathways are inpatient admissions for ED, ranging from 37% in the S-S pathway and 41% in the NS-S pathway to 72% in the NS-NS pathway. This is followed by individual outpatient treatments in the NS-NS and NS-S pathways, and family treatments (including individual family therapy, multi-family therapy and sessions for parents only) in the S-S pathway. While inpatient stays due to ED make up a large proportion of costs in the NS-NS pathway, standard deviations are large – indicating considerable variability between individuals. As a result, the difference in inpatient costs between pathways is not statistically significant. Together, ED and medical admissions account for over 70% of total costs in both pathways where the assessment is in a non-specialist service. The lower proportion of costs due to inpatient admissions in the S-S pathway reflects the lower probability of admissions.

Figure 5-1: Contributors to total cost of care, by care pathway







PREDICTORS OF TREATMENT COST

Table 5-6 shows the results of the univariate regression analysis identifying whether any participants' characteristics are associated with higher or lower total costs. Costs were positively associated with age and duration of illness (significant at the 90% level), and negatively associated with having another medical condition and vomiting at baseline. There were significant differences by care pathway as a whole, and in pairwise comparisons between the S-S and the NS-S pathway ($p = 0.088$) and the S-S and the NS-NS pathway ($p = 0.016$). There was no significant cost difference between the NS-S and NS-NS pathway.

Table 5-6: Predictors of treatment costs from univariate models

	Coef. (contribution to total costs)	SD	p
White British	8,933	8,306	0.285
Parents married or cohabiting	6,669	9,263	0.474
Living with parents	10,928	9,213	0.239
Parental occupational class:			
Class 1 or 2	18,456	17,842	0.305
Class 3 or 4	20,184	20,937	0.338
Baseline diagnosis AN vs EDNOS	10,840	7,907	0.174
Other medical condition	- 16,930	11,582	0.148
Any co-morbid psychiatric condition	-5,165	8,742	0.556
Co-morbid depression	-583	9,850	0.953
Co-morbid anxiety	-6,479	16,712	0.699
Co-morbid self-harm	-15,293	15,274	0.320
Co-morbid other psychiatric condition	-9,844	14,278	0.492
Taking psychiatric medication	-15,403	16,187	0.344
Bingeing	-8,090	15,341	0.599
Dietary restriction	3,223	8,252	0.697
Vomiting	-11,726	9,371	0.214
Laxative use	2,013	15,455	0.897
Intense exercise	-2,224	8,125	0.785
Care pathway:			
NS-S	13,638	10,057	0.197
NS-NS	23,148	10,311	0.027
Age (years), n = 81	-6,732	3,213	0.039
Duration of illness (months), n = 79	-864	535	0.111
Baseline weight/height, n = 80	-543	386	0.163
Number of psychiatric co-morbidities	-3,904	4,984	0.436

DISCUSSION

In this study, I analysed the treatments received and associated costs for a cohort of adolescents in four Greater London PCTs. This is the first study to take a comprehensive view on the costs of outpatient care in England. I then looked at variations in costs to determine if costs are associated with measures of clinical need, or with socio-demographic factors.

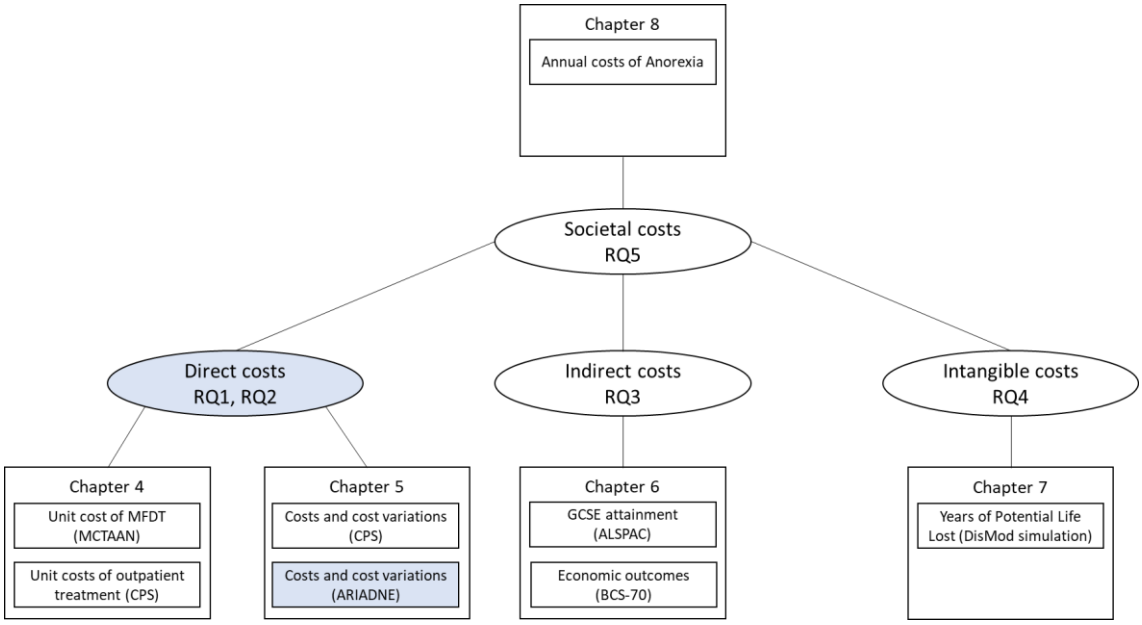
Across all pathways, inpatient admissions are the main drivers of costs. The composition of total costs is slightly different in the S-S pathway, where individual and family treatments combined account for almost 36% of costs and there are a lower proportion of inpatient admissions. The high percentage of costs due to medical inpatient admissions in the NS-S pathway (29%) may point to medical complications arising during treatment, leading to referral to specialist services. However, the data do not allow this hypothesis to be tested. It should be noted that medical admissions were generally short (around seven days), with two cases with exceptionally long admissions (average 63 days), and given the small sample size the data are sensitive to such outliers.

These service use patterns are reflected in the total costs, with the S-S pathway incurring the lowest total costs. While this cost difference is statistically significant, the small sample and limited data availability mean that it would not be appropriate to conclude that this means S-S pathways are the less costly option. Further, it is not possible to adjust for individual and service-level factors such as self-selection into the different pathways. In addition, there were missing data both at the service and individual level, so that these findings should be regarded as indicative rather than definitive.

Several limitations arise from the design of the Care Pathways study (see (House 2011) pp. 81-83): While the study was not an RCT design, these are rare in the study of ED services due to small case numbers and difficulties in maintaining adherence to the allocated treatment (e.g. (Gowers *et al.* 2010)). While 37 out of 44 eligible services provided data, some key services did not participate. These non-participating services were CAMHS services, which increased a bias towards specialist services in the sample. Greater London differs from the UK as a whole in terms of service availability, with a greater number of specialist NHS and private ED services. According to the study authors, this may have resulted in a 'de-skilling' of CAMHS services compared to CAMHS services in other areas of the country.

While this study focussed on one geographical area and transferability to other parts of the country is therefore limited, this study makes an important contribution to knowledge about the costs of ED treatment in outpatient services. No previous study has calculated treatment costs in outpatient services in England using a bottom-up approach, and looked at variation in treatment costs by individual characteristics.

PART 2: INDIVIDUAL-LEVEL COST VARIATIONS: EVIDENCE FROM THREE RCTS



INTRODUCTION

In this section, I extend the analysis from part 1, which covered variations in the costs associated with outpatient and inpatient treatment, to encompass a wider range of services. I explore service use, associated costs and variations in total costs across different agencies and budgets. This is part of my exploration of direct costs of AN and links to RQ1: Why do costs vary.

Using data collected alongside the CASIS (Goddard *et al.* 2013b), MOSAIC (Schmidt *et al.* 2013) and iMANTRA (Schmidt *et al.* 2017) trials I present an analysis of baseline data, collected from patients before receiving the RCT interventions.

First, I describe service use for each of the trials. Then, I calculate the associated costs by cost category, such as primary care, hospital or social services, and total costs for each participant. Finally, I present an exploratory analysis of cost variation for the CASIS and MOSAIC trials. This provides insight into the direct costs of treatment for AN Given the paucity of evidence regarding service use and costs, this analysis of service use data is an important addition to the UK evidence base.

METHODS

DATA SOURCES

Data were available from three RCTs:

- CASIS (Goddard *et al.* 2013b): The populations were patients aged 12 and over with a diagnosis of AN (n=178), randomised at the point of admission to inpatient care.
- MOSAIC (Schmidt *et al.* 2013): This trial recruited female adults aged 18-65 receiving treatment in specialist ED outpatient services.
- iMANTRA (Schmidt *et al.* 2017): Participants in this feasibility study were inpatients aged 16 and above recruited at the point of discharge.

As these were baseline data, data from participants in the intervention and control groups were combined for this analysis.

SAMPLE CHARACTERISTICS AND CLINICAL MEASURES

Socio-demographic variables and baseline clinical measures are available for these samples. Clinical measures included measures of ED symptom severity (EDE and EDE-Q), depression, anxiety and stress (DASS) and quality of life (WHO-QoL) – although not all these measures were collected for all three trials. More detail on each of these measures can be found in Chapter 3.

SERVICE USE AND COSTS

Participants completed the CSRI (Beecham & Knapp 2001) at baseline. The schedule covered a retrospective six-month period and was adapted for each study to include hospital services, specialist mental health services, primary care services and community-based services such as social work and alternative therapy alongside demographic information.

The costs associated with service use for each participant were calculated by identifying an appropriate unit cost and duration for each service contact and multiplying these by the number of contacts each person reported. They are described by reporting means, standard deviations and ranges

For most services, unit costs were drawn from publicly available sources (Curtis 2011; Department of Health 2011). Others were taken from previous studies or estimated using an equivalent method (Beecham 2000; Berridge *et al.* 2002), and from data collected as part of the Care Pathways Study (see Chapter 1, Part 1 for details).

Where service contacts were reported but the number of contacts was missing, the mean for all people in contact with that particular service was entered.

STATISTICAL ANALYSES

Service use and costs

Service use by participants for the 6-month period prior to the baseline assessment are described in terms of the number of people in the sample and the percentage of the sample using a given service. Service costs are presented as means with standard deviations and ranges by service category.

Cost variations

The relationship between costs, patient characteristics and clinical measures was explored using an expenditure function approach (Beecham *et al.* 1991; Knapp 1998). The aim was to identify if any particular characteristics of people with AN was associated with higher or lower costs.

This was an exploratory analysis using total service costs as the dependent variable, with patient characteristics and measures of clinical severity as explanatory variables in a regression-type framework. The Park test (see Chapter 3) was applied, with a resulting value of zero that suggested that different distributional assumptions did not provide a benefit over a linear model. To account for the skewed distribution of cost data, linear regression analysis was performed with 10,000 bootstrap replications. Means, standard errors and p-values are shown, in addition to the adjusted r-squared.

Given the exploratory nature of the analysis, all potentially relevant socio-demographic and clinical variables available at baseline were used. This includes variables that are potentially difficult to interpret when it comes to their relationship to costs over the baseline period, such as a current ED diagnosis. However, the main purpose of this analysis is to generate hypotheses for further investigation.

Table 5-7 shows the predictors used in the analysis of CASIS data, while Table 5-8 shows predictors considered in the analysis of MOSAIC data. Details on the clinical measures (WHO quality of life scales, DASS and EDE-Q) can be found in Chapter 3.

Table 5-7: Predictors in the analysis of CASIS data

Predictor	Coding
Age	Scale variable
Gender male	Binary – no/yes
Ethnicity	Binary – Other vs White British
English is first language	Binary – no/yes
Cohabiting	Binary – no/yes
Has children?	Binary – no/yes
Number of children	Scale variable
Years of education	Scale variable
Has a degree	Binary – no/yes
Economic activity status	Categorical: • Employment • Student • Economically inactive
Diagnosis	Binary – AN vs other
BMI (baseline)	Scale variable
Lowest BMI ever	Scale variable
Age of onset	Scale variable
Duration of illness	Scale variable
WHO quality of life rating	Scale variable
WHO health rating	Scale variable
DASS[1] depression score	Scale variable
DASS anxiety subscale	Scale variable
DASS stress subscale	Scale variable
Total DASS score	Scale variable
EDEQ[2]-Restraint subscale	Scale variable
EDEQ-Eating concern subscale	Scale variable
EDEQ-Shape concern subscale	Scale variable
EDEQ-Weight concern subscale	Scale variable
EDE-Q Global score	Scale variable
Number of hospitalisations	Scale variable

Table 5-8: Predictors in the analysis of MOSAIC data

Predictor	Coding
Age	Scale variable
Ethnicity	Binary - Other vs White British

[1] Measure of depression, anxiety and stress
[2] Measure of ED symptoms

Living with partner	Binary – no/yes
Degree vs no degree	Binary – no/yes
Diagnosis	Binary – AN vs other
BMI (baseline)	Scale variable
Age of onset	Scale variable
Duration of illness	Scale variable
EDEQ-Restraint subscale	Scale variable
EDEQ-Eating concern subscale	Scale variable
EDEQ-Shape concern subscale	Scale variable
EDEQ-Weight concern subscale	Scale variable
EDEQ Global score	Scale variable
Previous hospital admission	Binary – no/yes
Previous treatment for AN	Binary – no/yes
Taking antidepressants	Binary – no/yes

Predictors of costs that were statistically significant were selected and a multivariate model was fitted by stepwise removal of non-significant predictors from a full model.

A 90% confidence interval was used to determine statistical significance when identifying potential candidates for the multi-variate model because in economic analyses, there is less risk associated with type II errors than, for example, in studies of clinical outcomes where a false positive may put patients' health at risk (McCrone *et al.* 2003).

Within the set of potential predictors, there are variables that are closely related: duration of illness and age of onset, for example, are related to age in that age minus duration of illness is age of onset. The highest level of education or qualification achieved will also be related to age, and the EDE-Q global score is by definition correlated with its sub-scales. These cannot be fitted into the same multivariate model, so that in presenting the results, I selected the model with the variables that explained the highest proportion of variance.

RESULTS

PARTICIPANTS

Sample characteristics are shown for CASIS (Table 5-9) and MOSAIC (Table 5-10). Please note that sample characteristics for the iMANTRA trial are omitted because no analysis of costs was performed due to the fact that these would vary based on inpatient costs which is driven by length of stay, and it is unclear how variables collected at discharge would be related to length of stay.

Average age in CASIS was 26, the same as in MOSAIC but – given the wider population recruited – with a wider range. There was a marked difference in the proportion of participants who did not identify as white British (6.6% in CASIS vs 66.7% in MOSAIC). This may in part be driven by a more diverse population being treated in outpatient compared to inpatient settings, but it is partly due to differences in how response data were collected. In the MOASIC data, the ethnicity variable was not a fixed list of responses but a free-text response, and participants sometimes responded with "British" or "English", making it difficult to categorise them on the same basis as the CASIS sample. Here, only those explicitly identifying as white British are included in that category, and results regarding the ethnicity indicator in MOSAIC need to be treated with caution.

Age of onset in MOSAC is older with 17.7 years vs 16.5 years in CASIS. Duration of illness is longer in CASIS with an average of 9.8 years, compared to 8.1 years in MOSAIC. Average baseline BMI is lower in CASIS (14.3), with 16.6 in MOSAIC. This reflects the care pathway for AN, where more severe cases are more likely to be admitted for inpatient treatment.

Overall, the differences between the samples appear to be linked to the different recruitment pathways, as the three trials studied different populations. The CASIS trial recruited patients at the point of admission to inpatient treatment, while MOSAIC studied outpatients and iMANTRA focussed on the period following discharge from hospital.

Table 5-9: Sample characteristics: CASIS

Characteristic	Available n	Mean (SD) or n(%)	Range
Age	156	26.1 (9.04)	13-62
Gender male	157	7 (4.5%)	-
Ethnicity (Other vs White British)	152	10 (6.6%)	-
English is first language	154	148 (96.1%)	-
Cohabiting	154	32 (20.8)	-
Has children?	143	33 (23.1%)	-
Number of children	143	0.4 (0.84)	0.0-4.0
Years of education	146	15.2 (2.96)	7.0-25.0
Degree vs no degree	112	45 (40.2%)	-
Employment **Employed** **Student** **Inactive**	155	 26 (16.8%) 45 (29.0%) 84 (54.2%)	-
Diagnosis AN vs other	157	10 (6.4%)	-
BMI (baseline)	156	14.3 (2.05)	9.0-21.7
Lowest BMI ever	120	12.8 (1.82)	7.5-18.3
Age of onset	135	16.5 (5.55)	5.0-45.0
Duration of illness (months)	135	117.6 (102.69)	9.0-480.0
WHO QoL rating poor/very poor	150	82 (54.7%)	-
WHO health rating poor/very poor	151	83 (55.0%)	-
DASS depression score	152	28.6 (11.45)	0.0-42.0
DASS anxiety score	152	19.7 (9.97)	0.0-42.0
DASS stress score	152	29.0 (9.49)	0.0-42.0
Total DASS	152	77.3 (27.21)	0.0-126.0
EDEQ-Restraint	150	3.8 (1.82)	0.0-6.0
EDEQ-Eating concern	150	3.8 (1.28)	0.0-6.0
EDEQ-Shape concern	150	5.0 (1.13)	0.25-6.0
EDEQ-Weight concern	150	4.5 (1.36)	0.0-6.0
EDE-Q Global score	150	4.3 (1.20)	0.41 – 5.95
Number of hospitalisations	129	1.8 (2.79)	0.0-18.0

Table 5-10: Sample characteristics: MOSAIC

Characteristic	Available n	Mean (SD) / n (%)	Range
Age	141	26.0 (7.48)	18.0-52.0
Ethnicity (Other vs White British)	87	58 (66.7%)	-
Living with partner	136	27 (19.9%)	-
Degree vs no degree	116	56 (48.3%)	-
Diagnosis AN vs other	141	106 (75.2%)	-
BMI (baseline)	133	16.6 (1.25)	11.0-18.7
Age of onset	131	17.7 (6.55)	2.0-44.0
Duration of illness (years)	133	8.1 (7.1)	0.5-37
EDEQ-Restraint	141	3.7 (1.45)	0.0-6.0
EDEQ-Eating concern	141	2.9 (1.40)	0.0-6.0
EDEQ-Shape concern	141	3.5 (1.69)	0.25-6.0
EDEQ-Weight concern	141	3.2 (1.63)	0.0-6.0

Characteristic	Available n	Mean (SD) / n (%)	Range
EDEQ Global score	141	3.3 (1.28)	0.33-5.6
Previous hospital admission	140	30 (21.4%)	-
Previous treatment for AN	139	79 (56.8%)	-
Taking antidepressants	139	55 (39.6%)	-

SERVICE USE

Table 5-11 shows the number and percentage of participants in each trial using each type of service as well as the average number of contacts with the service and the corresponding standard deviations. Participants reported the highest contact rate with GPs for their EDs in CASIS, followed by outpatient services and dentists, while in MOSAIC, the highest percentage of participants was in contact with outpatient services, followed by GPs for EDs and for other reasons. In iMANTRA, where participants were recruited from an inpatient population, the high use of inpatient services was followed – by a wide margin – by GPs for EDs and psychiatrists/psychologists.

SERVICE COSTS

shows the costs associated with service use, summarising the different services presented in Chapter 4 into service categories. Reflecting the pathways of recruitment and the location of the interventions to be evaluated in the RCTs, average costs per person were highest for inpatient treatment in iMANTRA and CASIS, while outpatient treatment costs were the largest contributor to total costs in MOSAIC.

Table 5-11: Service use in the six months preceding baseline assessment, three trials

	CASIS		MOSAIC		iMantra	
Service	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***
Inpatient ED	79 (49%)	35.56 (67.27)	11 (8%)	6.19 (28.34)	41 (100%)	174.59 (15.33)
Inpatient other reason	26 (16%)	2.64 (12.43)	15 (11%)	0.67 (3.41)	1 (2%)	0.34 (2.19)
Outpatient ED	90 (56%)	6.92 (10.37)	126 (89%)	3.75 (8.620)	8 (20%)	-
Outpatient other	23 (14%)	0.72 (2.78)	34 (24%)	0.55 (1.44)	0 (0%)	-
Day hospital	0 (0%)	-	0 (0%)	-	0 (0%)	-
A&E ED	53 (33%)	0.8 (2.26)	27 (19%)	0.34 (.950)	2 (5%)	0.24 (1.41)
Gynaecologist	0 (0%)	-	0 (0%)	-	0 (0%)	-
Psychiatrist	51 (32%)	1.85 (4.74)	32 (23%)	0.96 (2.95)	6 (15%)	2.02 (6.07)
Psychologist	64 (40%)	2.99 (6.0)	27 (19%)	1.42 (4.72)	0 (0%)	-
Family therapist/MFDT	0 (0%)	-	0 (0%)	-	4 (10%)	0.56 (1.96)
Individual therapist/CBT/IAPT	0 (0%)	-	0 (0%)	-	4 (10%)	0.88 (3.87)
Psychotherapist	25 (16%)	2.33 (7.04)	10 (7%)	0.53 (2.71)	0 (0%)	-
CPN	40 (25%)	2.38 (7.930)	17 (12%)	0.85 (3.48)	0 (0%)	-
CAMHS/AMHS	0 (0%)	-	0 (0%)	-	10 (24%)	0.29 (1.33)
Crisis team	0 (0%)	-	0 (0%)	-	0 (0%)	-
Residential rehabilitation	0 (0%)	-	0 (0%)	-	0 (0%)	-
GP ED	137 (86%)	7.44 (7.79)	124 (88%)	4.53 (8.70)	6 (15%)	0.68 (2.14)
GP other	55 (34%)	1.24 (2.44)	96 (68%)	2.03 (2.64)	3 (7%)	0.41 (1.94)
Walk-in clinic	0 (0%)	-	0 (0%)	-	1 (2%)	-
Practice nurse ED	72 (45%)	4.88 (12.36)	32 (23%)	0.81 (2.64)	4 (10%)	0.34 (1.11)

	CASIS		MOSAIC		iMantra	
Service	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***
Practice nurse other	32 (20%)	0.45 (1.35)	38 (27%)	0.61 (2.24)	0 (0%)	-
Dietician/nutritionist	0 (0%)	-	0 (0%)	-	6 (15%)	0.78 (3.77)
Health visitor	0 (0%)	-	0 (0%)	-	1 (2%)	-
Other community nurse	13 (8%)	0.78 (3.58)	6 (4%)	0.18 (1.14)	0 (0%)	-
Dentist	88 (55%)	0.89 (1.17)	67 (48%)	0.82 (1.28)	4 (10%)	0.37 (1.88)
Optician	52 (33%)	0.38 (0.59)	36 (26%)	0.34 (0.69)	4 (10%)	0.15 (0.53)
Counsellor	44 (28%)	2.64 (6.18)	27 (19%)	1.07 (3.07)	0 (0%)	-
Alternative therapist	23 (14%)	0.67 (2.83)	9 (6%)	0.33 (1.64)	0 (0%)	-
Physiotherapist	0 (0%)	-	0 (0%)	-	1 (2%)	0.07 (0.47)
Occupational therapist	0 (0%)	-	0 (0%)	-	0 (0%)	-
Osteopath	0 (0%)	-	0 (0%)	-	0 (0%)	-
Police	0 (0%)	-	0 (0%)	-	0 (0%)	-
Solicitor/lawyer	7 (4%)	0.15 (0.87)	7 (5%)	0.09 (.51)	0 (0%)	-
Self-help/support group	18 (11%)	0.51 (2.24)	9 (6%)	0.42 (2.28)	1 (2%)	0.29 (1.87)
Helplines	7 (4%)	0.38 (2.22)	4 (3%)	0.16 (1.21)	0 (0%)	-
CAB	0 (0%)	-	0 (0%)	-	1 (2%)	0.02 (0.16)
Voluntary organisations/churches	0 (0%)	-	0 (0%)	-	0 (0%)	-
Websites	24 (15%)	1.12 (4.11)	12 (9%)	1.97 (15.63)	0 (0%)	-
Social worker	17 (11%)	0.33 (1.36)	14 (10%)	0.26 (1.36)	0 (0%)	-
Outreach/ family support worker	12 (8%)	0.11 (0.4)	5 (4%)	0.04 (.24)	0 (0%)	-
Family centre	0 (0%)	-	0 (0%)	-	0 (0%)	-
Carer	0 (0%)	-	0 (0%)	-	0 (0%)	-

	CASIS		MOSAIC		iMantra	
Service	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***	***Number using (%)***	***Mean contacts (SD)***
Extra help at school	23 (14%)	0.14 (0.35)	18 (13%)	0.13 (0.33)	0 (0%)	-

* In iMANTRA, these professionals were combined into one question

Table 5-12: Service costs in the six months preceding baseline assessment, three trials

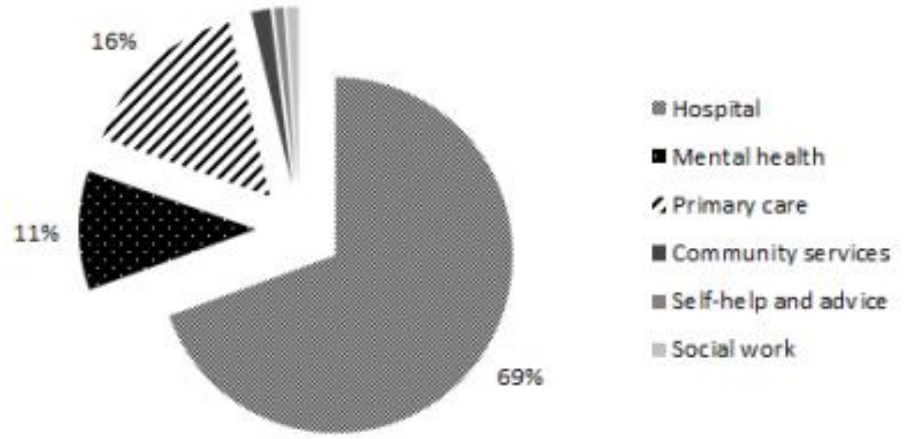
	CASIS			MOSAIC			iMANTRA		
Service category	***Mean £***	***SD £***	***Range £***	***Mean £***	***SD £***	***Range £***	***Mean £***	***SD £***	***Range £***
Hospital	21,045	30,370	0-215,172	4,547	14,403	0-87,794	81,304	12,029	21,672-87,651
Mental health	1,687	2,261	0-11,232	709	1,564	0-11,458	1,062	2,894	0-13,224
Primary care	1,650	1,409	0-7,360	1,046	1,304	85-12,272	229	493	0-2,076
Community services	286	489	0-1,752	115	247	0-1,460	3	16	0-105
Social work	95	397	0-3,780	70	383	0-3,549	49	293	0-1,872
Self-help and advice	32	99	0-673	59	394	0-4,500	0	n/a	n/a
Total costs	24,795	31,121	318-224,025	6,546	15,316	138-96,287	82,647	11,296	25,200-95,124

Note: Hospital includes: Inpatient, outpatient, A & E. Mental health includes: Psychiatrist, psychologist, CPN, psychotherapist, family therapist, MFDT, individual therapist, CBT, CAMHS, AMHS, crisis team, residential rehabilitation. Primary care includes: GP, practice nurse, community nurses, dentist, optician, dietician/nutritionist. Community services includes: Counsellor, alternative therapy, solicitor/lawyer, physiotherapy, occupational therapy, osteopathy, police. Self-help and advice includes: Self-help group, support group, CAB, helplines, websites. Social care includes: Social worker, outreach worker, family support worker, family centre, carer.

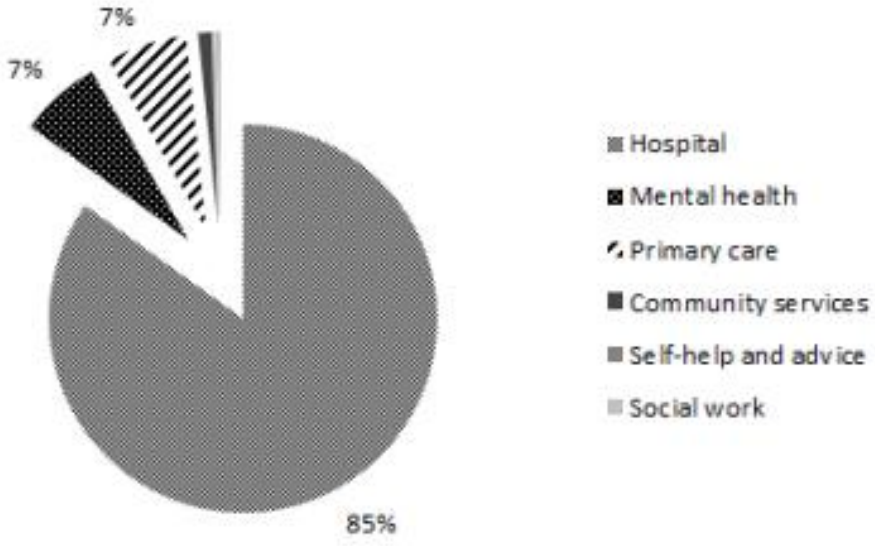
The proportion of total cost absorbed by each cost category for each trial is shown in Figure 5-2.

Figure 5-2: Costs by service category, three trials

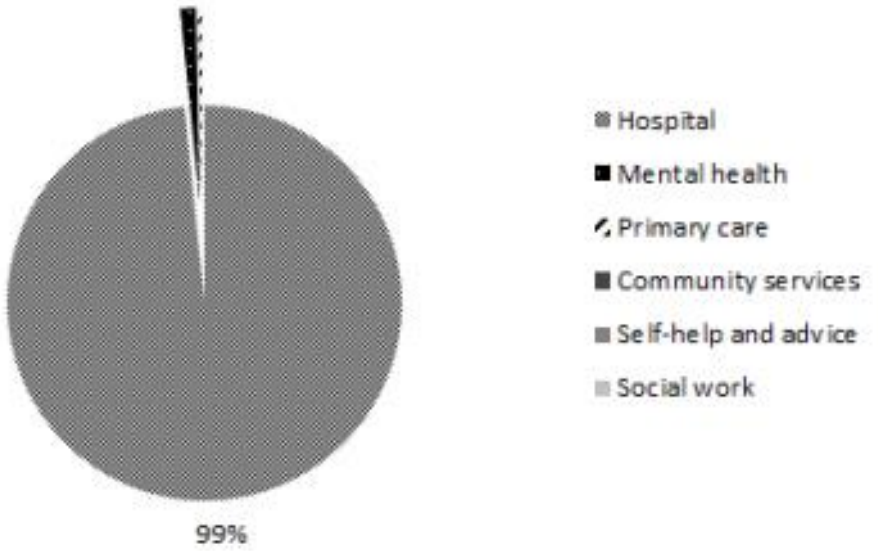
MOSAIC



CASIS



iMANTRA



Total costs over the six months prior to baseline were highest for the iMANTRA group in which all participants had used inpatient care over the previous six months; hospital costs accounted for 99% of total costs. In the CASIS group, who were also recruited from an inpatient population, hospital costs still accounted for 85% of total costs, and only around 6% of this was due to outpatient visits, reported by over 60% the participants. In the MOSAIC group – recruited through outpatient services – only 16% reported a hospital admission for ED or other reasons in the six months prior to the intervention. For all three studies, community, self-help and social work services contributed a very small proportion to total costs even though some of these services were used by over 10% of the study samples.

PREDICTORS OF SERVICE COSTS

I explored predictors of service costs in the MOSAIC and CASIS groups. Table 5-13 and Table 5-14 show the results of univariate regression models, relating participant characteristics to total costs, as well as a 'full' model with all predictors significant at the 90% level, and a 'fitted' model which maximises the proportion of variance in total costs explained (adjusted r-squared).Note that even though the number of previous

hospitalisations was statistically significant in the univariate models, this predictor has been omitted in the following models to avoid issues of endogeneity.

For the univariate models using CASIS data, there were significant positive associations with total costs for having English as a first language (coefficient 21,426), WHO health rating (coefficient 12,206), DASS stress score (coefficient 614), total DASS score (coefficient 179) and the number of previous hospitalisations (coefficient 3,723). There were significant negative associations between total costs and having children (coefficient-11,184), the number of children (coefficient -4,783), having a degree (coefficient -4,790), having a diagnosis of AN vs another diagnosis (coefficient -17,193), lowest BMI ever (-4,640) and age of onset (-635).

This points to patients not from a background of recent migration, higher stress and possibly a more protracted or severe course of illness as indicated by a higher number of hospitalisations, lowest ever BMI and earlier age of onset, and those with EDNOS incurring higher costs.

Those with children, a higher level of education, a later age of onset and a potentially less severe course of illness (as measured by the lowest BMI ever) incurred lower costs, pointing perhaps to less engagement with services for those with later or adult onset AN.

The largest coefficients are found for English as a first language, WHO health rating and a diagnosis of EDNOS, but some scale variables (previous hospitalisations, number of children, and lowest BMI also carry high coefficients that indicate the need for further investigation. Perhaps surprising is that a better WHO health rating is also associated with higher costs, and the relationship between WHO health rating and previous treatment and current severity of illness should be explored, especially since this is one of the largest coefficients.

Table 5-13: Predictors of service costs (CASIS)

	Univariate models			Full model			Fitted model		
Predictor	**Coef.**	**se**	**p**	**Coef.**	**se**	**p**	**Coef.**	**se**	**p**
Age	-118	235	0.615						
Gender male	7,615	9,121	0.404						
Ethnicity (Other vs White British)	3,054	15,637	0.845						
English is first language	21,426	28,11	<0.001	26,723	10,390	0.010	27,175	7,039	<0.001
Cohabiting	1,998	5,033	0.691						
Has children?	-11,184	5,060	0.027						
Number of children	-4,783	1,879	0.011						
Years of education	704	996	0.480						
Degree vs no degree	-4,790	2,696	0.076	8,790	7,997	0.272			
Employment									
• **Student**	-6,288	6,376	0.324						
• **Economically inactive**	-2,397	6,343	0.706						
Diagnosis AN vs other	-17,193	3,836	<0.001	-20,352	11,125	0.067			
BMI (baseline)	-1,010	951	0.288						
Lowest BMI ever	-4,640	1,567	0.003	-7,155	1,989	>0.001	-7,997	2,031	<0.001
Age of onset	-635	681	0.096	-684	452	0.130			
Duration of illness	-27	18	0.138						
WHO quality of life rating	7,929	5,025	0.115						
WHO health rating	13,206	4,812	0.006	18,090	6,933	0.009	18,267	6,726	0.007
DASS depression score	355	264	0.178						
DASS anxiety score	287	193	0.137						
DASS stress score	614	171	<0.001	920	1,026	0.369	603	267	0.024
Total DASS score	179	73	0.015						
EDEQ-Restraint	17	1,203	0.989						
EDEQ-Eating concern	1,835	2,057	0.372						

	Univariate models			Full model			Fitted model		
Predictor	**Coef.**	**se**	**p**	**Coef.**	**se**	**p**	**Coef.**	**se**	**p**
EDEQ-Shape concern	714	2,346	0.761						
EDEQ-Weight concern	1,665	1,713	0.331						
EDE-Q Global score	1,239	1,861	0.505						
Number of hospitalisations	3,723	1,246	0.003						
Adjusted R^2									**0.197**

Table 5-14: Predictors of service costs (MOSAIC)-

	Univariate models			Full model			Fitted model		
Predictor	***Coef.***	***se***	***p***	***Coef.***	***se***	***p***	***Coef.***	***se***	***p***
Age	-243	137	0.075	-83	130	0.524			
Ethnicity (Other vs White British)	3,142	3,586	0.381						
Living with partner	-3,371	1,693	0.047	18	1,671	0.991			
Degree vs no degree	-4,790	2,696	0.076	-2,425	1,665	0.145			
Diagnosis AN vs other	-5,563	1,781	0.002	2,331	1,173	0.047	4,031	1,318	0.002
BMI (baseline)	-850	614	0.166						
Age of onset	-317	147	0.031	-100	127	0.433			
Duration of illness	-23	99	0.815						
EDEQ-Restraint	-1,448	1,306	0.271						
EDEQ-Eating concern	617	847	0.466						
EDEQ-Shape concern	-401	1,005	0.690						
EDEQ-Weight concern	-965	881	0.273						
EDEQ Global score	-850	1,305	0.521						
Previous hospital admission	16,254	5,137	0.002						
Previous treatment for AN	5,120	2,018	0.011						
Taking antidepressants	5,433	2,543	0.033	5,286	2,601	0.042	4,847	1,875	0.010
Adjusted R^2									**0.041**

In the final fitted model, the only predictors retained are English as a first language (coefficient 27,175), lowest BMI ever (coefficient -7,997), WHO health rating (coefficient 18,267) and DASS stress score (coefficient 603). While the coefficient on the DASS stress score is approximately the same as in the univariate model, the size of the other coefficients has increased as is perhaps expected, with the coefficient for lowest BMI ever increasing from -4,640 to -7,997. It should be noted that the fitted model explains less than 20% of variation (adjusted R^2=0.197), leaving much of the variation in cost unexplained.

In the models for MOSAIC, there is a significant positive association between total costs and taking antidepressants (coefficient 5,433), and there are significant negative associations with age (coefficient -243), living with a partner (coefficient -3,371), having a degree (coefficient -4,790), a diagnosis of AN vs another diagnosis (coefficient -5,563) and age of onset (coefficient -317).

These are similar trends to what we see in CASIS, with psychiatric co-morbidity (depression) and a potentially longer duration of illness (age of onset) associated with higher costs. Negative associations with age, living with a partner and having a degree are potentially related, as the latter two are more likely to be true for older people.

The final fitted model only retains the variable for diagnosis (coefficient 4,031) and taking antidepressants (coefficient 4,847). Note that the former switches sign in the multivariable models, pointing to missing explanatory variables missing from these models. This is further supported by the adjusted R^2 of 0.041, i.e. explained variation of only 4.1%.

Further analysis should explore whether there are separate effects for level of education and having a family (children or partner), and which aspects of severity of illness and illness duration are likely to contribute to higher costs.

DISCUSSION

This section contributes to the evidence base by a) describing the service use by patients with ED before commencing an evidence-based treatment and associated costs and b) analysing why these costs vary between individuals. Aside from the TOUCAN study (Byford *et al.* 2007a), to my knowledge these are the largest datasets of wider service use associated with AN in England that have been analysed to date.

The data presented were taken from three studies each with a different recruitment pathway. This was reflected in both the service use data and the costs, as, for example, all participants in iMANTRA (who were recruited from inpatient units) predictably reported inpatient stays. The MOSAIC group, recruited through outpatient services, was the most diverse in terms of the range of service use, and also reported the lowest average costs.

While the literature on cost variations is only starting to emerge, some trends can be observed:

- Health care costs associated with ED are higher than for those without ED (Samnaliev *et al.* 2015).
- Hospital costs associated with AN are higher than for other ED (Haas *et al.* 2012a).
- The presence of bingeing/purging behaviours is associated with higher outpatient costs (Stuhldreher *et al.* 2015).
- Longer duration of illness is associated with higher outpatient costs (Stuhldreher *et al.* 2015).
- Lower BMI at admission is associated with higher costs in AN and vice versa (Haas *et al.* 2012b, 2012a; Toulany *et al.* 2015).
- Higher BMI following hospitalization is associated with higher retrospective costs, i.e. a longer inpatient stay is associated with a higher BMI (Stuhldreher *et al.* 2015).
- Co-morbid mental health problems and conditions are associated with higher costs in inpatients (Haas *et al.* 2012b, 2012a) and outpatients (Stuhldreher *et al.* 2015), although some studies do not find this effect.

Factors associated with poor outcomes in the AN literature (Steinhausen 2002; Treasure & Russell 2011) , such as low BMI, a diagnosis of AN vs EDNOS and longer duration of illness, were also associated with higher treatment costs in this study, in line with previous literature summarized above. These findings suggest that patients with the highest needs in these domains are receiving the most intensive service response when presenting to secondary or tertiary care.

There were some differences between the studies. Higher age was associated with slightly lower treatment costs in MOSAIC. Previous treatment for AN (number of previous hospital admissions in CASIS and a binary indicator of previous hospital admissions in MOSAIC) were associated with higher treatment costs – the latter being in line with other literature (Stuhldreher *et al.* 2015). Interpretation is difficult, as it is unclear whether this simply reflects treatment costs immediately prior to the study, or a prolonged engagement with services due to severity or chronicity of AN, and these predictors have therefore been omitted from the multivariate models.

English as a first language was also associated with higher treatment costs in CASIS, which may point to differences in treatment uptake among minority population groups (House 2011) – but in the univariate models, this is not reflected in a significant cost impact of the variable.

The findings in this study broadly reflect the existing literature but identifies additional potentially relevant predictors of costs: age and English as a first language. Notably, mental health co-morbidity - a significant predictor of costs in several previous studies – was not significant in the multi-variate model.

CHAPTER SUMMARY

Little is known about the treatment received in outpatient services, the associated costs and whether those costs vary by clinical need or by other characteristics. There is a particular gap in the knowledge of costs of treatment for AN provided by outpatient services, especially in community-based services. In this chapter, I explored treatments received by a cohort entering outpatient treatment in four Greater London PCTs (CPS) and participants in two large RCTs (CASIS, MOSAIC). I then analysed the associated costs and explored variations based on individual level characteristics, and additionally based on level of service specialisation for the former.

Key findings with regard to treatment in the CPS received can be summarised as follows:

- Single-family therapy was the most commonly received treatment, followed by individual outpatient and medical outpatient treatment.
- Other forms of treatment, such as day patient or parent-only sessions were much less common.
- The S-S and N-S pathways had similar rates of inpatient admissions.
- The NS-NS pathway had the highest rate of admissions and the highest average length of stay.
- Prior to inpatient admission GP consultations and outpatient services for ED and dentist were the most reported services (CASIS).
- Prior to commencing outpatient treatment, the most commonly seen services were outpatient services and GPs for ED and other reasons (MOSAIC).

The following key findings relate to service-level variations in costs:

- Patients on the S-S pathway had the lowest average cost, while those on the NS-NS pathway had the highest, but this difference was not statistically significant
- Costs associated with inpatient treatment for ED were the largest contributor to total costs for all pathways, with 37% in the S-S pathway, 41% in the NS-S pathway and 72% in the NS-NS pathway.
- In both NS-S and NS-NS pathways, total inpatient costs accounted for over 70% of total costs, compared to 46% in the S-S pathway.

At the individual level, costs were positively associated with:

- Age and duration of illness in the CPS;
- English as a first language, WHO health rating and DASS stress scale in CASIS;
- Previous hospital admission in MOSAIC.

Costs were negatively associated with:

- Vomiting and co-morbid medical condition in the CPS;
- The S-S pathway compared to the NS-NS pathway in the CPS;
- Lowest BMI in CASIS;
- Age and a diagnosis of AN vs other diagnosis in MOSAIC.

The largest contributors to costs in the RCT groups were

- Inpatient admissions in CASIS, with 50% reporting an admission;
- Outpatient services in MOSAIC, with inpatient costs accounting for only 8%.

In conclusion, costs appeared to be driven by care pathway and the associated risk of admission, although the direction of causality is unclear and cannot be tested with the available data. In the RCTs, the recruitment pathway is reflected in reported service use. Cost variations are related to some indicators of severity (e.g. low BMI, duration of illness, vomiting) and some demographic characteristics (age, English as a first language).

CHAPTER 6

Indirect costs: Evidence on the productivity-related impacts of Anorexia nervosa from two British cohorts

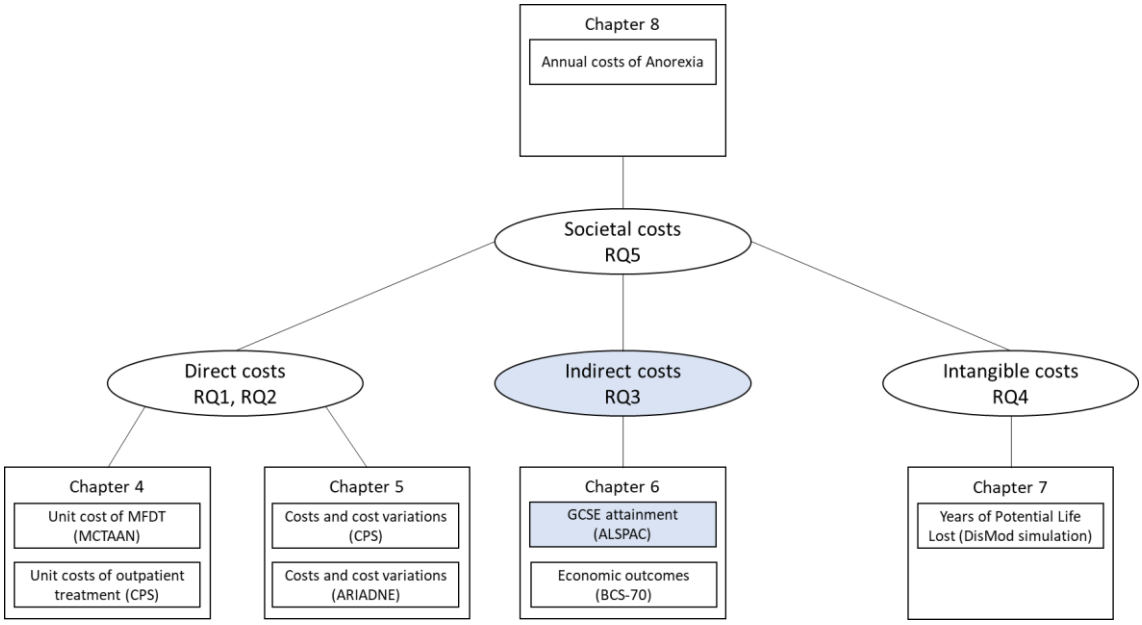
CHAPTER INTRODUCTION

The previous two chapters focussed on the direct costs of AN. In this chapter, I focus on some of the indirect costs associated with AN to answer RQ3: "What is the impact of AN on education, employment, income and related outcomes?"

Productivity losses – productivity not realised as a result of an illness – are an important aspect of these indirect costs, and often make up a large percentage of the overall cost of illness. The theoretical framework for the two studies presented here is the human capital approach, where productivity is seen as a dividend from a "stock" of capital that can be built and maintained by productivity-enhancing activities. One such activity (or indicator of activity) is education attainment. Productivity itself is measured in terms of output and the market valuation of this output. Wages and income can be used as a proxy measure of productivity, although it is an imperfect one.

This chapter first explores the impact of AN on human capital accumulation, measured by education attainment at GCSE-level using data from the ALSPAC, and secondly the impact of AN on productivity and related outcomes as measured by employment status, income, disability and benefit receipt in adulthood using BCS-70 data.

PART 1 – THE EFFECT OF ANOREXIA NERVOSA ON GCSE ATTAINMENT. EVIDENCE FROM THE ALSPAC COHORT.



INTRODUCTION

AN is associated with long and frequent periods of hospitalisation. While there is commonly some on-site education, such long hospitalisations can mean that young people spend long stretches of time out of education (Byford *et al.* 2007a). Byford and colleagues (Byford *et al.* 2007a) found that in addition to hospital stays, the young people in their study spent long stretches of time out of education. It seems that in the face of severe illness, education often comes second, although it is a concern to parents (Tierney 2005) and seen as an important determinant of quality of life (de la Rie *et al.* 2007). For those who remain within mainstream school, special provisions may have to be made to accommodate sickness absences.

School absences are likely to characterise the education pathway of young people with AN. Usually, however, absences are a policy concern because they are linked to truancy and associated behavioural difficulties and crime (National Audit Office 2005).

At the same time, some features of AN may mitigate any detrimental impact on attainment. People with the disorder are thought to have a higher than average IQ (Lopez *et al.* 2010) and better working memory (Kothari *et al.* 2012), and may have higher achievement than those with a comparable IQ (Dura & Bornstein 1989). Higher levels of perfectionism are also associated with AN (Lloyd *et al.* 2014), although it is not clear whether this would necessarily lead to improved school performance.

There is some evidence that the illness does not affect educational outcomes in the longer term: there was no statistically significant difference between young women with AN and their healthy co-twins five years after recovery from AN (Keski-Rahkonen *et al.* 2007), and a greater proportion of patients admitted to hospital with AN had completed post-secondary education compared to controls (Hjern *et al.* 2006). In contrast, Patton and colleagues (Patton *et al.* 2008) found young people with EDNOS-AN more likely to be not in education or employment than cohort members without ED. However, I am not aware of any study looking at educational outcomes controlling for other characteristics, such as parental socio-economic status.

Persistent purging behaviours are associated with lower education attainment (Allen *et al.* 2013), and patients falling into the purging subtype of AN may experience lower quality

of life than the restricting type (Mond *et al.* 2005) – although this has more recently been challenged as the result of a review of the literature (Baiano *et al.* 2014). In this chapter, I explore whether sickness absence and purging behaviour have a detrimental effect on education outcomes for young people with AN.

I use ALSPAC data to test the following hypotheses:

- Young people with anorexia nervosa will not differ from non-disordered controls in terms of GCSE attainment, controlling for confounding factors such as socio-economic status and parental level of education.
- Young people with anorexia nervosa with bingeing/purging have lower GCSE attainment than non-disordered controls.
- Level of school absences due to sickness will not affect GCSE attainment of young people with AN more than those without disordered eating patterns.
- Absences will negatively affect GCSE outcomes in those with bingeing/purging behaviours, but not those where these behaviours are absent.

While a recent Swedish study found that school achievement was positively related to the risk of AN in both females and males (Sundquist *et al.* 2016), I am not aware of a study of education outcomes in AN for England.

METHODS

DATA AVAILABILITY AND ACCESS

This is a longitudinal prospective study with comparison groups and inclusion of potential confounders. It uses data from the ALSPAC (Golding *et al.* 2001), a longitudinal birth cohort study, which enrolled all pregnant women living within Avon, England, due to give birth between the 1st April 1991 and 31st December 1992. It is estimated that approximately 85-90% of those eligible for inclusion chose to participate and the sample has been shown to be representative of the UK population, although deprived households are under-represented in the sample (Bristol University 2014). The core ALSPAC sample consists of 14,541 pregnancies, and data were obtained on 14,272 with a known birth outcome via postal questionnaires. 13,988 children survived the first year, and at age 7, another 713 children were enrolled.

Data access was facilitated by Dr Nadia Micali, University College London, through the NIHR-funded project 'Adolescent eating disorders and related behaviours: longitudinal course and risk factors'[17]. Questions about eating behaviours that will enable the researchers to obtain DSM-IV diagnoses have been included in the sweeps at ages 16 and 18. The focus is on risk factors contributing to adolescent EDs, and particularly the transgenerational effect of maternal EDs.

For the present study, eligibility criteria were aligned with Dr Micali's study. Participants were considered eligible if they had not withdrawn consent and could be contacted for data collection at ages 14 and 16. Where there was more than one participant from the same family (i.e. in case of a multiple birth), one twin was randomly removed to preserve independence. At age 14, 6,140 out of 10,581 eligible participants returned questionnaires on ED behaviours, with 5,069 out of 9,702 at age 16.

In addition, availability of GCSE outcome data determined whether participants were included in this analysis. GCSE data were available through linked data so that they were not reliant on survey responses. Given the high amount of missing data in the ED variables and the hypothesised causal relationship between ED and GCSE performance,

[17] http://www.iop.kcl.ac.uk/sites/edu/?id=191

the outcome variable was used in the multiple imputation model to utilise the information in the outcome variable (GCSE) about the predictor variable, AN status (Sterne *et al.* 2009).

PREDICTORS

Data on eating behaviours were available at ages 14 and 16. At age 14, there was evidence of AN for n=102 females, while at age 16, there was evidence for n=69. For a small number (n=13), there was evidence of AN at both time points.

For this analysis, a combined indicator was calculated that reflected whether the study participant had a diagnosis of anorexia nervosa, derived by the researchers based on DSM-IV criteria (Micali *et al.* 2017a) at either age 14 or age 16. Data on self- and parent reported bingeing and purging behaviours were collected at the same time. Additionally, school absences due to illness over the last two weeks were available at age 16. Data were re-coded to suit the analysis (see Table 6-1). Those with a diagnosis of AN at either age 14 or age 16 are of primary interest to this study, while those with no ED formed the comparison group.

Table 6-1: Coding of eating behaviours and ED diagnosis at age 14 and age 16

Characteristic	**Coding**
Bingeing or purging at age 14 or age 16	Binary – no/yes
ED diagnosis at age 14 or age 16	Categorical • No ED • Anorexia • Other ED
Days absence due to illness last two weeks	Scale

OUTCOMES

The main outcome measure was educational attainment at Key Stage 4, measured as a) the total point score and b) whether 5 or more 'good' GCSEs (grades A*-C) were achieved. The latter is a commonly used indicator of good educational attainment and the total point score is useful for comparison with other studies.

CONFOUNDERS AND CO-VARIATES

The literature on education research is vast and there are many potential predictors of educational attainment. An analysis of attainment in the Chicago Longitudinal Study (Ou & Reynolds 2008) found the strongest predictors to be maternal educational attainment, school absences and mobility, grade retention and the young person's educational expectations. Student characteristics such as gender (Arnot *et al.* 1998; Gray *et al.* 2004), ethnicity (Demack *et al.* 2000), (parental) socio-economic status or occupational class (Connolly 2006; Demack *et al.* 2000; Power & Manor 1992), mental health problems including depression and psychological distress (Fergusson & Woodward 2002; Rothon *et al.* 2010; Shahar *et al.* 2006; Wilson & Marcotte 1996), learning disabilities, for example ADHD (Wilson & Marcotte 1996) as well as ability or intelligence (Furnham *et al.* 2009) are possible predictors of educational achievement. At the school level, characteristics such as school sector (Smith & Naylor 2005), school size (Newman *et al.* 2006), school resources (Steele *et al.* 2007) and the proportion of poor students (Noden & West 2009) may be associated (positively or negatively) with achievement. There is also evidence that school-level characteristics, such as the proportion of parents in higher occupational classes, influence the chance of developing eating disorders, independent of individual-level characteristics (Bould *et al.* 2016).

Three sets of confounders and co-variates were identified, following an analysis presented by Vignoles and colleagues (2010), and a review and analysis of risk factors by Nicholls and Viner (2009). The first includes ALSPAC core variables that provide demographic information on parents and child, household characteristics and key information related to pregnancy and birth outcome (see Table 6-2).

Table 6-2: Set 1 - ALSPAC core variables

Characteristic	**Coding**
Mother's age at delivery	Scale variable
Preterm birth or low birth weight, defined as born at gestational age <37 weeks or born at gestational age >= 37 weeks with a birth weight <2,500 grams.	Binary – no/yes
Parity	Binary – single vs multiple birth
Gender of child	Binary – female/male
Child ethnicity	Binary – white/other
Smoking in pregnancy	Binary – ever smoked no/yes
Housing tenure	Categorical:

Characteristic	Coding
	• Owner-occupied • Social housing • Private rented • Other
Marital status	Categorical: • Never married • Married (regardless of number of marriage) • No longer married (regardless of reason)
Occupational class	Categorical: Lowest occupational class, combining data on mother and father. • I • II • III non-manual • IV manual • V
Maternal education	Categorical: Mother's highest educational qualification • CSE • Vocational • O-level • A-level • Degree

The second set of predictor variables includes additional child and family characteristics (see Table 6-3).

Table 6-3: Set 2 - Child and family characteristics

Characteristic	Coding
Number of children in household	Scale
Pupil eligibility for FSM (KS4)	Binary – no/yes
IDACI deprivation indicator	Scale (range 0-1)
YP expectation of obtaining 5+ good GCSEs	Categorical • Very likely • Fairly likely • Not very likely • Not at all likely
Emotional and behavioural difficulties	Binary – ever, no/yes
School Action or School Action Plus (KS4)	Binary – no/yes
School absences due to sickness last 2 weeks	Scale – range 0-14

The final set of variables includes school-level characteristics (see Table 6-4).

Table 6-4: Set 3 - School-level characteristics

Characteristic	Coding
School reputation (parent report)	Categorical • Very good • Good • Poor • Very poor • Don't know (recoded to missing)
Sex of school	Binary • Mixed • Single sex
School identifier	Nominal variable, used for clustering

Additional characteristics, such as institution type, were considered for analysis, but there was a perfect correlation with independent schools and single-sex schools. Given that the literature suggests that the proportion of females in a school is positively related to the risk of developing eating disorders (Bould *et al.* 2016), preference was given to the sex of school indicator, which was re-coded from a categorical variable (mixed, male only, female only) to a binary variable (mixed vs single sex).

MISSING DATA

Missing data were analysed and multiple imputation was performed using chained equations with the - mi impute - command (Royston & White 2011) in Stata 14 (StataCorp 2015). M=40 sets were imputed.

Scale variables were imputed using the predictive mean matching procedure (-pmm-), considering the three next neighbours. Truncated regression (-truncreg-) was used for scale variables with a limited range, such as the IDACI, which has a range of zero to one. Logistic regression (logit) was used for binary variables, ordered logit (-ologit-) for ordinal variables, and multinomial regression (-mlogit-) for nominal variables. The augment option was used selectively where perfect prediction was encountered.

ANALYSIS MODELS

Analysis models were developed by first identifying sets of variables representing characteristics with a theoretical backing for their impact on education outcomes and anorexia nervosa. The model can be described as

$$A_i = f(E_i, X_i, I_i, S_i, U_i)$$

Where A_i is individual GCSE attainment, as a function of

- E_i , representing the individual's eating behaviours and diagnosis;
- X_i, a set of demographic and socio-economic characteristics from the ALSPAC core variable set;
- I_i, a set of child and parent characteristics shown to be linked to both eating behaviours and attainment;
- S_i, a set of school characteristics;
- U_i, an error term.

Starting with a simple linear model

$$\text{Model 1: } A_i = \alpha + \beta E_i + U_i \text{ ,}$$

the analysis is extended by adding additional sets of variables:

$$Model\ 2\text{: } A_i = \alpha + E_i + X_i + U_i \text{ ,}$$

$$Model\ 3\text{: } A_i = \alpha + \beta E_i + X_i + I_i + U_i \text{ ,}$$

$$Model\ 4\text{: } A_i = \alpha + \beta E_i + X_i + I_i + S_i + U_i.$$

Similarly, for the binary outcome denoting whether a young person achieved 5 good GCSEs, and where V_i represents the three sets of variables, the logit regression equivalent is as follows:

$$p(A_i = 1|V_i) = \frac{e^{(\beta_0+\beta_1 E_i+\beta_1 X_i+\beta_2 I_i+\beta_3 S_i)}}{e^{(\beta_0+\beta_1 E_i+\beta_1 X_i+\beta_2 I_i+\beta_3 S_i)} + 1}$$

With $p(Y = 1|X)$ interpreted as the probability of a positive outcome conditional on X, written as the odds ratio

$$\ln\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 E_i + \beta_1 X_i + \beta_2 I_i + \beta_3 S_i$$

Analyses for Model 4 were run with the -vce(cluster)- option, with KS4 school ID as the clustering variable.

Model fit is assessed by comparing the four resulting models for each of the two outcome variables on the adjusted R^2 for linear regression models using the user-written -mibeta- command in STATA 14. The selected model was used in the following logit regression to ensure comparability. Residual plots (-qqnorm-) were inspected to confirm assumptions about normality of residuals for 10 imputed datasets.

Following selection of the most efficient model to address hypothesis 1, hypotheses 2-4 are tested by extending this model to include interactions between the AN indicator variable and bingeing/purging behaviours, absences, or both, as appropriate to answering the respective research question.

SUB-GROUP ANALYSES

To ensure consistency with other estimates in the literature and throughout this thesis, analyses were repeated for females only. In addition, I tested whether the imputation of the predictor variable (ED diagnosis) changed the results (Sterne *et al.* 2009) – as presence of an ED could conceivably be related to missingness – and ran the analysis for females including only those cases that provided data on the ED behaviour questions (n=1,024).

RESULTS

SAMPLE

Overall, data on KS4 attainment (whether has attained 5 good GCSEs; GCSE total point score) is available for n=11,997. No data were available for 3,087. After removal of participants without data on GCSE total score, whether they had achieved 5 'good' GCSEs and missing information on sex, 9,511 cases remained, and 9,492 had information on KS4 school ID which was used for clustering. These 9,511 cases form the sample for analysis without the clustering variable, and n=9,492 form the sample for analyses with clustering. There are n=4,751 and n= 4,745 in the samples for the analysis relating to females only.

DESCRIPTIVES

In the unimputed data set, data on absences in the last two weeks due to sickness were available for n=2,831. Information on ED diagnosis was available for 2,452, with n=195 in the group with AN. Data on bingeing and purging behaviours were available for 2,273, with 114 experiencing these at either age 14 or age 16.

Sample information for the group without an ED and the group with AN is shown in Table 6-5.

There are differences in several sample characteristics. Those with AN are more likely to be female, and less likely to be a member of an ethnic minority. Findings regarding socio-economic status are difficult to interpret. While those with AN are less likely to live in social housing (defined as either rented from a council or a housing association) and more likely to have parents whose lowest combined occupational class is I, they appear to be under-represented in occupational classes II and III-non-manual, and over-represented in class III-manual. Eligibility for free school meals is low across the sample, and 25% lower in the group with AN than in the group without ED.

Table 6-5: Sample characteristics and data availability

	No ED		With AN	
	%	*available n*	*%*	*available n*
Parity - Multi	51.61%	1,953	54.44%	180
Sex of child - female	44.31%	1,995	76.92%	182
Child ethnicity - not white	4.24%	1,933	3.37%	178
Mother ever smoked - yes	61.11%	1,978	59.22%	179
Housing tenure		2,008		184
• **Owner-occupied**	84.96%		84.24%	
• **Social housing**	7.87%		5.43%	
• **Private rented**	4.73%		5.98%	
• **Other**	2.44%		4.35%	
Maternal marital status		2,028		184
• **Never married**	12.82%		14.13%	
• **Married**	82.64%		80.43%	
• **No longer married**	4.54%		5.43%	
Occupational class		1,877		175
• **I**	2.88%		3.43%	
• **II**	12.31%		8.57%	
• **III nm**	29.94%		25.71%	
• **III m**	27.38%		29.71%	

	No ED		With AN	
	%	*available n*	*%*	*available n*
• **IV**	28.72%		28.00%	
• **V**	4.10%		4.57%	
Maternal education		1,959		181
• **CSE**	11.84%		10.50%	
• **Vocational**	7.45%		9.39%	
• **O-level**	33.84%		33.70%	
• **A-level**	28.13%		30.94%	
• **Degree**	18.73%		15.47%	
Pupil eligibility for FSM (KS4) - yes	3.51%	2,106	2.67%	187
YP expectation of obtaining 5+ good GCSEs		1,686		146
• **Very likely**	62.93%		60.96%	
• **Fairly likely**	31.14%		32.88%	
• **Not very likely**	4.39%		4.79%	
• **Not at all likely**	1.54%		1.37%	
Emotional and behavioural difficulties – yes	4.32%	1,320	0.87%	115
School Action or School Action Plus (KS4) – yes	9.65%	2,052	8.65%	185
School reputation (parent report)		1,747		156
• **Very good**	39.15%		30.13%	

	No ED		With AN	
	%	*available n*	*%*	*available n*
• **Good**	57.18%		67.31%	
• **Poor**	3.32%		1.92%	
• **Very poor**	0.34%		0.64%	
Sex of school		2,171		191
Mixed	94.80%		93.72%	
Male only	1.70%		0.52%	
Female only	3.50%		5.76%	
	Mean (SD)	***available n***	***Mean (SD)***	***available n***
Mother's age at delivery	29.35 (4.45)	1,995	29.52 (4.90)	182
Gestation period	39.48 (1.81)	1,995	39.63 (1.68)	182
Birthweight	3,437.87 (535.56)	1,971	3,348.79 (464.57)	181
IDACI deprivation indicator	0.13 (0.13)	2,222	0.14 (0.15)	195
Number of children in household	2.24 (0.80)	1939	2.29 (0.84)	182
Days school absences due to sickness last 2 weeks	-0.04 (0.89)	1579	-0.01 (0.96)	136

Those in the AN group were less likely to have report experiencing emotional and behavioural difficulties, with only one person reporting problems for every five reporting them in the comparison group.

Perceived school quality differed between groups, presenting a mixed picture. Fewer participants in the group with AN attended a 'very good' school, but more attending a 'good' school. While they were less likely to attend a 'poor' school, they were more likely to attend a 'very poor' school – although the proportion in these categories was small across the sample. Plausibly linked to the distribution of sex between the groups, participants with AN were more likely to attend a female only school, and less likely to attend a male only school.

On the (mean-centred) variable showing days of absences from school due to illness, those with AN had a lower average deviation from the mean than the comparison group. However, this variable is highly skewed, with 4,249 out of 4,928 participants with data available reporting zero days absence due to illness.

REGRESSION ANALYSES

In the following section, I present summary results for the various models. The fully expanded models can be found in Appendix 4.

Table 6-6 shows a summary of models 1-4, estimating the effect of reporting AN vs reporting no ED on GCSE total score, where

- Model 1 is a model including only the AN/no ED dummy variable;
- Model 2 additionally includes variables from set 1 above;
- Model 3 additionally includes variables from set 2 above and
- Model for additionally includes variables from set 3 above.

Table 6-6: Impact of anorexia on GCSE total score (full sample)

	Model 1 – coeff. (SE)	**Model 2**	**Model 3**	**Model 4**
Anorexia	0.45 (14.25)	-9.38 (11.41)	-1.66 (7.80)	-1.18 (7.97)
Prob > F	0.976	0.413	0.831	0.88

The coefficient on the AN category is not significant in any of the four models, as indicated by the result of the F-test. To facilitate choice between these models, the adjusted R-squared was analysed and while this increases most between models 1 and 2, there is still an increase to model 3 upon the inclusion of school variables. There is little change between models 3 and 4, which is perhaps expected given the limited number of variable added to the model, and model 3 is selected for the analyses that follow.

Table 6-7 shows the results of this model, corresponding to the hypotheses stated above:

- Model 3a is Model 3 above and includes variables from sets 1 and 2 alongside the AN indicator;
- Model 3b additionally includes the indicator for bingeing and purging behaviours (BP) and an interaction term between the AN and the BP indicators;
- Model 3c includes the AN indicator, the variable reporting days of sickness absence from school, and the interaction term between the two and
- Model 3d includes the AN and BP indicators, the absence variable and a three-way interaction term.

Table 6-7: Impact of anorexia, binging/purging and absences on GCSE total score (full sample)

	Model 3a– coeff. (SE)	**Model 3b**	**Model 3c**	**Model 3d**
Anorexia	-1.66 (7.80)	-2.49 (8.47)	-1.51 (7.76)	-1.08 (7.83)
Bingeing/purging	-	-11.90 (18.11)	-	-1.76 (4.96)
AN x BP	-	14.30 (22.86)	-	-
Absences	-	-	-5.41 (2.25)*	-5.23** (1.81)
AN x Absences	-	-	0.49 (1.36)	-
AN x BP x Absences	-	-	-	0.57 (1.32)
Prob > F	0.831	0.59	0.90	0.948

* p<0.05
** p<0.01

The only significant coefficient in these models is on the variable for absences in Models 3c and 3d. Note that GCSE score ranges from 0-1,281, so that a 5-point difference per day of absence above the mean is judged to be a small effect.

The same process is repeated for the logit modelling the impact of AN on whether a study participant achieved 5 or more good GCSEs.

Table 6-8: Impact of anorexia on 5 good GCSEs

	Model 1 – OR (se)	**Model 2 – OR (se)**	**Model 3 – OR (se)**	**Model 4 – OR (se)**
Anorexia (OR)	1.13 (0.19)	1.02 (0.18)	1.20 (0.25)	1.20 (0.25)
Prob > F	0.464	0.889	0.401	0.403

The findings in Table 6-8 show the same pattern observed above, and again model 3 is selected for the investigation that follows.

In Table 6-9, results of the logit models are shown. None of the coefficients reach statistical significance, with the exception of absences (without the interaction with AN) in Model 3d, meaning that a relationship between AN, BP, absences and their interactions with the odds of achieving 5 or more good GCSEs cannot be shown in this model.

Table 6-9: Impact of anorexia, binging/purging and absences 5 good GCSEs (full sample)

	Model 3a – OR (se)	**Model 3b – OR (se)**	**Model 3c – OR (se)**	**Model 3d – OR (se)**
Anorexia	1..20 (0.25)	1.21 (0.28)	1.20 (0.25)	1.22 (0.26)
Bingeing/purging	-	0.76 (0.37)	-	0.93 (0.11)
AN x BP	-	1.25 (0.71)	-	-
Absences	-	-	0.92 (0.05)	0.93* (0.038)
AN x Absences	-	-	1.01 (0.04)	-
AN x BP x Absences	-	-	-	1.01 (0.37)
Prob>F	0.401	0.454	0.376	0.3485

*p<0.1

SUB-GROUP ANALYSES

The sub-group analysis using the sample of females only shows essentially the same results, with the only difference that the absence variable is no longer significant in Model 3d for the '5 good GCSEs' outcome (see Table 6-11).

Table 6-10: Impact of anorexia, binging/purging and absences on GCE total score (females only)

	Model 3a– coeff (SE)	**Model 3b**	**Model 3c**	**Model 3d**
Anorexia	-0.65 (9.27)	-1.51 (10.78)	-0.61 (9.22)	-0.49 (9.38)
Bingeing/purging	-	-11.55 (32.10)	-	-0.37 (5.51))
AN x BP	-	13.72 (36.37)	-	-
Absences	-	-	-4.80 (3.74)	-5.00 (2.88)* (2.58)
AN x Absences	-	-	10.07 (2.16)	-
AN x BP x Absences	-	-	-	0.27 (1.90)

* p<0.1

Table 6-11: Impact of anorexia, binging/purging and absences 5 good GCSEs (females only)

	Model 3a – OR (se)	**Model 3b – OR (se)**	**Model 3c – OR (se)**	**Model 3d – OR (se)**
Anorexia	1.13 (0.33)	1.26 (0.41)	1.23 (0.33)	1.25 (0.35)
Bingeing/purging	-	0.81 (0.63)	-	0.96 (0.12)
AN x BP	-	1.14 (1.01)	-	-
Absences	-	-	0.94 (0.09)	0.92 (0.06)
AN x Absences	-	-	0.99 (0.06)	-
AN x BP x Absences	-	-	-	1.15 (0.67)

For the sample including only females for whom information on the predictor variable was available, there were no significant associations between AN and education in the models.

DISCUSSION

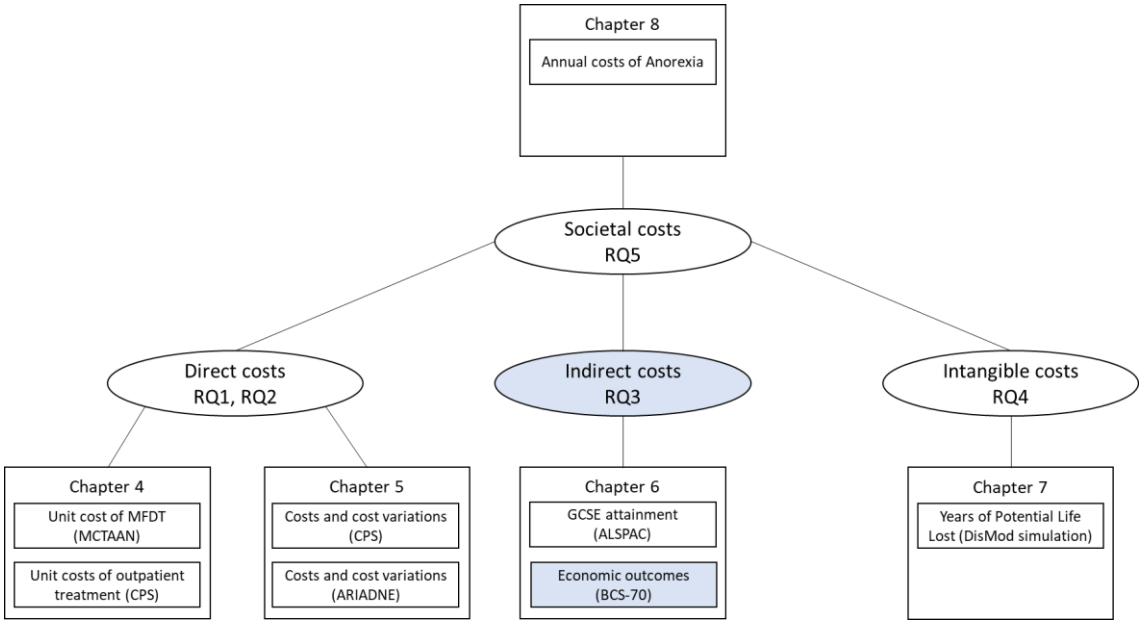
To my knowledge, this is the first study of the impact of AN on GCSE attainment. In accordance with my hypotheses, young people with AN did not differ from controls without ED in terms of their GCSE achievement. However, counter to my hypotheses, the presence of bingeing/purging behaviours did not affect GCSE attainment. These results held when the analysis was repeated for females only, and for those who provided data on ED behaviours. The latter analysis was performed to see whether the imputation changed the direction of results, as in the unimputed data, there was a trend towards higher GCSE scores in young people with AN.

The process of model fitting shows that, in terms of r-squared, socio-demographic variables and characteristics in childhood that are predictive of AN and education are more important than the school-level variables tested, and more important than the presence of ED behaviours.

There are several limitations to this study. Data on ED behaviours and diagnoses was available for ages 14 and 16, and these were combined in the predictor variable to increase sample size. This may dilute any effect of current AN on education. Across all variables in the analysis, including in the cross-tabulations of predictors and outcomes, there was a fair amount of missing data. This was addressed using multiple imputation procedures.

The main finding from this study will inform my estimate of productivity losses associated with AN. Based on these analyses, there is no evidence of an impact of AN on GCSE attainment, nor evidence of an effect of bingeing and purging behaviours. No costs associated with lover attainment will therefore be included in the CoI estimate.

PART 2 – LONGER-TERM ECONOMIC OUTCOMES ASSOCIATED WITH ANOREXIA NERVOSA IN THE BCS-70



INTRODUCTION

This section delves further into the indirect costs associated with AN and contributes towards answering RQ3: "What is the impact of AN on education, employment, income and related outcomes?". To my knowledge, this is the first study of long-term economic outcomes in AN using UK cohort data.

As described in Chapter 3, a common way of valuing productivity losses is to determine the amount of lost employment and applying a wage rate to estimate total productivity lost. I use BCS-70 data to investigate the association of self-reported AN with economic outcomes in adulthood, including employment and income to estimate excess unemployment and income forgone due to AN. This information can then be used to calculate productivity losses due to AN.

The following hypotheses are tested:

- Women with lifetime AN will have a lower chance of being in employment compared to women with no ED;
- Women with lifetime AN will have a lower income (conditional on being in employment);
- Women with lifetime AN will have a higher chance of being disabled and
- Women with lifetime AN will have a higher chance of being in receipt of benefits.

I describe those with AN and those without an ED in terms of their long-term economic outcomes and develop logistic regression and general linear models to estimate the effect of AN, controlling for a range of risk factors identified by Nicholls and Viner (2009) in the same dataset.

METHODS

DATA

The British Cohort Study (BCS-70) includes over 17,000 babies born in the UK in one week in April 1970 and is representative of the UK population. At the time the analysis was undertaken, data were available for seven sweeps up to age 38, so participants could be tracked well into adulthood. Use of the data is free of charge, and this study has been registered with the Economic and Social Data Service.

PREDICTOR

No formal diagnosis of ED is included in the BCS-70, but at age 29/30, there is a set of questions about self-reported lifetime ED, age of onset and type of ED.

Table 6-12: Questions relating to eating disorders in the BCS-70 (age 29/30 sweep)

Characteristic	**Coding**
Ever had eating problems	Binary – no/yes
Name of eating problem (up to 4 problems)	Categorical: Bulimia or compulsive eating Anorexia nervosa Problems with swallowing Some other kind of eating problem Don't know
Age first had ED	Scale variable
Eating disorder in last 12 months	Binary – no/yes
Seen a doctor about ED in last 12 months	Binary – no/yes

From these data, it is possible to determine:

- Lifetime ED: Whether the cohort member ever had an ED, and the type of ED (multiple EDs possible);
- Age of onset of ED;
- Current ED: Whether the cohort member had an ED in the last 12 months.
- Whether the cohort member has seen a doctor about the ED in the last 12 months.

The analysis presented here was modelled on a study by Nicholls and Viner (2009), who reviewed the literature on childhood risk factors for AN and reported whether these risk factors predicted self-reported lifetime AN in the BCS-70.

I used the same case definition as Nicholls and Viner, comparing those with AN only (i.e., no other ED reported) to those with no self-reported ED. Participants were therefore included in this study if they had answered the question about lifetime ED at age 29/30 and either reported AN only (AN group) or no eating problems (comparison group).

OUTCOMES

The economic outcomes in adulthood considered in this analysis were related to education, employment and benefit receipt. Table 6-13 describes these outcomes and how they were coded for the analysis. With the exception of income (scale variable), outcomes were categorical variables in the original BCS-70 data and were re-coded as binary variables to ensure a sufficient number of participants with AN were available in each cell. These binary categories were developed in preliminary analyses of the outcome variables to ensure there were sufficient which is presented below.

Table 6-13: Characteristics and coding

Characteristic	Coding
Education outcomes	
High level of education, defined as having a degree (undergraduate or postgraduate qualification; 2004 sweep)	Binary – no/yes
Employment-related outcomes	
Participation in paid employment and other activities that build skills and human capital, e.g. participation in education and training. (2000 sweep)	Binary – no/yes
Whether cohort member is an employee (2000 sweep)	Binary – no/yes
Whether cohort member is employed full-time (conditional on being employed; 2000 sweep)	Binary – no/yes
Whether cohort member is employed part-time (conditional on being employed; 2000 sweep)	Binary – no/yes
High social class (class I or II), based on occupation (conditional on being employed; 2000 sweep)	Binary – no/yes
Economic activity status is 'sick' or 'disabled' (2000 sweep)	Binary – no/yes
Self-reported weekly wage at age 29/30 (2000 sweep)	Scale variable
Benefit receipt	

Characteristic	Coding
Income-related benefits: Whether cohort member receives income support, council tax benefit or housing benefit	Binary – no/yes
Family-related benefits: Whether cohort member receives child benefit or family tax credit not paid as lump sum	Binary – no/yes

CONFOUNDERS

In developing the analytical approach, I used a recent paper looking at risk factors for AN in the BCS-70 (Nicholls & Viner 2009) as a starting point. This looked at risk factors identified in the literature and tested whether there was a significant relationship in the data.

As much as possible, I replicated the coding used in the Nicholls & Viner analyses, informed by discussions with the authors and the researchers who conducted the analyses that were the basis for some of their coding choices. The variables and their coding are shown in table 6-13.

Table 6-14: Characteristics and coding of confounders.

Characteristic	Coding
Female sex	Binary – no/yes
Mother report of frequent feeding problems in first 6 months (1975 sweep)	Binary – no/yes
Maternal psychological morbidity, defined as scoring >=7 on the Malaise Inventory[18] (1975 sweep)	Binary – no/yes
Ever separated from mother for longer than one month (1975 sweep)	Binary – no/yes
Child BMI, defined as weight divided by height squared (1980 sweep)	Categorical: Overweight – one SD or more above mean Normal weight – within one SD above or below mean Underweight – one SD or more below mean
Under-eating age 10	
Self-esteem measured on LAWSEQ (Lawrence 1981) (1980 sweep)	Categorical: High – one SD or more above mean Average – within one SD above or below mean Low – one SD or more below mean

[18] https://www.ukdataservice.ac.uk/teaching-resources/malaise/background

Characteristic	Coding
Conduct and hyperactivity domains of the Rutter Scale (Rutter 1967), based on teacher report (1980 sweep)	Categorical: High – one SD or more above mean Average – within one SD above or below mean Low – one SD or more below mean
Attention problems domain of the Rutter Scale, based on teacher report (1980 sweep)	Categorical: High – one SD or more above mean Average – within one SD above or below mean Low – one SD or more below mean

Table 6-15 shows those predictors that were identified as being significant in univariate models:

Table 6-15: Significant predictors of AN in the BCS-70 cohort (adapted from Nicholls & Viner 2009, p. 794)

Predictor	n	Adjusted odds ratio*	p
Female sex	10,340	34.8 (8.0-143)	<0.0001
Report of frequent feeding problems in first 6 months	9,023	2.1 (1.32-3.7)	0.01
Maternal psychological morbidity (Malaise Inventory high scorer >=7)	9,036	2.1 (1.3-3.6)	0.004
Separation from mother >1 month	9,150	2.5 (1.1-5.8)	0.04
Child BMI Overweight >1 SD Age 10 (3 cats)	8,675	0.4 (0.2-1.1)	0.08
Under-eating age 10	9,668	3.0 (1.5-6.6)	0.003
Self-esteem high >=1SD above mean	8,408	0.7 (0.5-0.9)	0.02
Conduct and hyperactivity problems teacher report >=1 SD above mean	8,598	2.0 (1.0-4.0)	0.05
Attention problems teacher report >=1 SD above mean	8,276	1.9 (1.0-3.7)	0.06

*Odds ratios adjusted for "sex, occupational class, maternal education at 5 or 10 years as appropriate, and occupational class at 30 years." (Nicholls & Viner 2009, p. 794)

Confounders to be included in a model should be associated with both treatment and outcome, and the literature on the BCS-70 suggests that this is the case for the variables identified as significant predictors of AN (Dearden *et al.* 2004; Knapp *et al.* 2011).

ANALYSIS APPROACH

The Nicholls & Viner analysis showed female sex to be highly predictive of AN status. The literature on AN suggests that (maybe because male cases are so rare) treatment and outcomes for males tend to be very different to females, indicating that an analysis for males and females likely to be worthwhile – especially in the context of exploring variations in societal costs of AN. However, only 5 male participants with a self-reported lifetime AN were found in this sample. A decision was therefore made to exclude males from this analysis.

Another issue to be considered was the choice of analytical approach. Nichols and Viner employed a multi-variate regression model (Cepeda *et al.* 2003). However, I was concerned about the potential for multicollinearity, given the relatively large number of binary and categorical variables on one hand, and the small number of cases in the AN group on the other hand. It has been suggested that in this situation, a propensity score can be calculated that is a summary indicator of the likelihood of an outcome being achieved, without needing to worry about overfitting the propensity score model (Shepherd 2001).

The propensity score is calculated using a logistic regression model with the treatment allocation as the dependent variable. In this case, whether or not the cohort member reported AN vs no ED. The variables thought to be associated with both predictor and outcome are used as predictors. The model estimates

$$p(x) \stackrel{\text{def}}{=} \Pr(T = 1|X = x),$$

Where p(x) is the propensity score, T is the binary outcome variable and X are the confounders. This score is then used as a co-variate in in a second stage regression.

I calculated a propensity score based on the risk factors for anorexia identified by Nicholls and Viner (see above). I attempted to use k-3 nearest neighbour matching, but matches could not be found for all participants in the AN group, further reducing the analysis sample. I therefore employed a simpler model, using the propensity score as a co-variate in logistic regression models to estimate the effects of AN on economic outcomes at age

29/30. This approach has been applied successfully to BCS-70 data before (Dearden *et al.* 2004) and reduces bias in the estimate of the treatment effect (D'Agostino 1998).,

The models were estimated using the logit command in STATA v.12 (StataCorp. 2011) and STATA v. 14 (StataCorp 2015) with the - vce(cluster) - option to reflect the clustering within individuals across several time points typical for longitudinal data. The difference in weekly income was estimated using a generalised linear specification with a gamma family and log link, as suggested by the Park test.

MISSING DATA

Missing data patterns in longitudinal data take a specific form and have received a lot of attention, both in epidemiology and in relation to, for example, clinical trials. Consequently, the development of multiple imputation procedures has led to their application to longitudinal data. Questions that arise are whether multiple imputation is in fact necessary (Twisk *et al.* 2013), whether outcomes (i.e. the dependent variable) should be imputed e.g. (Groenwold *et al.* 2012), and which imputation model is (structurally) the most appropriate (Ferro 2014). However, as discussed in the Chapter 3, imputation is generally preferred.

Missing values imputed using chained equations and 20 imputations. The chained equations procedure was chosen because of the inter-relatedness of the various predictor variables. I tested relationships between predictors and constructed the imputation model accordingly. The imputation was performed prior to constructing the propensity score.

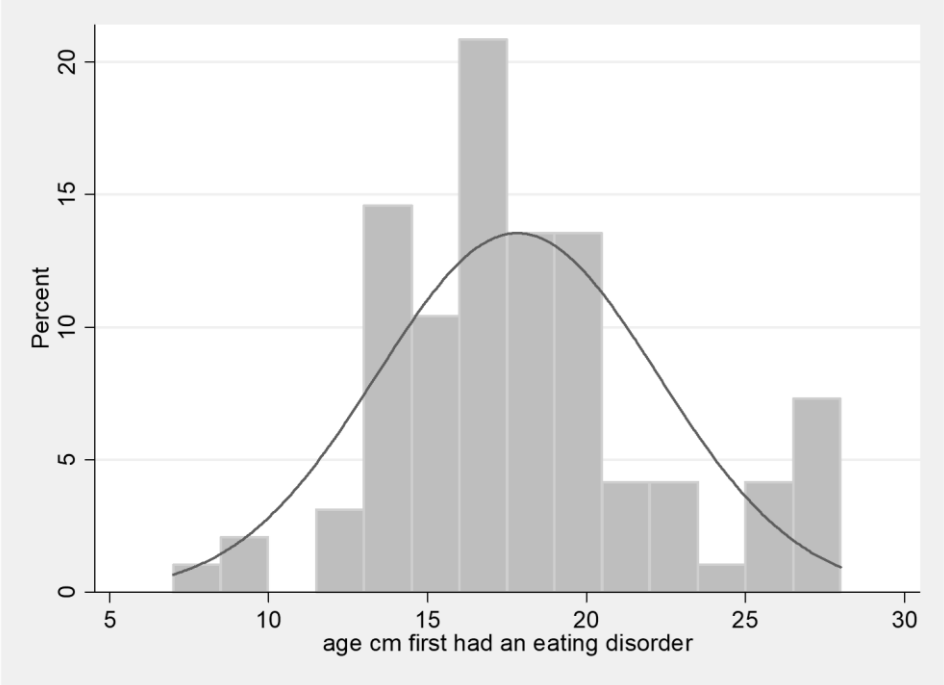
RESULTS

SAMPLE

At age 29/30, 11,261 cohort members were followed up. Information on eating problems is available for 11,211 (99.6%). Overall, 407 reported having had eating problems, and 116 participants reported lifetime AN. Of these, 101 reported AN only. The proportion of males with AN was very small, with only 5 male participants reporting AN. Consequently, the AN group consists of 96 female participants reporting lifetime AN. In the comparison group (i.e. cohort members reporting no ED), there are 5,070 participants.

Descriptives are reported for the original (i.e. unimputed) data. The average age of onset was 17.82 years (SD 4.42, range 7-28) with a median of 17 and a mode of 18. Early onset anorexia (age of onset <13 years) was reported by 6 women. A large proportion (n=44) reported onset between 13 and 17, and 46 between 18 and 28. Figure 6-1 shows the distribution of age of onset.

Figure 6-1: Distribution of age of onset of self-reported AN in the BCS-70 cohort



Of the 96 women, 22 had anorexia in the past 12 months. Of these women with a current ED, 13 had seen a doctor about the eating disorder. The average age of onset for this group was 20.0 years (SD 5.72). There were seven women with a current ED who reported age of onset at 23 years or older, i.e. report a duration of illness of 6 years or less and could therefore be considered to have a short-term experience of AN. The average age of onset for this group was 26.4 years (SD 1.72). Those with a current ED and age of onset younger than 23 years (n=14) reported an average age of onset of 16.8 (SD 3.95).

Figure 6-2 shows the distribution of the cohort member's father's or mother's occupational class at birth (of the cohort member), while Figure 6-3 shows the highest level of maternal education at age 5.

Figure 6-2: Distribution of father's or mother's occupational class at CM birth

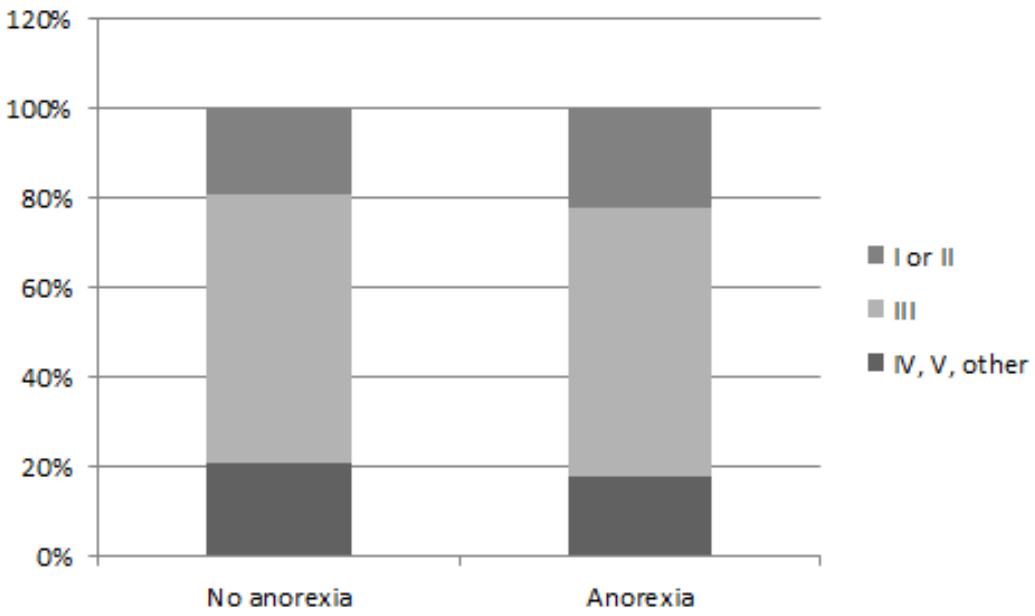
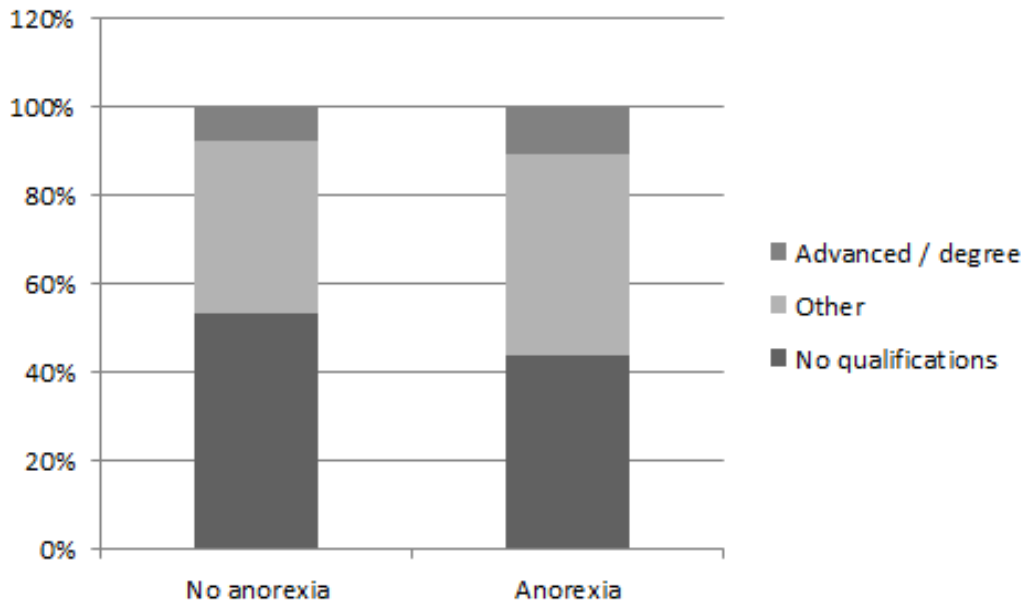


Figure 6-3: Level of maternal education at age 5



ANALYSES OF OUTCOMES

Unadjusted results

This section shows simple comparisons in outcomes between the group with AN and the group without ED, i.e. not adjusting for the propensity score.

The distribution of father's or mother's occupational class at birth of the cohort member[19] and level of maternal education at age 5 (considered to be relevant confounders) are shown in Figure 6-2 and Figure 6-3. There were no statistically significant differences between cohort members with and without self-reported AN.

Education attainment

Data on highest educational qualification is available at ages 30 and 34. Summary information (including age the participant left full-time education) is shown in Table 6-16 and Table 6-17. The only significant difference is that those with anorexia left full time education at age 20, compared to age 18 among those with no anorexia.

[19] Mother's social class was used where the father's was not available.

Table 6-16: Highest educational qualification at age 30

	No ED			Anorexia		
	Mean (SD)	***Range***	***n***	***Mean (SD)***	***Range***	***n***
Number of O-levels	6.09 (3.04)	0-15	2,490	6.57 (2.95)	0-12	42
Number of CSEs	3.97 (2.89)	0-12	865	3.35 (2.80)	0-12	17
Number of a-levels	2.65 (1.07)	0-7	1,083	2.38 (0.97)	1-4	24
Age left full-time education*	18.71 (3.87)	14-34	4,504	20.0 (4.77)	15-34	77

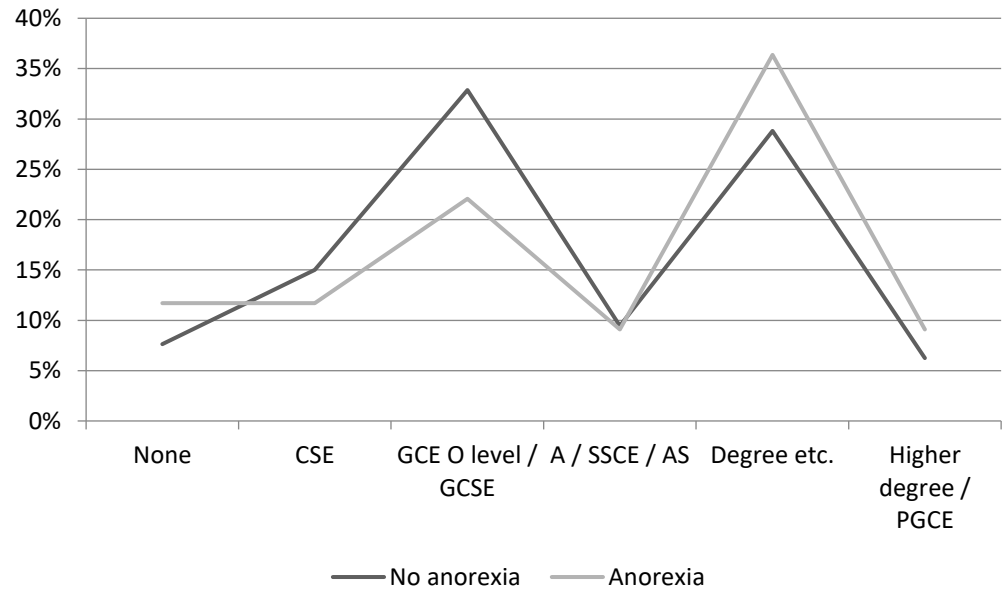
*Difference significant at the 95% level

Table 6-17: Highest educational attainment at age 34

	No ED (n=4,500)		Anorexia (n=77)	
	n	***%***	***n***	***%***
None	343	8%	9	12%
CSE	675	15%	9	12%
GCE/O-level/GCSE	1,479	33%	17	22%
A/SSCE/AS	425	9%	7	9%
Degree etc.	1,297	29%	28	36%
Higher degree/PGCE	281	6%	7	9%

As shown in Table 6-16 and Table 6-17, there are a lot of missing cases for these particular questions. Given the small numbers, data were plotted in a graph (see Figure 6-4), and visual inspection suggested that there may be differences between those with and without reporting anorexia in terms of those obtaining a highest qualification that is below and above A-levels (or equivalents). Please note that while line graphs are not usually an appropriate choice for these type of data, they were chosen because they effectively highlight differences between the two groups as the level of education increases.

Figure 6-4: Highest educational attainment age 34



There were 1,578 (35%) in the comparison group with a degree or higher degree, and 34 (45%) in the anorexia group. This difference was significant at the 90% level (p=0.058 for Chi-square and p=0.071 for Fisher's exact test).

Employment status

Employment status at age 29/30 was explored in a similar way. The original variable had 12 categories, with very few people with anorexia in each cell. Table 6-18 shows the original variable, and the same variable recoded into

- 'Economically active' vs not
- Employed (full-time or part-time) vs other
- Employed vs unemployed vs other

This reflect different theoretical and practical distinctions. None of the distinctions showed a significant difference between those with and without AN. Those with anorexia were no more likely than those without to be in part-time employment (see Table 6-18).

Table 6-18: Employment status at age 29/30

	No ED (n=5,449)		Anorexia (n=95)	
Category	*n*	*%*	*n*	*%*
Full-time paid employment	2,647	49%	43	45%
Part-time paid employment	1,150	21%	17	18%
Full-time self-employed	153	3%	3	3%
Part-time self-employed	87	2%	3	3%
Unemployed seeking work	116	2%	0	0%
Full-time education	73	1%	3	3%
Government training scheme	5	0%	0	0%
Temporarily sick/disabled	17	0%	0	0%
Permanently sick/disabled	84	2%	10	11%
Looking after home/family	1,030	19%	14	15%
Wholly retired	1	0%	0	0%
Other	86	2%	3	3%
Not economically active	1,334	24%	27	28%
Employed	4,037	74%	66	69%
Full-time work	2,800	51%	46	48%
Part-time work	1,237	23%	20	21%

Employment-based occupational class

Another possible impact beyond the probability of employment or working time is on choice of the type of job, which determines occupational class in some classification systems. As a result, data on occupational class is only for those who are in paid employment or self-employed. The breakdown is shown in Table 6-19.

Table 6-19: Employment-based occupational class, age 29/30

	No ED (n=4,033)		Anorexia (n=65)	
Category	*n*	*%*	*n*	*%*
I - Professional	179	4%	3	5%
II- Managerial – technical	1,430	35%	32	49%
III.i - Skilled, non-manual	1,579	39%	17	26%
III.ii - Skilled, manual	304	8%	4	6%
IV - Partly skilled	451	11%	7	11%
V - Unskilled	84	2%	2	3%
Others	6	0%	0	0%

Figure 6-5 plots these data as a simple graph, showing potential differences in Class II and Class IIIn. Figure 6-6 shows the same data, but cumulates them over time. It appears that a useful cut-off might be after Class II.

Figure 6-5: Occupational class at age 29/30

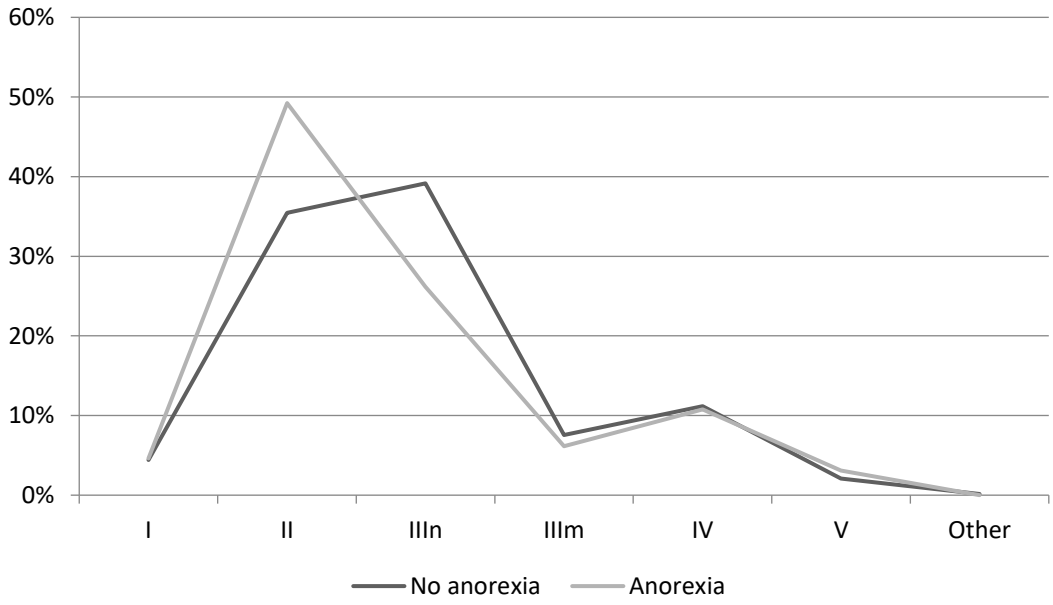
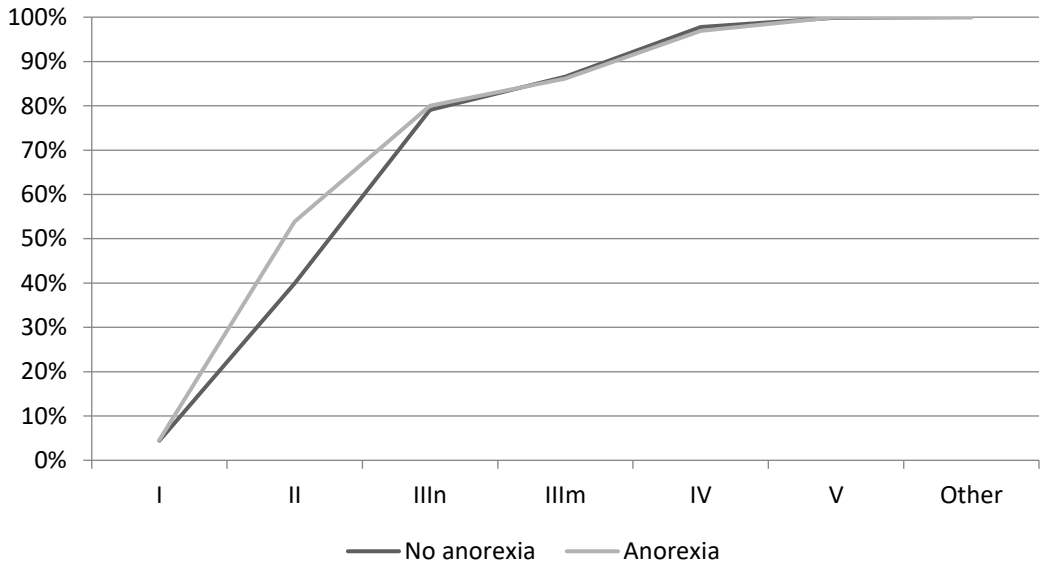


Figure 6-6: Occupational class at age 29/30, cumulative



The proportion of those with anorexia (35/65) is Classes I and II is significantly greater (at the 95% level; add p-value) than for those without anorexia (1,609/4,033).

Benefit receipt

Benefit receipt at age 29/30 is detailed in Table 6-20. Given the large number of available benefits, the most commonly received benefits were pragmatically divided into income-related benefits (income support, council tax benefit and housing benefit) vs family-related benefits (child benefit, family tax-credit not paid as lump sum). Those with anorexia were more likely to receive income-related benefits, potentially pointing to a lower income.

Table 6-20: Benefit receipt, age 29/30

	No ED (n=5,449)		**Anorexia (n=96)**	
Category	***n***	***%***	***n***	***%***
Statutory sick pay	32	1%	0	0%
Child benefit	2,853	52%	48	50%
JSA	110	2%	0	0%
Income support*	444	8%	16	17%
Family tax credit (non-lump)	391	7%	8	8%
Family tax credit (lump sum)	35	1%	0	0%
Council tax benefit	523	10%	13	14%
Housing benefit*	536	10%	16	17%
Maternity allowance	37	1%	0	0%
Statutory maternity pay	102	2%	0	0%
Income-related benefits*	780	14%	21	22%
Family-related benefits	2,905	53%	48	50%

*difference in proportion significant at 95% level

Income

Self-reported mean weekly income at age 29/30 was £298 for those with and £279 for those without AN, a non-significant difference. The income variables in the BCS-70 are problematic. While the data provider has promised to share a cleaned version of the variable in the near future, at the time of this analysis, only an 'informal' and incomplete fix was available. This fix is based on work by Lorraine Dearden and Alissa Goodman, who reviewed the earnings data in the BCS-70 and tried to address problems and

inconsistencies (Appendix 4 to Shepherd 2001). The results presented here are based on this fix, which its authors acknowledge is incomplete, and results relating to the income variable therefore need to be interpreted with caution.

Multi-variate models

Propensity score

The result of the propensity score model is shown in Table 6-21. While the purpose of a propensity score model is not to maximise explained variance or to retain only significant co-variates in a final model, but to incorporate as much relevant information as possible, some large (significant) contributors to the chance of being in the AN group can be highlighted. Early Feeding problems, early separation from the mother and high maternal malaise scores are the largest contributors to an increased risk of being in the AN group, followed by high scores on the conduct problems and hyperactivity scale. High self-esteem on the other hand is the largest contributor to a decreased risk of being in the AN group.

Table 6-21: Propensity score model.

	Coef.	**SE**	**p-value**
Social class at birth			
• **III**	1.13	0.33	0.675
• **IV, V or other**	1.19	0.45	0.633
Maternal qualifications			
• **Qualification – not degree**	1.32	0.34	0.280
• **Degree**	1.73	0.79	0.229
Frequent feeding problems in first 6 months	1.74	0.47	0.041
Separated from mother >1 month	1.76	0.80	0.216
Under-eating	1.67	0.65	0.188
Malaise Inventory			
• **Low scorer**	1.30	0.50	0.503
• **High scorer**	1.87	0.53	0.027
Child BMI category age 10			
• **Low BMI**	0.70	0.24	0.305
• **High BMI**	0.64	0.26	0.277
Maternal BMI	0.97	0.03	0.299
Self-esteem			

	Coef.	SE	p-value
• **Low self-esteem**	0.81	0.26	0.505
• **High self-esteem**	0.61	0.22	0.178
Conduct problems and hyperactivity			
• **Low scorer**	1.01	0.53	0.992
• **High scorer**	1.60	0.44	0.082
Ethnicity	0.53	0.54	0.538

Economic outcomes

Table 6-22 shows economic outcomes in adulthood for those with and without AN. There is a statistically significant difference between those with and without AN for three of the eight outcomes. The statistically significant difference in income-related benefits reflects the higher probability of those with AN receiving income support (17% vs 8%) and housing benefit (17% vs 10%).

Table 6-22: Overview of economic outcomes for people with and without anorexia, age 29/30 or 34

	No ED		Anorexia (n=96)	
Category	**%**	**Available n**	**%**	**Available n**
Degree vs not*	29%	5,449	35%	96
Economically active vs not	76%	5,449	72%	96
Employed vs other	74%	5,449	69%	96
Full-time work vs not	51%	5,449	48%	96
Sick/disabled vs not*	2%	5,449	10%	96
Occupational class I or II vs lower*	40%	4,033	54%	65
Receiving income-related benefit vs not*	14%	5,449	22%	96
Family-related benefits vs not	53%	5,449	50%	96

*Difference statistically significant at 95% level

Table 6-23 shows the odds ratio for each of these outcomes, adjusting for AN risk factors (the propensity score). The only significant difference between those reporting AN and the group with no ED is that those with AN were 6.32 times as likely to be long-term sick or disabled. For those in employment, there was no difference in weekly income.

Table 6-23: Odds ratios for economic outcomes of anorexia, adjusted for propensity score

Outcome	Age measured	Odds ratio (SE)	p-value
Long-term sick/disabled**	30	6.32 (2.33)	<0.01
Employed	30	0.75 (0.17)	0.19
Occupational class I or II if employed	30	1.02 (0.36)	0.960
Receives income-related benefits	30	1.30 (0.34)	0.31
Has a degree	34	1.29 (0.53)	0.533

DISCUSSION

The current evidence base on the economic circumstances of people with AN and the potential adult consequences of a severe disorder is small. This study is the first to look at the longer-term economic consequences of AN in England, and therefore adds considerably to the knowledge base in this area.

While there were significant differences between those with AN and those with no ED in terms of the (unadjusted) proportion in employment, the proportion in a high social class if employed, the proportion receiving income-related benefits and the proportion with a degree, these differences did not carry through in the multi-variate analysis. In those surviving into adulthood, a lifetime occurrence of AN did not appear to affect employment prospects or wages – a similar finding to a study in the US that found no statistically significant impact of ED on chance of employment or wages (Samnaliev *et al.* 2015). These findings highlight the need to adjust for potential confounders.

One possible explanation for the lack of impact only those participants provide data who a) survive into adulthood and b) did not drop out of the cohort study, potentially due to the severity of their illness. This calls into question the missing at random assumption underlying the MI procedure.

The advantage of using a cohort that is representative of the general population, rather than a 'clinical' sample recruited, for example, through specialist ED services, is that it does not capture just the top end (in terms of need) of the affected population. This could potentially disguise a significant result that might have been found if only those with a strict clinical diagnosis were considered. But while sometimes concerns are raised about the reliability of self-reported diagnoses, simple questions such as have been shown to be as good as more elaborate screening instruments in identifying ED in community samples (Keski-Rahkonen *et al.* 2006).

Those with AN did have much higher odds of being sick or disabled (adjusted OR 6.32). While another study found that 35% of those with AN received benefits in a Canadian study (Su & Birmingham 2003), in this sample, only 10% were sick or disabled.

Further work is needed to determine why AN does not appear to affect employment prospects in this cohort with high levels of disability.

CHAPTER SUMMARY

The evidence for the impact of AN on economic outcomes is mixed. The studies presented here were the first to use the respective dataset to investigate productivity-related outcomes in adulthood for people with AN. In summary, the studies showed that:

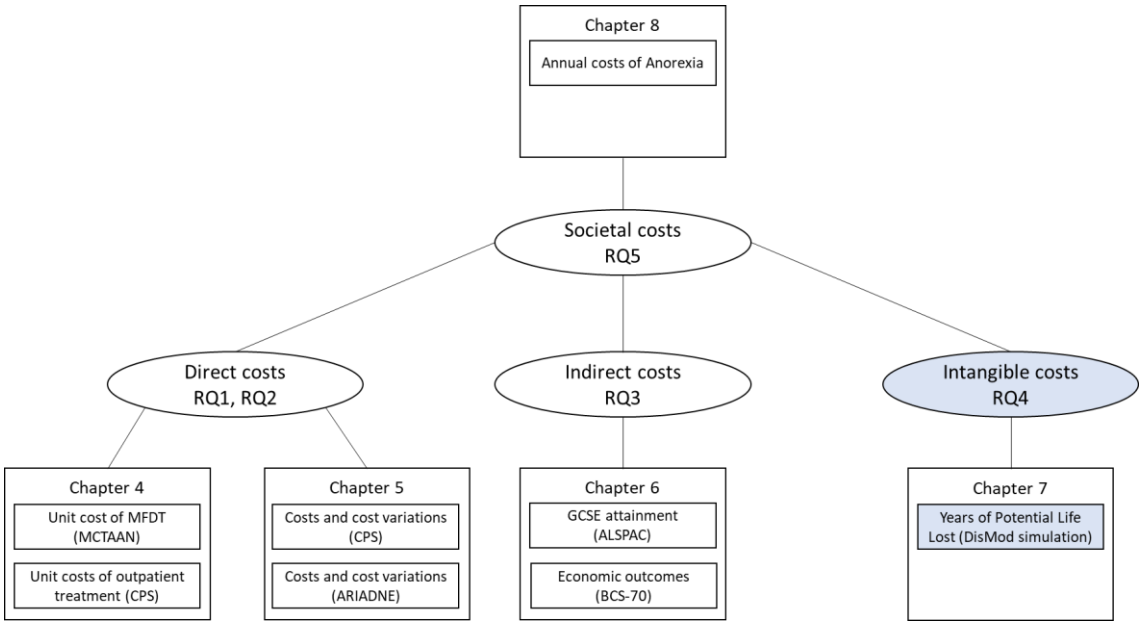
- There was no impact of AN on GCSE attainment.
- There was no interaction between AN and absences.
- The presence of bingeing/purging behaviours did not alter these relationships.
- Those with AN were not more likely to be unemployed.
- They were not more or less likely to be in a higher occupational class (classes I or II) if employed.
- They were more likely to be long-term sick or disabled.
- They were not more likely to receive income-related benefits.
- There was no difference in weekly wages for those in employment.

These findings are broadly in line with the existing literature. A previous study from Finland did not find an impact of AN on education in the long term (Keski-Rahkonen *et al.* 2007). In contrast to these findings, a sample with AN was found to have a higher chance of having a degree (Hjern *et al.* 2006). The same study showed the rate benefits receipt to be high, as was the chance of disability in a Canadian study (Su & Birmingham 2003). Finally, a recent US study found no impact of AN on the likelihood of employment or on wages (Samnaliev *et al.* 2015).

These findings will be used in Chapter 8 to inform the CoI estimate of AN: If no impact on education, employment or wages can be found, no costs should be included, as there will be no impact on productivity. However, there was a significant impact on disability, which will be explored in terms of costs to the public sector and in terms of productivity.

CHAPTER 7

Intangible costs: Years of Potential Life Lost from Anorexia nervosa



CHAPTER INTRODUCTION

This chapter shows disease modelling results estimating the annual prevalence and case fatalities from AN for England and therefore contributes to answering RQ4: "What is the loss of life associated with AN in England?"

While many studies have estimated the prevalence of AN, most focus on at risk populations because general population studies typically find few cases of AN (Solmi *et al.* 2016). This makes it difficult to obtain an empirical prevalence figure for AN.

I use the DisMod-II disease modelling software to combine information on the English population (distribution, mortality rate) and information on AN (incidence, duration of illness and SMR) to estimate prevalence by 5-year age group and case fatalities. I apply the method suggested by Harbottle and colleagues (Harbottle *et al.* 2008) to English data to estimate the life expectancy of women with AN at various ages of onset. I calculate years lived with disability (YLD) and Years of Potential Life Lost (YPLL) and discount them to age of onset so that a monetary value to calculate intangible costs associated with AN can be applied in Chapter 8.

A previous iteration of this study was recently published (Schmidt *et al.* 2017). I have since updated the model and provide two additional scenarios, exploring the impact of a) a higher incidence to reflect the population not in contact with health services and b) a lower mortality rate to simulate more effective treatments.

METHODS

DISMOD-II MODEL

The DisMod-II software (Barendregt *et al.* 2003) is publicly available and contains a set of equations for a simple disease model. The equations relate the following disease parameters to each other:

- Incidence
- Prevalence
- Case fatality
- Time to remission

At least three of the above are required as inputs to generate the remaining as model outputs. In addition, information on the underlying population (number of people, all-cause mortality) are required to populate the model. The software allows the user to estimate a more complete picture of a disease where full information is not available.

POPULATION DATA

Data on the English population was drawn from the Office for National Statistics mid-year estimate for 2011. Given the lack of data on AN in males, only data on females were used.

INCIDENCE

Incidence rates for females were entered in 5-year age groups, based on the most recent estimate from an analysis of the GPRD by Micali (2013), as rates per 100,000.

MORTALITY RATE AND SMR

The general population mortality rate between age x and age x+1 was taken from National Life Tables (ONS) for 2010-2012. The SMR for AN of 5.86 was taken from a review of 36 studies (Arcelus *et al.* 2011).

LIFE EXPECTANCY IN AN

Life expectancy at ages 10-100 was calculated by applying the SMR for anorexia to the mortality rate for England. Applying the method for constructing life tables provided by the ONS, the number of deaths at each age was calculated by multiplying the mortality rate by the population. Life expectancy at each age was then calculated by first calculating years alive at each age, then summing years alive from age x to the oldest age (in this case, 100), and dividing this by the population at age x. Full details of the calculations can be found in Chapter 3.

DURATION OF ILLNESS

In a widely cited study by Herzog and colleagues (1997), 50% of those admitted to hospital for AN recovered after 6 years. This input parameter was used for the median duration of ED.

SCENARIO ANALYSIS

To model the impact of unmet treatment need on mortality, I re-ran the base scenario but doubled the incidence rate. In a second variation, I assumed that mortality from medical complications is reduced by 50%, i.e. an overall reduction of 25%.

YEARS OF POTENTIAL LIFE LOST AND YEARS LIVED WITH DISABILITY

YPLL were calculated for the age of onset within each 5-year age group (by first determining whether a person with age of onset at age x was alive or not alive at a given future age up to 82, based on life expectancy at age x. Future YPLL were discounted to age of onset, using a discount rate of 3.5%.

Years lived with disability were calculated by multiplying the model output for duration of illness for each five-year age group by the number of incident cases in that age group. Future years lived with disability were discounted to age of onset, using a discount rate of 3.5%.

RESULTS

OVERVIEW OF SCENARIOS

Table 7-1 shows the results of the DISMOD II analysis, estimating a prevalence of approximately 13,000 cases and an incidence of ca. 2,000 new cases in the base scenario. The largest proportion of cases is at ages 20-24 (21%), given that most cases have their onset between ages 15-19. Table 7-2 and Table 7-3 show the same information for the two additional scenarios.

PREVALENCE RATE

The prevalence rate for the three scenarios is plotted in Figure 7-1. The high incidence scenario doubles prevalence. The highest prevalence is found between age 20-24, given that the highest incidence rate is in the age 15-19 age group.

Figure 7-1: Estimated prevalence per 100,000, three scenarios

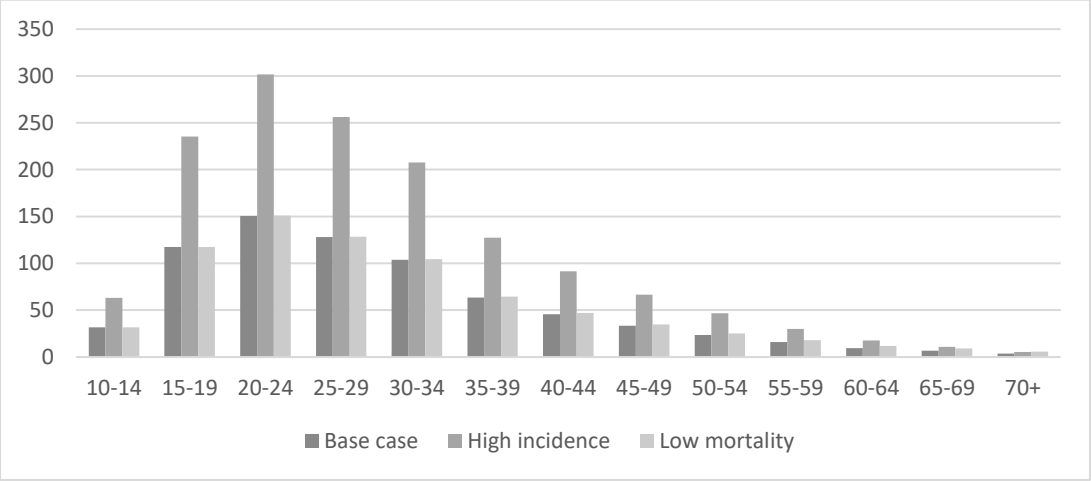


Table 7-1: Prevalence, morbidity and mortality for AN in England, base case

Age group	Incidence per 100k	Number new cases	Prevalence per 100k	Total cases	% of total cases	Duration of illness	Age of onset	Case fatalities
10-14	21.5	322	31.6	474	4%	4.5	13	0
15-19	44.5	722	117.5	1,907	15%	5.4	18	2
20-24	23.3	415	150.6	2,681	21%	6.6	22	4
25-29	17.7	324	128.0	2,344	18%	7.6	27	4
30-34	5.6	99	103.7	1,830	14%	8.5	31	5
35-39	2.5	44	63.6	1,124	9%	9.4	38	5
40-44	1.5	29	45.7	896	7%	9.7	42	6
45-49	1.0	19	33.3	655	5%	8.9	47	7
50-54	0.5	8	23.5	405	3%	8.0	53	6
55-59	0.4	6	16.0	243	2%	7.3	57	6
60-64	0.3	5	9.6	155	1%	5.7	64	6
65-69	0.4	5	6.8	89	1%	5.1	66	5
70+	0.2	12	3.5	73	1%	3.4	74	12
All ages	7.5	2,036	47.8	12,899	100%	6.1	22	69

Table 7-2: Prevalence, morbidity and mortality for AN in England, high incidence case

Age group	Incidence per 100k	Number new cases	Prevalence per 100k	Total cases	% of total cases	Duration of illness	Age of onset	Case fatalities
10-14	43.0	644	63.2	946	4%	4.5	13	1
15-19	89.1	1446	235.2	3,818	15%	5.4	18	5
20-24	46.6	830	301.5	5,368	21%	6.6	22	7

Age group	Incidence per 100k	Number new cases	Prevalence per 100k	Total cases	% of total cases	Duration of illness	Age of onset	Case fatalities
25-29	35.4	648	256.3	4,694	18%	7.6	27	9
30-34	11.3	199	207.7	3,664	14%	8.5	31	10
35-39	4.9	87	127.3	2,249	9%	9.4	38	9
40-44	3.0	59	91.6	1,794	7%	9.7	42	12
45-49	2.0	39	66.6	1,310	5%	8.9	47	14
50-54	0.7	12	46.7	806	3%	8.1	52	12
55-59	0.4	6	30.1	456	2%	7.3	57	11
60-64	0.3	5	17.6	283	1%	5.8	64	11
65-69	0.4	5	11.0	144	1%	5.1	67	9
70+	0.2	12	5.4	100	0%	3.4	74	15
All ages	15.0	4,033	95.1	25,665	100%	6.2	22	126

Table 7-3: Prevalence, morbidity and mortality for AN in England, low mortality case

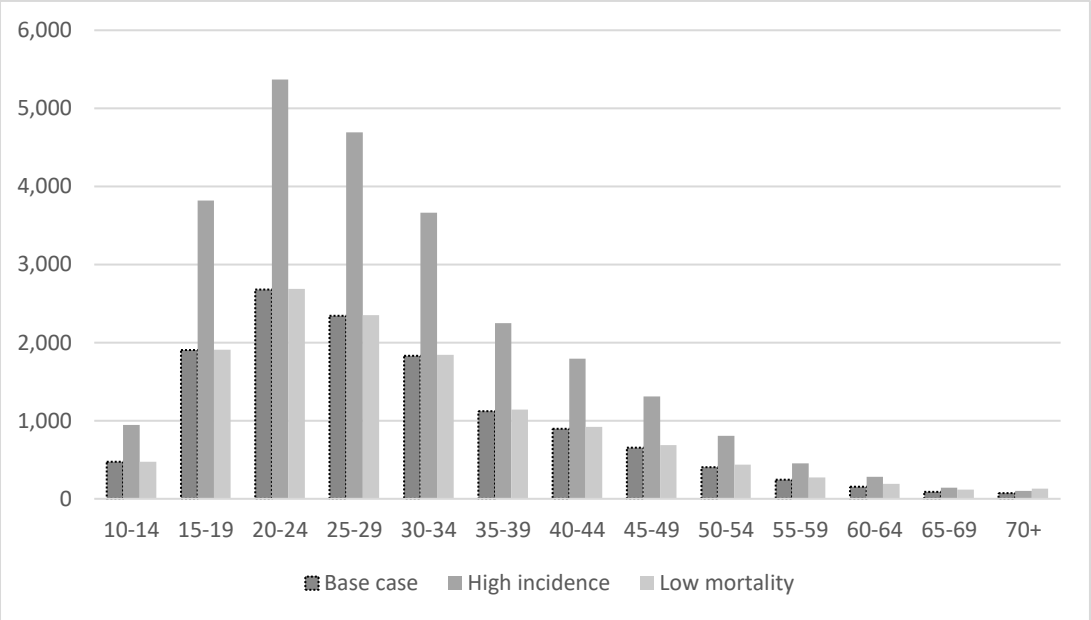
Age group	Incidence per 100k	Number new cases	Prevalence per 100k	Total cases	% of total cases	Duration of illness	Age of onset	Case fatalities
10-14	21.5	322	31.7	474	4%	4.5	13	0
15-19	44.5	722	117.6	1,909	14%	5.4	18	1
20-24	23.3	415	150.9	2,687	20%	6.7	22	1
25-29	17.7	324	128.6	2,354	18%	7.8	27	2
30-34	5.6	99	104.6	1,844	14%	8.8	31	2
35-39	2.5	44	64.6	1,142	9%	10.0	38	2
40-44	1.5	29	47.0	921	7%	10.5	42	2

Age group	Incidence per 100k	Number new cases	Prevalence per 100k	Total cases	% of total cases	Duration of illness	Age of onset	Case fatalities
45-49	1.0	19	34.9	686	5%	9.9	47	3
50-54	0.5	8	25.4	437	3%	9.2	53	3
55-59	0.4	6	18.1	275	2%	8.6	57	3
60-64	0.3	5	11.8	191	1%	7.2	64	3
65-69	0.4	5	9.0	118	1%	6.7	66	3
70+	0.2	12	5.6	131	1%	4.9	74	10
All ages	7.5	2,035	48.9	13,195	100%	6.3	22	35

TOTAL CASES

Similarly, total cases are highest in the high incidence scenario (see **Error! Not a valid bookmark self-reference.**), and slightly higher in the low mortality scenario

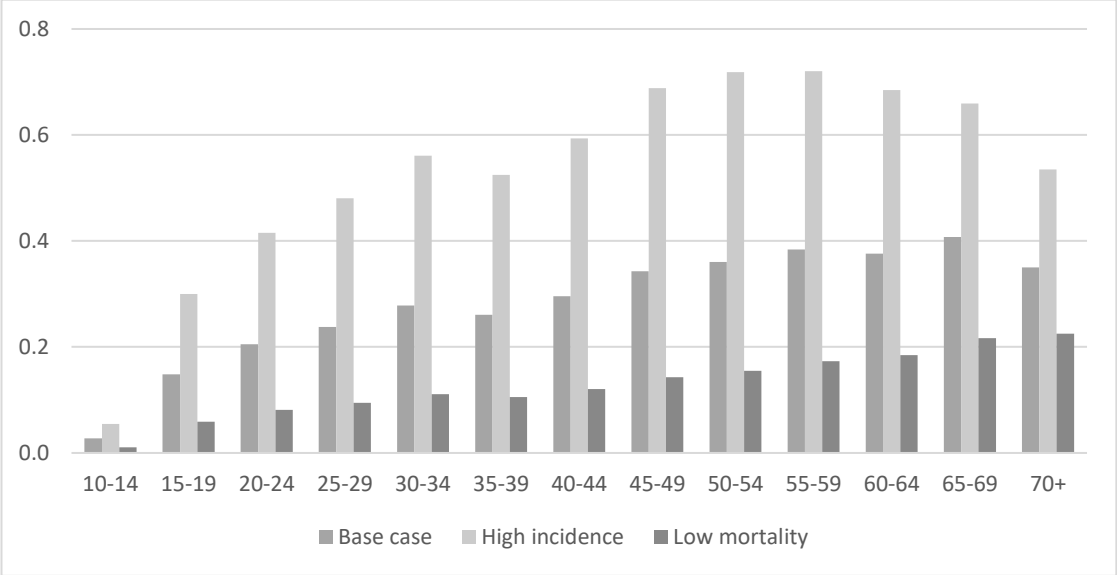
Figure 7-2: Total cases, three scenarios



MORTALITY RATE

Figure 7-3 plots mortality rates. The impact of higher incidence while constraining other parameters means that the mortality rate has to adjust in the high incidence scenario.

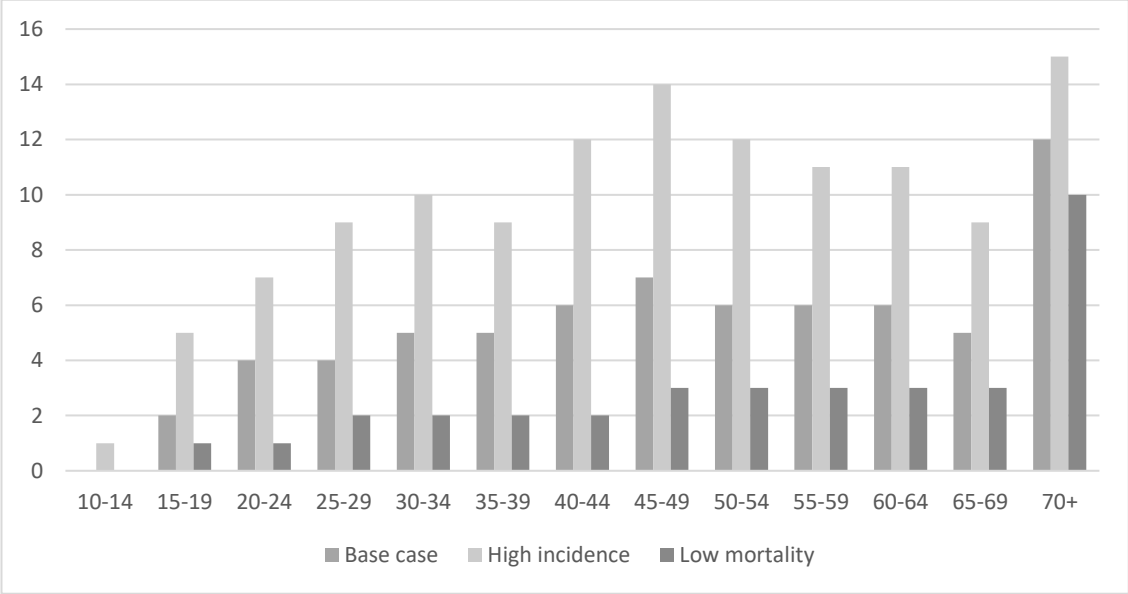
Figure 7-3: Mortality rate, three scenarios



CASE FATALITIES

Finally, Figure 7-4 shows case fatalities. In the base scenario, there are an estimated 69 fatalities per year.

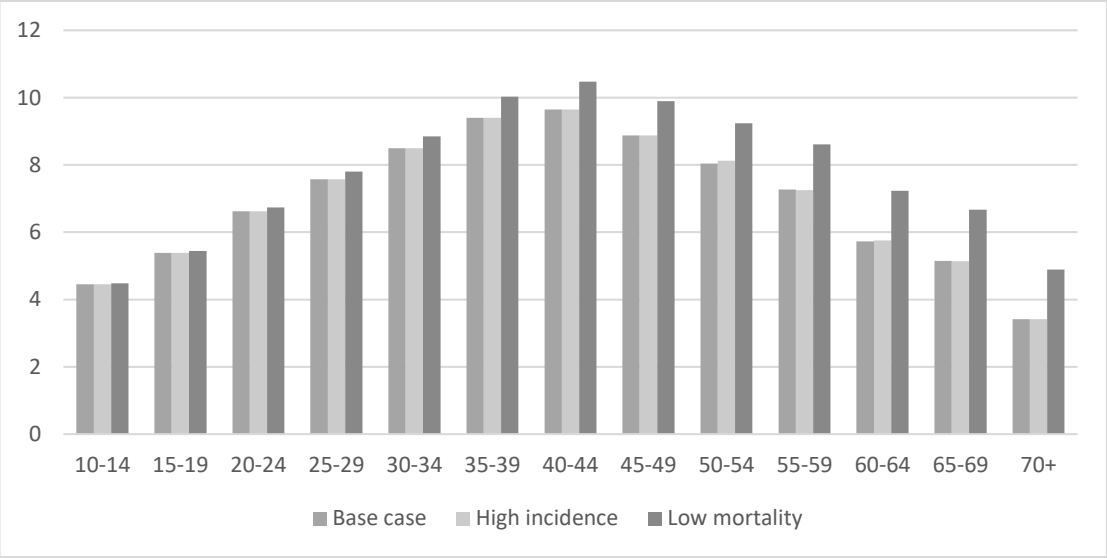
Figure 7-4: Case fatalities, three scenarios



DURATION OF ILLNESS

Duration of illness was modelled to retain the average of around six years, while also reflecting a likely shorter duration in the case of a younger age of onset. Here, we see the impact of the lower mortality rate, which - all else being equal – leads to a longer duration of illness (see Figure 7-5).

Figure 7-5: Duration of illness, three scenarios



YEARS OF POTENTIAL LIFE LOST

Table 7-4 shows estimated life expectancy and average YPLL by age of onset. Combining the results of the base case with an analysis by Harbottle & Birmingham (Harbottle *et al.* 2008) and recent projections for life expectancy in England, I estimate that 6,000 life years are lost to AN each year (discounted to present value; see Table 7-5). The present value of YPLL across all age groups is on average 3 years. As expected, for the low mortality scenario, the estimate is halved, while it is doubled for the high incidence scenario.

Table 7-4: Life expectancy and YPLL

Age	Chance of death age x	Life expectancy age x	YPLL for AN onset age x
10	0.0004	55.0	17.8
11	0.0005	54.0	17.8
12	0.0006	53.1	17.8
13	0.0005	52.1	17.8
14	0.0007	51.1	17.7
15	0.0008	50.2	17.7
16	0.0010	49.2	17.7
17	0.0012	48.2	17.6
18	0.0012	47.3	17.6
19	0.0014	46.4	17.6
20	0.0013	45.4	17.5
21	0.0014	44.5	17.5
22	0.0013	43.5	17.4
23	0.0015	42.6	17.4
24	0.0014	41.7	17.3
25	0.0016	40.7	17.3
26	0.0017	39.8	17.2
27	0.0020	38.8	17.2
28	0.0020	37.9	17.1
29	0.0020	37.0	17.1
30	0.0023	36.1	17.0
31	0.0024	35.2	17.0
32	0.0027	34.2	16.9
33	0.0029	33.3	16.8
34	0.0032	32.4	16.8
35	0.0036	31.5	16.7
36	0.0038	30.6	16.6
37	0.0041	29.8	16.5
38	0.0045	28.9	16.4
39	0.0047	28.0	16.3
40	0.0055	27.1	16.2
41	0.0061	26.3	16.1
42	0.0063	25.4	16.0
43	0.0070	24.6	15.9
44	0.0078	23.8	15.8
45	0.0084	23.0	15.6
46	0.0093	22.1	15.5
47	0.0096	21.3	15.4
48	0.0107	20.5	15.2
49	0.0119	19.8	15.1

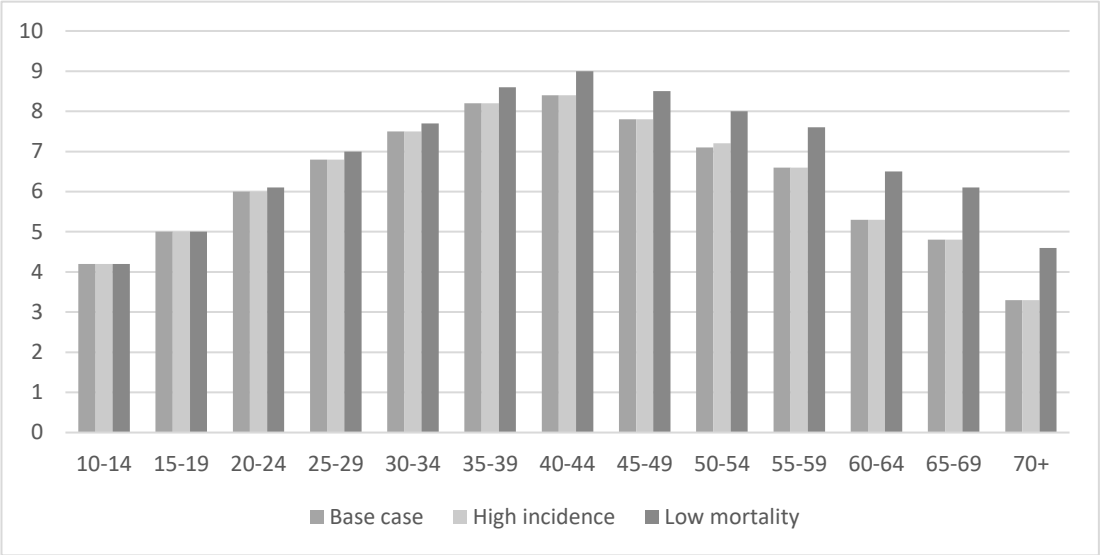
Table 7-5: Reduction in life expectancy and present value of YPLL

Age group	Age of onset	New cases	Reduction in life expectancy	Present value YPLL
10-14	13	322	17.77	735
15-19	18	722	17.61	1,957
20-24	22	415	17.42	1,196
25-29	27	324	17.19	1,109
30-34	31	99	16.96	359
35-39	38	44	16.42	203
40-44	42	29	16.02	154
45-49	47	19	15.37	101
50-54	53	8	14.37	52
55-59	57	6	13.52	37
60-64	64	5	11.78	28
65-69	66	5	11.24	26
70+	74	12	8.80	38
Total		***2,010***		***5,995***

YEARS LIVED WITH DISABILITY

Years lived with disability is closely related to duration of illness, but is shown here to include discounting of future years of life. As with duration of illness, years lived with disability is not affected by assumptions about incidence, but is increased by assuming a lower mortality rate for AN (see Figure 7-5). The total number of years lived with disability (discounted to present value) in the base case is 47,131, with 48,460 in the low mortality case. The small difference in estimates arises from the distribution of age of onset, where incident cases are more likely to fall into age brackets with shorter durations of illness.

Figure 7-6: Years lived with disability, three scenarios



DISCUSSION AND SUMMARY

In this short chapter, I present the results of a disease modelling study with the aim of calculating life years lost from AN in England. I then apply a valuation and discount to present value to obtain an estimate of the annual intangible costs associated with AN. This estimate will be combined with estimates of direct costs and indirect costs to calculate the CoI of AN in England.

In the base case,

- New cases per year are estimated at 2,036;
- Prevalence is estimated at 48.9 cases per 100,000;
- Total cases are estimated at 12,895;
- Fatalities are estimated at 69 per year;
- The reduction of life expectancy is up to 17 years;
- The total present value of YPLL is around 6,000;
- The total present value of YLD is around 47,000.

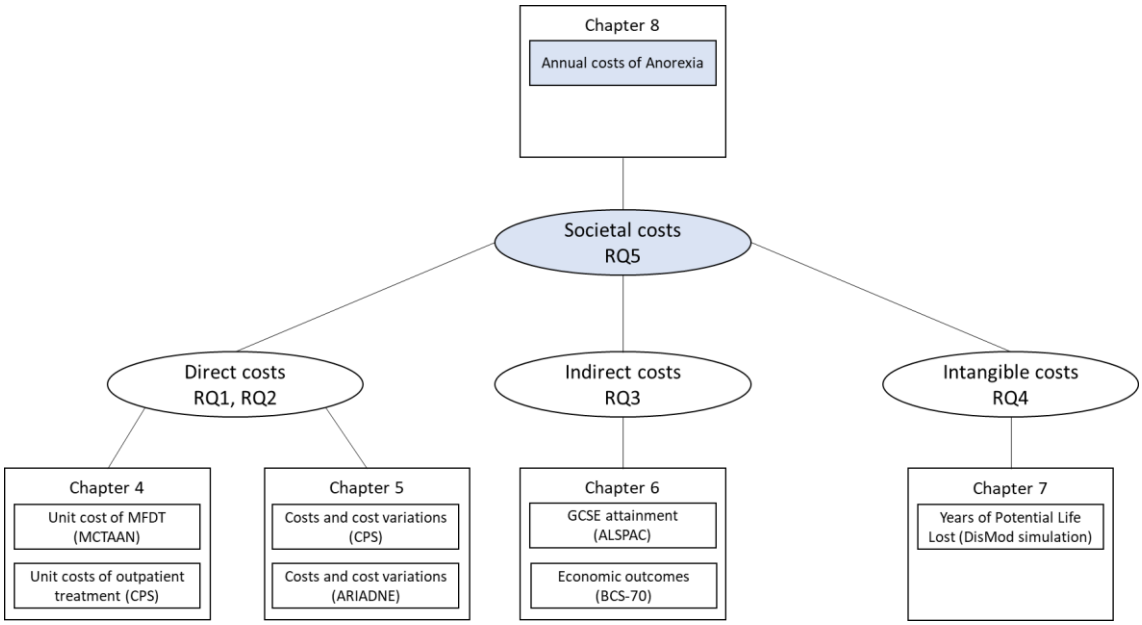
While the incidence figure is based on the most recent estimate available and therefore rooted in the literature, although it is lower than incidence figures derived from calculations based on incidence rates for the population as a whole. In contrast, the King's Fund estimated that in 2007, here were nearly 27,000 people with AN.

The scenarios reflecting a) higher incidence and b) lower mortality illustrate that changing any one parameter will alter the model to accommodate this change. Given that incidence is fixed and even a large reduction in SMR does not seem to affect prevalence by much, it is possible that the estimate of duration of illness – around six years – is too low. The low mortality scenario also illustrates how a lower mortality rate can increase duration of illness. While mortality is avoided, the number of years lived with an illness will be higher.

This small study aimed to produce an estimate of prevalence, life years lost and years lived with disability.

CHAPTER 8

The annual costs of Anorexia nervosa to English society, 2010/11



CHAPTER INTRODUCTION

This chapter pulls together information from the preceding empirical chapters (Chapters 4-7) to estimate the annual societal costs of AN for England. The chapter draws on data collected alongside the various RCTs from the ARIADNE programme, the Care Pathways Study, the analyses of BCS-70 data as well as publicly available data and parameters from the literature review.

Previous estimates of the cost of AN in England have adopted a perspective limited to the cost of inpatient care (Office of Health Economics 1994) or relied on assumptions drawn from international cost estimates when it comes to estimating the costs of outpatient treatment (King's Fund *et al.* 2008).

More recently, the charity ProBono Economics estimated the annual cost of EDs to be between £1.26 and £9.6 billion (ProBono Economics 2012). This estimate does not distinguish between different types of ED and is to a large extent based on the previous work by the King's Fund (2008). It includes a burden of disease figure associated with disability from AN of £950m in the lower-cost scenario, so that approximately £80m are due to increased health care costs and £230m due to productivity losses.

The study presented here endeavours to address some of the shortcomings of previous estimates. A particular gap was the lack of data on the costs of outpatient treatment. In the context of a shift in the focus of treatment from inpatient towards outpatient treatment, this was a significant blind spot. Providing estimates from English data reduce the reliance on international figures, which allows me to better reflect the English health care context. This is important because as we have seen, service consumption such as length of stay can vary significantly between countries, and it is reasonable to assume that the ratio of inpatient to outpatient costs will vary as well.

There is no single data source that would allow the calculation of a cost-of-illness for AN. In particular, there is a paucity of data on the short- and longer-term patterns of service use and associated costs. It is common in economic analyses to make use of modelling techniques to synthesise and analyse evidence from various different sources(Philips *et al.* 2004). Use of modelling approaches allows for evidence to be synthesised so that CoI studies are possible even for conditions with low prevalence

because gaps in the evidence, and uncertainties arising from small sample sizes can be addressed by the use of sensitivity analysis.

In this chapter, I present a 'conservative estimate' based on publicly available data that provides a touch stone for comparisons with previous estimates, and a 'high estimate' incorporating additional potential costs where assumptions and recourse to non-routine data sources were necessary. Given the limited availability of reliable data sources, I have combined top-down estimates (breaking down total figures to arrive at a per-case figure) and bottom-up estimates (starting with the individual case and aggregating up). Judging by my review of the existing literature, this study is the most comprehensive estimate of the costs associated with AN in England to date.

METHODS

LITERATURE AND DATA REVIEW

A literature and data review was performed at the outset of the project to identify known costs of AN, and any gaps in the existing research.

I reviewed available datasets to identify potential sources of parameters for the cost of illness estimate. This included routine datasets and large population surveys.

In particular, I searched for sources of data on:

- Incidence of AN and related disorders for England;
- Detection rates in primary care;
- Referrals to secondary/tertiary care;
- Care pathways;
- Treatments provided for AN;
- Service use;
- Economic outcomes, including education attainment, employment and income.

Where no current figures for England were available, estimates from the studies presented in this thesis were used, and several of the studies (see Chapters 6 and 7) were designed specifically to address gaps in the data.

Any remaining gaps were filled using parameters from a literature search. This search had several elements, and formed the basis of Chapter 2 as well as this CoI estimate:

- A scoping search on PubMed;
- Snowball search from recent key publications, such as the NICE guidance documents on eating disorders, and the most recent review of cost-of-illness studies available;
- Search of indexes of key journals (International Journal of Eating Disorders and European Eating Disorders Review);
- Expert consultation with colleagues at the IoP and KCL;
- Grey literature searches using the Google search engine.

Following this initial search, a PubMed alert was set up to monitor new publications with the keywords *anorexia* and *eating disorder* in the abstract or title.

SENSITIVITY ANALYSIS

To address the uncertainty arising from the fact that data from different sources are combined, and the uncertainty surrounding individual parameters, perform deterministic sensitivity analysis by presenting two scenarios:

- A 'conservative estimate', based on publicly available data sources such as the Hospital Episode Statistics (HES) and data on benefit receipt from the Deportment for Work and Pensions (DWP). Productivity losses are based on DWP claimants data. The approach of using publicly available data means that this estimate is (to some extent) comparable to previous work by The King's Fund (2008) and ProBono Economics (ProBono Economics 2012).
- A high cost estimate' that incorporates assumptions and parameters from the literature and data from studies that were part of the ARIADNE programme to account for other potential costs that may not be reflected in the publicly available data. This 'high cost estimate' includes potential additional admissions and outpatient contacts due to AN recorded under different diagnoses, family expenditure on private sector inpatient provision (either out of pocket or funded by insurance), estimates of A&E visits and primary care costs.

Additionally, productivity losses are calculated from estimated lost earnings associated with disability based on

- DWP claimants data and
- An estimated number based on results from Chapter 6.

Finally, estimated losses associated with Years Lived with Disability (YLD) are calculated for possible valuations of a year at full health of £15,000, £20,000 and £30,000.

Therefore, I present two scenarios each for service costs and productivity losses, and three scenarios for losses associated with loss of life and reduction in quality of life.

DATA SOURCES

PREVALENCE OF AN

The likely prevalence of AN by age group was estimated based on the most recent analysis of incidence in the General Practice Research Database (Micali *et al.* 2013) and parameters for the average duration (Steinhausen 2009) and mortality rates from AN based on a review of the recent literature (Arcelus *et al.* 2011) using the freely available DISMOD II software (Barendregt *et al.* 2003). These results are presented in Chapter 7.

PRIMARY CARE COSTS

The conservative estimate of primary care costs draws on estimates from the ProBono Economics report (ProBono Economics 2012), which combined information on the number of GP contacts by patients with AN presented by NICE (National Institute for Clinical Excellence 2004) – in turn based on the Third National Survey of Morbidity in General Practice – and a prevalence estimate for AN to arrive at a figure of three GP visits per year for each prevalent case of AN. Little is known about the service use of people with AN prior to entering treatment, but there is some evidence on elevated service use up to five years prior to diagnosis (Lask *et al.* 2005; Ogg *et al.* 1997). For the higher cost estimate, this study draws on baseline information from the three trials presented in Chapter 5 to estimate a plausible range of primary care costs (GP services, nurses, dieticians) incurred prior to an inpatient admission or outpatient treatment. Where treatment is provided exclusively in primary care, it is assumed that each person is in contact with their GP three times per year, as in the conservative estimate. National unit costs for GP visits were applied (Curtis 2011).

SECONDARY AND TERTIARY CARE

The Hospital Episode Statistics (HES) provides information on admissions to NHS hospitals in England and outpatient treatment in hospitals. Summary data are routinely published on an annual basis, so that no analysis of HES data was undertaken for this thesis. Classification is based on ICD-10 diagnostic codes. Summary data are publicly available by primary diagnosis, and since 2013/14 also by all diagnosis, i.e. including

additional diagnoses. It includes non-residents treated in English hospitals and private patients treated in the NHS.

HES include data on the number of inpatient, outpatient and A&E contacts at NHS hospitals in England (HESonline 2011). The proportion of cases treated primarily on an inpatient and outpatient basis were calculated by combining HES data with the prevalence estimate (number of cases) and information from the literature review as follows: I assume that around a third of AN cases are treated exclusively in primary care (Currin *et al.* 2006). Based on the number of episodes recorded in HES, I estimate that around 11% of prevalent cases are treated as inpatients each year. This suggests that 56% are treated primarily on an outpatient basis.

COST OF INPATIENT AND OUTPATIENT TREATMENT

The number of inpatient admissions, number of bed days and outpatient contacts recorded under a primary diagnosis of AN were obtained from the publicly available data from the Hospital Episode Statistic for 2010/1120 and the Special Interest Topic on ED for the same year (HESonline 2011). Since a detailed breakdown by age was not available, the ratio of adult (63%) to child (37%) of Finished Consultant Episodes (FCEs) from the Special Interest Topic report was applied when costing inpatient stays. This served as a lower-bound estimate for inpatient costs because admissions that are causally related to AN may not be recorded under a primary diagnosis of AN, but under the primary presenting problem such as cardiac problems. To obtain a higher bound estimate, the ratio of costs for medical inpatient admissions to ED admissions from the Care Pathways Study was applied. The higher estimate also includes potential additional outpatient care costs, based on the ratio of the costs of ED-related and medical outpatient appointments to ED inpatient costs from the Care Pathways Study, across all three pathways (38% and 27%, respectively). This includes treatment provided in community settings. An ad-hoc analysis of data relating to patients treated in the private sector (also from the Care Pathways Study) indicates that outpatient treatment makes up a much smaller proportion of costs than in the public sector. I therefore apply this additional cost only to NHS beds (51% of ED inpatient costs).

[20] Note that this was not an analysis of individual-level HES data.

COST OF INDEPENDENT SECTOR PROVISION

The likely cost to the NHS of inpatient treatment provided by the independent sector, and additional costs of privately funded treatment are calculated based on the assumption that 49% of ED beds are provided by the private sector (Royal College of Psychiatrists 2012), and 90% of independent beds are NHS funded (O'Herlihy *et al.* 2003b). The remaining 10% were assumed to be funded privately or through private insurance.

BENEFIT RECEIPT

Social security benefit payments made to people due to ED were obtained from the Department for Work and Pensions. There were on average 810 female claimants of Employment Support Allowance (ESA) for ED per quarter, with an average weekly amount of £90.25. Incapacity Benefit (IB) or Severe Disablement Allowance (SDA) was paid to 1,308 females each quarter, with a weighted average weekly amount of £56.04. As the statistic does not distinguish between different EDs, I assumed that the proportion of benefits paid to people with AN corresponded to the proportion of ED admissions for AN in HES (71% of FCEs). For the high cost scenario, the number of people receiving benefits for AN were estimated based on the finding from my analysis of the BCS-70 (see Chapter 6) that showed people with AN to be 6.3 times as likely to be disabled in adulthood. This resulted in 824 claimants for ESA and 2,399 for IB or SDA.

LOST PRODUCTIVITY

Lost productivity from an increased risk of disability (see Chapter 7) was calculated based on the number of claimants as above. For those claiming ESA, the amount forgone was calculated as the difference between median full time and median part time annual wages for females, while for those on IB and SDA, it was calculated as the median full-time wage from the Annual Survey of Hours and Earnings (ASHE, table 1.7a). Assumptions for discounting to present value were an average age of women with AN of 26, based on my prevalence calculations (see Chapter 7), and a retirement age of 62.3. This was adjusted for the average probability of unemployment for women, the average between the estimate from the Census and the Labour Force Survey of 4.1%. Lost earnings for someone claiming ESA is therefore estimated at £13,892, and for someone claiming IB or SDA at £22,492.

YEARS LIVED WITH DISABILITY AND YEARS OF POTENTIAL LIFE LOST

YLD and YPLL were calculated based on based a survival analysis by Harbottle and colleagues (2008), an average life expectancy of 82 a standardised mortality rate of 5 and a discount rate of 3.5%. YPLL were valued at £30,000 (with sensitivity values of £15,000 and £20,000), and a 46% reduction was applied to account for the likely disability weight of AN. Details on the methods and full results of the disease modelling study used to generate these data can be found in Chapter 7.

OVERVIEW OF PARAMETERS AND ASSUMPTIONS

Table 8-1 provides an overview of parameters and assumptions for the 'conservative' and the 'high' estimate.

Table 8-1: Parameters and assumptions used in the CoI estimate

Parameter	Assumptions conservative estimate	Assumptions high estimate
ED inpatient costs children	1,370 admissions for females with AN (HESonline 2011) (71% of ED admissions, HESonline 2011) Average length of stay 55.1 days (HESonline 2011) 37% of FCEs for AN in people < age 18 (HESonline 2011) Unit costs: £473 adults, £491 children	Additionally: Medical inpatient costs were 29% of ED inpatient costs (Care Pathways Study; Chapter 5)
ED inpatient costs adults		
Private sector NHS funded	N/A	90% of independent beds are NHS funded (O'Herlihy *et al.* 2003b)
Privately funded treatment	N/A	• 49% of beds provided by the independent sector (Royal College of Psychiatrists 2012) • 90% of independent beds are NHS funded (O'Herlihy *et al.* 2003b)
Outpatient costs children	110 first appointments (HESonline 2011) 8,025 subsequent appointments (HESonline 2011) 78 telephone appointments (HESonline 2011) Unit costs:	• Ratio: Outpatient costs due to ED are 38% of inpatient costs (Care Pathways Study) • Ratio: Medical outpatient sessions are 27% of inpatient costs (Care Pathways Study)
Outpatient costs adults		
A & E	N/A	Distribution of treatment assumption from A&E contacts in CASIS and MOSAIC: • 32% of later inpatients with average 2.5 contacts for ED • 19% of later outpatients with average 1.8 contacts for ED
Primary care	3 GP visits per person with AN (prevalence based, from ProBono Economics 2012) Unit costs:	Distribution of treatment assumption (Currin, Schmidt et al. 2006, HESonline 2011) GP (CASIS, MOSAIC): • 86% of later inpatients, average 8.9 contacts • 88% of later outpatients, average 6.2 contacts

Parameter	Assumptions conservative estimate	Assumptions high estimate
		Nurse (CASIS, MOSAIC): • 46% of later inpatients, average 11.3 contacts • 56% of later outpatients, average 6.2 contacts Dietician (CASIS, MOSAIC): • 6% of later inpatients, average 6.4 contacts • 8% of later outpatients, average 6.4 contacts
Productivity losses	£13,892 per ESA claimant £22,492 per IB or SDA claimant Discount rate 3.5% Unemployment rate 4.2%	• £13,892 per ESA claimant • £22,492 per IB or SDA claimant • Discount rate 3.5% • Unemployment rate 4.2%
Years Lived with Disability and Years of Potential Life Lost	N/A	Disease modelling Chapter 7, following (Harbottle *et al.* 2008) • Mortality and life expectancy for AN based on ONS data • SMR anorexia 5.68 (Arcelus *et al.* 2011) • Discount rate 3.5% • Value per life year £30,000 (sensitivities: £15,000, £20,000) • Disability weight 0.54 (Kruijshaar *et al.* 2005)
Benefit receipt (transfer payments)	Proportion of benefit claimants attributable to AN vs other ED is the same as the proportion of ED admissions due to AN (71%,) Employment & Support Allowance (ESA); DWP data: 810 claimants per quarter Average weekly amount £90.25 Incapacity Benefit (IB)/Severe Disability Allowance (SDA); DWP data: 1,308 claimants per quarter Average weekly amount £56.04	• Odds ratio of disability is 6.3 for women with AN (BCS-70 study) • Female population of England is 26.97m (ONS figures) ESA, from DWP data: • 299.6k claimants per quarter → 824 claimants with AN • Average weekly amount £76.75 IB/SDA from DWP data:

Parameter	Assumptions conservative estimate	Assumptions high estimate
		• 850.3k claimants per quarter →2,399 claimants with AN • Average weekly amount £57.39

RESULTS

Table 8-2 shows the results of the low and high estimates for 2010/11 by type of cost (direct, indirect, intangible or transfer payment) and cost category.

Table 8-2: Conservative and high estimate of the annual costs of AN in England (2010/11 prices)

Type of cost	Cost category	Conservative*	High*
Direct costs	ED inpatient adults	£20,900,000	£27,000,000
	ED inpatient children	£12,700,000	£16,300,000
	Private sector NHS funded	£0	£14,800,000
	Privately funded	£0	£1,600,000
	Outpatient adults	£900,000	£13,700,000
	Outpatient children	£600,000	£8,100,000
	A&E	£0	£400,000
	Primary care	£5,000,000	£7,000,000
Indirect costs	Productivity	£40,700,000	£65,700,000
Intangible costs	YPLL	£0	£97,100,000
Transfer payments	Benefits	£4,900,000	£10,400,000

*Rounded to nearest 100k

Between the conservative and the high estimate, there is a £6 million difference between the estimates for adults, and over £3 million for children. But the difference in the cost of outpatient treatment is ever more striking, with £11.8 million for adults and £7.5 million for children. As a percentage change, the difference in productivity losses is relatively small, at a multiple of 1.6, and similarly, the estimated size transfer payments roughly doubles.

Figure 8-1 illustrates the relative magnitudes of costs. Intangible costs are presented using a QALY valuation of £30,000. Using the alternative valuations of £15,000 and £20,000, the value reduces to £48,550,00 and £64,733,000, respectively. Years Lived with Disability are not included in this estimate.[1]

[1] Assuming an estimated YLD of around 47,000 per year, the associated loss is around £1.1bn based on a disability weight of 0.224 (Salomon *et al.* 2015) for a valuation of a disability-adjusted life year of £30,000, with £550m and £730m at valuations of £15,000 and £20,000, respectively. Given the uncertainty surrounding the disability weight and the lack of methodological robustness stemming from the use of a QALY valuation to value DALYs, these figures should be treated with caution.

Table 8-3 and

Table 8-4 show the annual costs associated with AN in 2010/11 for the conservative and high estimate, respectively, by cost perspective. Annual societal costs in the conservative estimate are £80.8 million, evenly split between healthcare costs and indirect costs, compared to £251.8 million in the high cost estimate where direct costs make up 30%, with 22% going to indirect and 48% to intangible costs. Societal costs in the high cost scenario are 3.1 times as high as in the conservative estimate.

Figure 8-1: Comparison of conservative and high cost estimate, by cost category

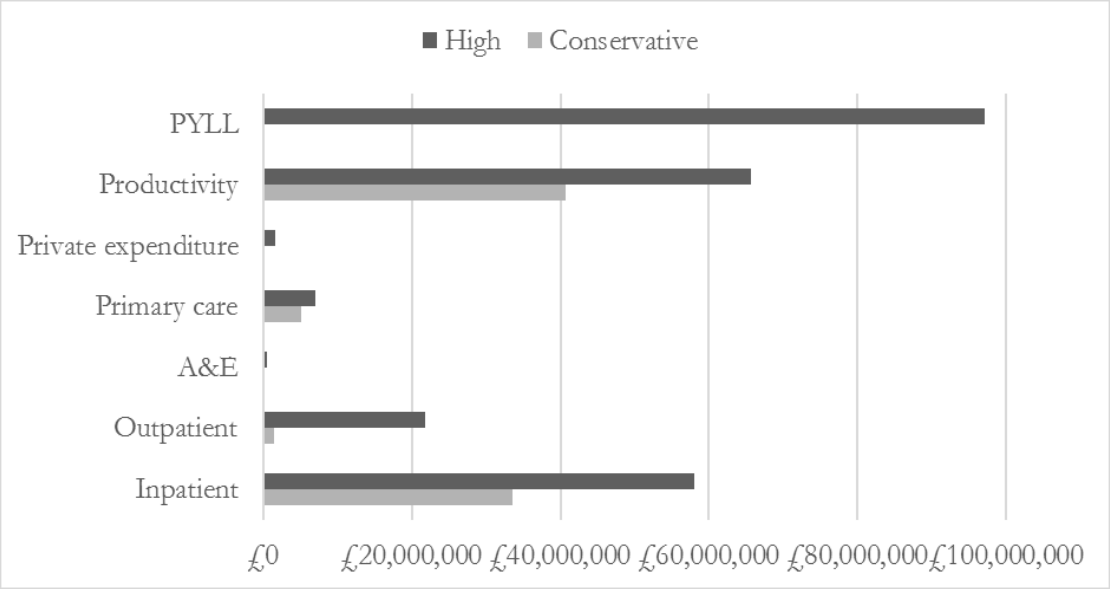


Table 8-3: Annual costs associated with AN in 2010/11, conservative estimate

	Perspective			
	Health system	***Government***	***Patients***	***Societal***
Direct costs	£40,100,000	£40,100,000	£0	£40,100,000
Indirect costs	£0	£0	£40,700,000	£40,700,000
Intangible costs	£0	£0	£0	£0
Transfers	£0	£4,900,000	£0	£0
Total	£40,100,000	£45,000,000	£40,700,000	£80,800,000

Table 8-4: Annual costs associated with AN in 2010/11, high estimate

	Perspective			
	Health system	***Government***	***Patients***	***Societal***
Direct costs	£87,300,000	£87,300,000	£1,600,000	£89,000,000
Indirect costs	£0	£0	£65,700,000	£65,700,000
Intangible costs	£0	£0	£0	£97,100,000[2]
Transfers	£0	£10,400,000	£0	£0
Total	£87,300,000	£97,800,000	£67,300,000	£251,800,000

In the conservative estimate, costs to the health care system are around £40 million, which more than doubles in the high estimate to £87 million where the costs of (potential) additional admissions, outpatient appointment and expenditure on private services are considered. Costs in the government perspective, which additionally includes transfer payments, also more than double from £45m to £97.8m. In addition to the doubling of health care costs, this is driven by the large increase in the estimated number of people receiving IB or SDA. From the perspective of patients and families (which is represented here in a very limited way), costs increase by 70%.

In the conservative estimate, over 40% of costs are due to inpatient treatment (Figure 8-2). Outpatient treatment accounts for only 2%, or 4% of all healthcare costs. In our high estimate, outpatient treatment accounts for 8% of total costs (see Figure 8-3) and 25% of healthcare costs. The cost of outpatient treatment in the high cost scenario are over a third of the costs of inpatient treatment.

[2] Using the alternative valuations of £15,000 and £20,000, the value reduces to £48,550,00 and £64,733,000, respectively.

Figure 8-2: Distribution of costs, conservative estimate

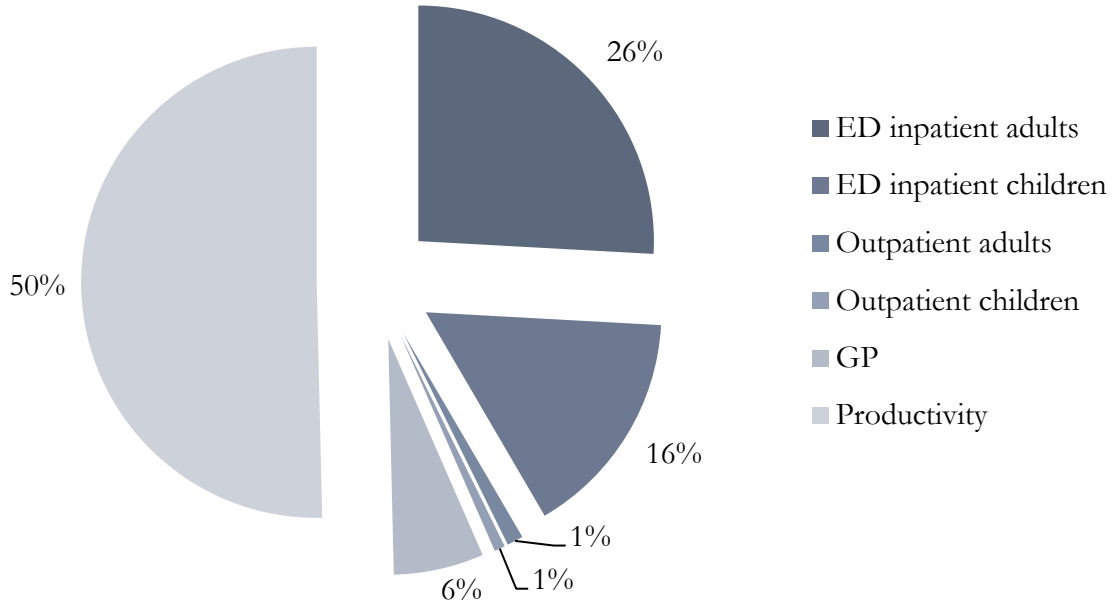


Figure 8-3: Distribution of costs, high estimate

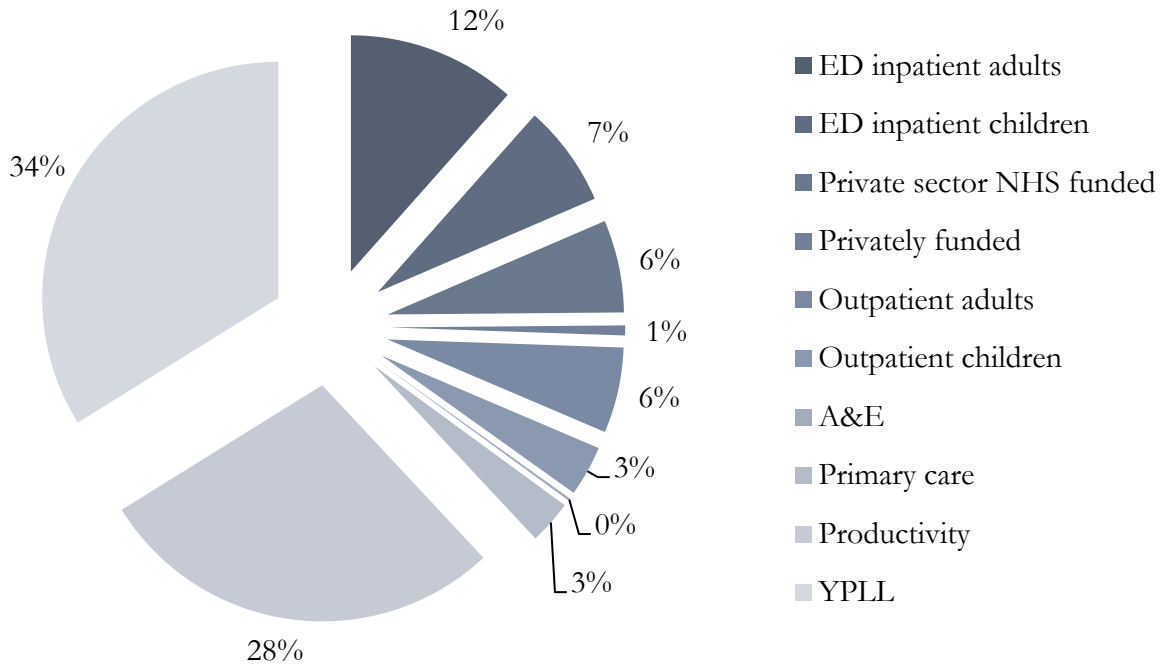


Figure 8-4 and Figure 8-5 show the impact of varying the cost-effectiveness threshold from £15,000 to £20,000 and £30,000. As expected, with an increasing valuation there is a linear increase in the estimate of intangible cost, and the contribution of intangible costs to total costs increases.

Figure 8-4: Total societal costs by scenario

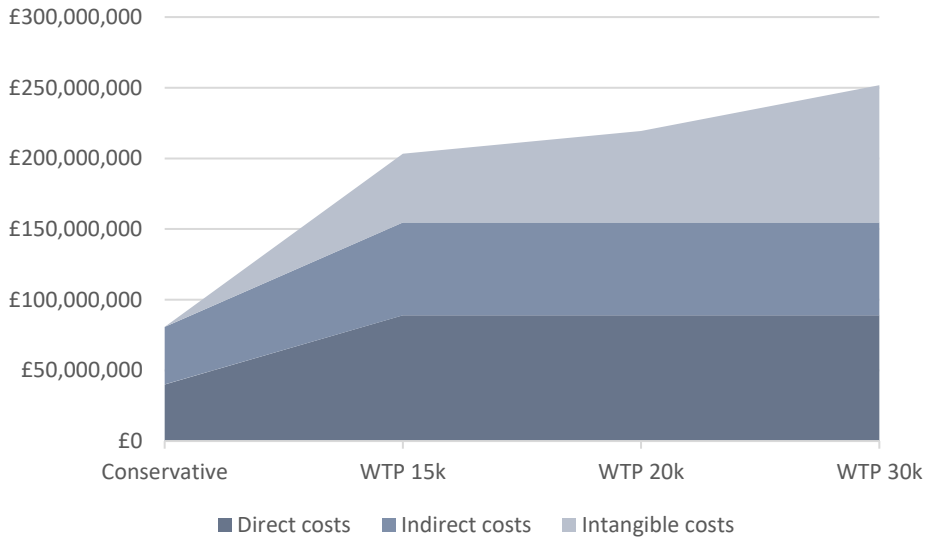
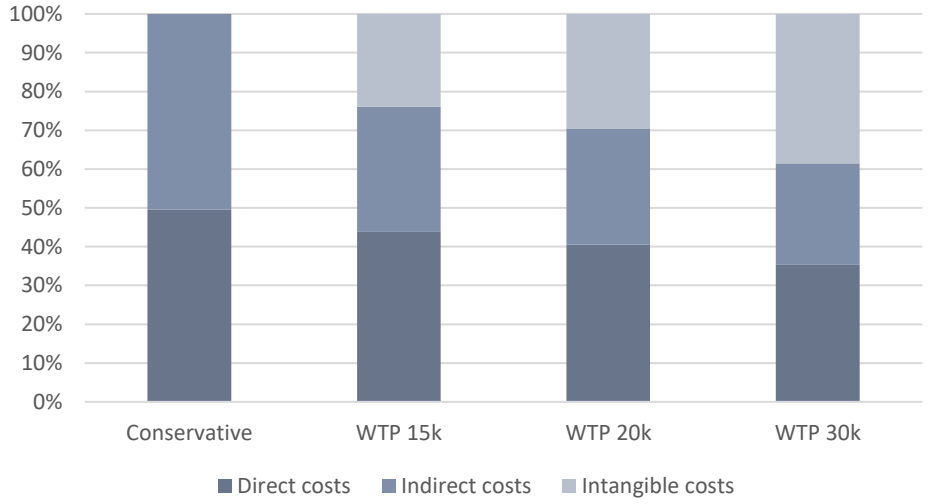


Figure 8-5: Proportion of total costs attributable to cost categories, by scenario



DISCUSSION AND SUMMARY

Any study of the social costs of AN is currently limited by poor data availability, in part due to the small number of cases that make it difficult to recruit sufficient numbers for research, and pose confidentiality issues in routinely collected data. Assumptions are therefore needed to come up with reasonable estimates. While there are many potential points of contention in the assumptions made to put together the estimate above, a few are likely to have a significant impact on results and are worth discussing.

It is unclear how many people with AN receive treatment and in what setting. Our assumption focusses on the main treatment setting, while in reality, there will be overlaps, with people admitted for inpatient treatment who previously or subsequently receive outpatient treatment, and who may have concurrent input from their GP.

Moreover, it is difficult to account for undetected cases. The 'true' prevalence of AN may be 2-3 times as high as estimated from either self-report or within services(Hoek 1991), and it is unclear what the cost implications of this may be. Similarly, it is currently not possible to estimate costs related to sub-threshold AN, as few data are available. In addition, there is a tendency in the literature to report research findings without distinguishing sub-threshold anorexia and bulimia – which is in line with the current diagnostic manual for psychiatric conditions.

Estimating the exact amount of benefits paid due to AN is difficult despite the availability of DWP data. While the majority of claimants received benefits for five or more years, this calculation may overestimate benefit receipt because the data do not show how many people start or stop claiming benefits within a quarter. The available data breakdown is not very precise due to the small number of claimants for AN, and the need to protect the identity of these individuals.

Finally, there are uncertainties surrounding the data from Hospital Episode Statistics. Data are available by diagnosis, but admissions linked to AN may happen for various reasons, such as cardiac problems, self-harm or other medical problems. This is apparent from the Care Pathways data. Further, the average length of stay reported in HES is much lower than that reported by a recent RCP survey of ED services in the UK (Royal College of Psychiatrists 2012) which reported a length of stay of over 18 weeks, and a recent study on

the duration of stay in UK Specialist ED Units reported an average length of stay of 26 weeks for adults and of 29 weeks for adolescents(Goddard *et al.* 2013a). One possible explanation is that HES conflates stays in psychiatric or ED units (typically for weight restoration or other mental health concerns such as self-harm) and stays in medical or paediatric units often linked to acute medical issues, which tend to be much shorter. In addition, HES data may not be entirely reliable(Brennan *et al.* 2012). To account for this, I assumed that inpatient treatment may be much more frequent that the diagnosis-based data suggest in our high cost scenario. Given that a high proportion of AN cases is likely treated on an outpatient basis, and given that the number of sessions required is generally high, the small contribution of outpatient costs in our conservative estimate is surprising, and it is possible that there are again issues with the underlying data. Here, I therefore estimated potential additional costs in the high cost scenario, but uncertainty remains.

It is difficult to compare this estimate to the recent work by ProBono Economics (ProBono Economics 2012) because it did not distinguish costs by type of ED. However, some differences are due to different unit costs applied to incidents of service use and differences in data sources. For example, while HES showed around 8,000 outpatient contacts for 2010/11, the ProBono Economics estimate cites unpublished data suggesting the number may be much higher (18,000). Other differences arise from the way private sector healthcare costs were treated. While HES reports data on both NHS beds and NHS commissioned private sector services, the ProBono Economics estimate assumed the HES data referred only to NHS beds, thus arriving at a much larger figure for additional private costs (£45m vs £1.6m).

Two areas of costs outside the public sector should also be mentioned. While the study using BCS-70 data did not show an impact on earnings in adulthood, there is reason to believe that AN is associated with productivity losses both from absenteeism (time taken off due to illness) and presenteeism (lower productivity when at work due to illness), and that the impact may be large. While no estimate of the reduction in productivity associated with AN is available, Goetzel and colleagues (Goetzel *et al.* 2004) reported an average impairment of daily productivity due to depression, sadness or mental illness of 10.7%. Moreover, with an average length of stay of over 50 days, the impact of hospitalisation on the ability to attend work is clearly severe. These reductions in productivity likely not only

affect patients, but also carers and partners, who often experience high levels of psychological distress, depression and anxiety (Zabala *et al.* 2009).

Cost related to informal care provided to people with AN by their family and friends have also been excluded from this estimate. The analysis of data collected in the CASIS study shows that up to three quarters of carers spent nearly a full day per week providing ED-related care (Raenker *et al.* 2013), with potential impacts not only on their health and wellbeing but also on their capacity to engage in paid employment. This is a relevant impact that should not be ignored, especially in the context of service developments that shift provision from inpatient to outpatient treatment, where higher levels of informal care may replace formal provision.

While I attempted to integrate findings from the ARIADNE studies into the estimate, the limited data available did not allow for a reliable estimate of total costs by ethnicity, gender and ED severity, although costs are distinguished by broad age group where possible. As more data from the ARIADNE studies and the large cohort studies become available, it may be possible to address the gaps in the estimate highlighted here.

However, to my knowledge, this is the most comprehensive and detailed estimate of the societal costs of AN for England to date, and fills a significant gap in the literature that has been repeatedly highlighted (Striegel Weissman & Rosselli 2017). It improves upon existing estimates by incorporating data beyond what is available through routine collection. This approach means that costs can be stratified further, and additional cost categories can be included. A full comparison of this CoI estimate against existing estimates for England is provided in Chapter 9.

While the data sources used in the conservative estimate are potentially more reliable, limiting a CoI estimate to such data is also likely to lead to an underestimation of actual costs. The high cost estimate incorporates a broader range of costs and is therefore more suited to capturing the complexities of AN. At the same time, these additional parameters may not be representative of the population with AN as a whole, as they are drawn from clinical studies. Another caveat is that there are still categories of costs that are omitted, such as caregiver burden, wider service use such as involvement of police or social care, travel costs necessary to attend for treatment, and out-of-pocket expenditure (e.g. for child care or additional foods or diet aids). There is also no estimate for males. On balance, both

estimates are likely to be 'wrong' in various ways, but the 'high' estimate is more likely to capture the broader burden of AN on individuals and society.

This study combined the results from the preceding empirical chapters with publicly available data and previous findings from the literature to estimate the annual costs of Anorexia nervosa to society in England for 2010/11. This addresses RQ5: "What are the annual societal costs of AN in England?" and accomplishes the overarching aim of this thesis.

In addition to carefully updating the evidence on the costs of AN to society, this study is the first in England to estimate costs of outpatient services beyond figures published in the Hospital Episode Statistics.

- Direct costs ranged from £40.1 million to £89 million.
- Indirect costs ranged from £40.7 million to £65.7 million.
- Intangible costs in the high cost scenario were calculated at £49 million to £97.1 million.
- Transfer payments were estimated from £4.9 million to £10.4 million.
- Total societal costs ranged from £80.8 million to £251.8 million.
- In the conservative estimate, direct and indirect costs each account for 50% of costs.
- In the high estimate, direct costs account for 30% of costs, indirect costs for 22% and intangible costs for 48%.

The largest relative increase in costs from the conservative to the high estimate is seen in the costs associated with outpatient treatment, reflecting a large uncertainty regarding the data arising from a discrepancy between routine data sources and reporting in the literature.

The ratio of costs associated with inpatient treatment to the costs associated with outpatient treatment in the conservative estimate is 22.4:1 (£33.6 million to £1.5 million), reducing to 2.7:1 in the high estimate (£59.7 million to £21.8 million). This is a better representation of the English health care context than figures drawn from international studies.

Several limitations remain. There is uncertainty around the magnitude of costs associated with outpatient services and wider service use. A cautious approach was taken to including

productivity losses and costs from excess mortality. Insufficient data were available to estimate costs associated with caregiving, travel or out-of-pocket expenditure.

CHAPTER 9

Discussion and policy implications

CHAPTER INTRODUCTION

The aim of this thesis was to present the annual societal costs associated with AN in England, and to explore why these costs may vary between individuals. The contribution of this thesis to the evidence base is an updated estimate of these societal costs, including a range of direct costs beyond hospital-based treatment, a more appropriate treatment of productivity losses based on analyses of economic outcomes using two major cohort studies and an estimate of costs associated with excess mortality using disease modelling techniques.

My survey of the available literature – focussing on information for England – showed that there was a particular gap in information about the costs of treatment provided in an outpatient setting. Little was also known about what treatments and wider services people with AN receive, the costs associated with this service use, and why costs may vary.

Using a range of econometric and economic modelling techniques, the thesis addressed each of these gaps in turn. The research questions were as follows:

- RQ1: What treatments are provided for AN in an outpatient context, what are the associated unit costs, and why do these costs vary?
- RQ2: What services do people use while being treated for AN on an outpatient basis, what are the associated costs, and why do these costs vary?
- RQ3: What is the impact of AN on education, employment, income and related outcomes?
- RQ4: What is the loss of life associated with AN in England?
- RQ5: What are the annual societal costs of AN in England?

The thesis is situated within the theoretical context of economic decision analysis. Three types of economic costs linked to health conditions are commonly distinguished, and my research questions map onto these types of costs as follows:

- RQ1 and RQ2: Direct costs arising directly from a condition, such as health care expenditure;
- RQ3: Indirect costs that are related to the condition but are not cash expenditure, such as productivity losses.

- RQ4: Intangible costs are those that are not easily quantified in monetary terms, for example the value of a life lost due to premature mortality.
- RQ5 is an overarching question that ties together the three types of economic costs under the umbrella of societal costs.

In this final chapter, I discuss my findings with regard to the societal costs of AN in England in the context of previous estimates and the wider literature to highlight the distinct contribution to knowledge. I summarise the strengths and limitations of the study and discuss the implications of my findings for policy, practice and future research. Concluding thoughts follow.

THE SOCIETAL COSTS OF ANOREXIA NERVOSA IN ENGLAND: WHAT HAVE WE LEARNED?

The aim of this thesis was to present an estimate of the annual societal costs of AN in England. In Chapter 8, I presented the estimate for 2010/11:

- Direct costs ranged from £40.1 million to £89 million.
- Indirect costs ranged from £40.7 million to £65.7 million.
- Intangible costs in the high cost scenario were calculated at £49 million to £97.1 million.
- Transfer payments were estimated from £4.9 million to £10.4 million.
- Total societal costs ranged from £80.8 million to £251.8 million.

Different cost perspectives were also considered. Notably, the cost to the health care system accounted for 50% of costs in the conservative estimate, and for 30% of costs in the high estimate. The implication is that a considerable burden of the cost of AN falls on individuals.

Previous estimates of the costs of AN for England were uprated to 2010/11 prices using the Gross Domestic Product deflator to allow for a more direct comparison (see Table 9-1). Below, I compare the studies in terms of direct, indirect and intangible costs, with a particular focus on the most recent estimate (ProBono Economics 2012)..

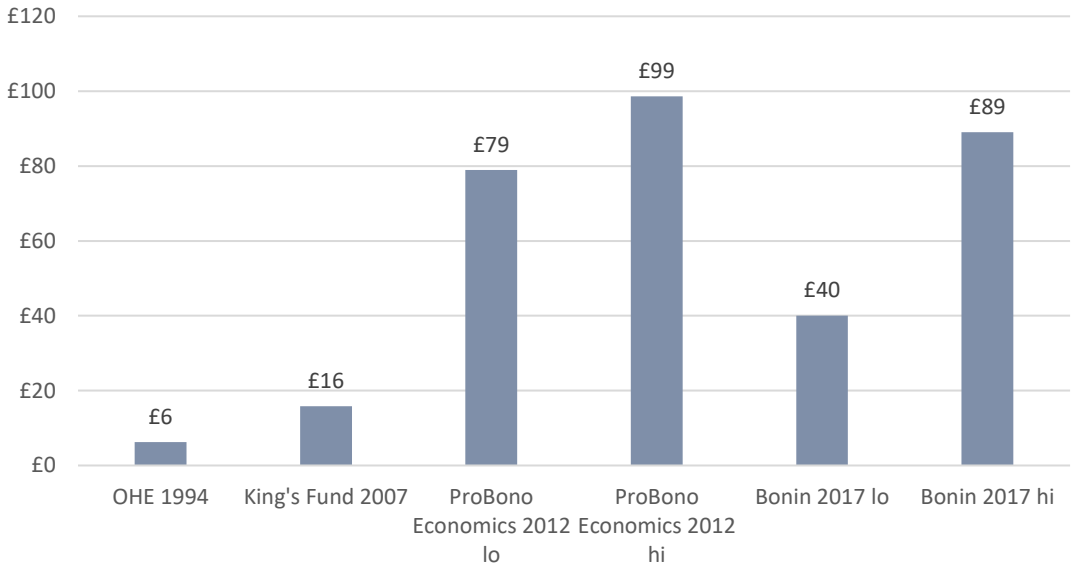
Table 9-1: Comparison of CoI estimates for England, 2010/11 prices (£million)

Study	Direct	Indirect	Intangible	Total costs
OHE 1994	£6	-	-	£6
King's Fund 2007	£16	£35	-	£51
ProBono 2012 lo	£79	£178	£158	£414
ProBono 2012 hi	£99	£2,219	£888	£3,205
Bonin 2017, lo	£40	£41	-	£81
Bonin 2017, hi	£89	£66	£97	£525

DIRECT COSTS

Estimates of direct costs per year increased from £6 million in 1994 to up to £99 million in 2012, with my conservative scenario of £40 million falling approximately in the middle (see Figure 9-1). But what are the reasons for this heterogeneity?

Figure 9-1: Comparison of estimates of direct costs of AN, 2010/11 prices (£million)



COSTS OF INPATIENT CARE

A closer look at the cost of inpatient care helps to illustrate the potential causes. All four estimates use routine data sources to estimate the costs of inpatient treatment, namely Hospital Episode Statistics (HES) or, in the case of the Office of Health Economics estimate, the Hospital Inpatient Enquiry. Comparing the three studies using HES-type data, I find the following differences and commonalities in the approach:

All studies used inpatient bed days as the basis for their calculations.

- King's Fund: 73,153 bed days for AN and BN combined. The assumption was that 95% of these were due to AN.
- ProBono Economics: 98,000 bed days for AN and BN combined.
- Bonin: 76,644 bed days in females with AN.

All studies made an assumption about the proportion of admissions occurring in younger vs older patients, although the age range of interest varied. This had implications for the unit cost applied (ProBono Economics, Bonin) and the proportion of total inpatient days included in the estimate (King's Fund).

- King's Fund: ¾ of inpatient days occurred in people below age 35, who were the focus of the study.
- ProBono Economics: Assumes that adult admissions cost about twice as much as children's.
- Bonin: 37% of FCEs for AN occur in patients aged under 18.

All studies drew on publicly available unit costs for inpatient days (presented here in 2010/11 prices):

- King's Fund: £213, based on the PSSRU unit cost volume 2006 (Curtis & Netten 2006).
- ProBono Economics: £503 based on the average of unit costs for specialist ED services and children's specialist services from the PSSRU unit cost volume for 2009/10 (Curtis 2010), which reports on NHS reference costs.
- Bonin: £480, weighted cost of ED inpatient days based on NHS reference costs (Department of Health 2011).

This analysis demonstrates that even though similar assumptions and data were used to derive these estimates, differences in assumptions can lead to a wide variation in costs – in this case, ranging from £11 million from the King's Fund estimate to £49 million in the ProBono Economics estimate (although this includes inpatient costs for BN).

COSTS OF OUTPATIENT CARE

The largest relative increase in costs between my conservative and high estimates is seen in the costs associated with outpatient treatment, reflecting a large uncertainty regarding the data arising from a discrepancy between routine data sources and reporting in the literature.

Here, estimation methods diverge between the three estimates compared above. While HES data on outpatient appointments have been published since 2003, they do not appear to

have been available at the time the King's Fund's estimate was put together, and their calculations are based on the ratio of outpatient costs to inpatient costs by Striegel-Moore (2000), 41%. The ProBono Economics estimate uses the same estimate as the King's Fund for its lower bound estimate, while the higher bound is based on unpublished HES data (ProBono Economics 2012, p. 19).

My estimate advances the approach. The ratio of costs associated with inpatient treatment to the costs associated with outpatient treatment in the conservative estimate is 22.4:1 (£33.6 million to £1.5 million), reducing to 2.7:1 in the high estimate (£59.7 million to £21.8 million).

Given that HES data on outpatient appointments are now easily accessible, they form the basis for my conservative estimate. My high estimate, on the other hand, applies what may be termed the 'ratio approach' employed by the previous estimates (i.e., applying a ratio between inpatient and outpatient treatment costs found elsewhere in the literature to new data), but I use data from the CPS – an estimate more appropriate to the English context. However, the ratio is similar to the Striegel-Moore estimate: 38% in the CPS vs 41% in the American study (Striegel-Moore *et al.* 2000). For this reason, the lower-bound ProBono Economics estimate of £20 million is very similar to my higher-bound estimate of £21.8 million. It should be noted, however, that patients in the Care Pathways Study where specifically entering for outpatient treatment, with the aim of preventing hospital admissions. It is unclear to what extent this cohort is representative of the population with AN as a whole, and it is possible that this cost ratio over-estimates outpatient treatment if scaled up to the national level. At the same time, HES data only report on outpatient appointment in hospital settings, so that there is likely a large amount of costs associated with treatment in community-based services that an estimate based on HES data would ignore.

A related issue is that of unit costs. The process of deinstitutionalisation, as outlined in Chapter 2, is defined by a shifting of service provision from a hospital to a community setting. At the unit cost level, all else being equal, service provision in a hospital is more costly than in a community setting (see data in Curtis 2011). The weighted average cost of an outpatient attendance for paediatric services from the same source was £775. The cost of an MFDT session, the most intensive form of therapy provided within the outpatient services in our study, was around £325 per family. The most commonly provided

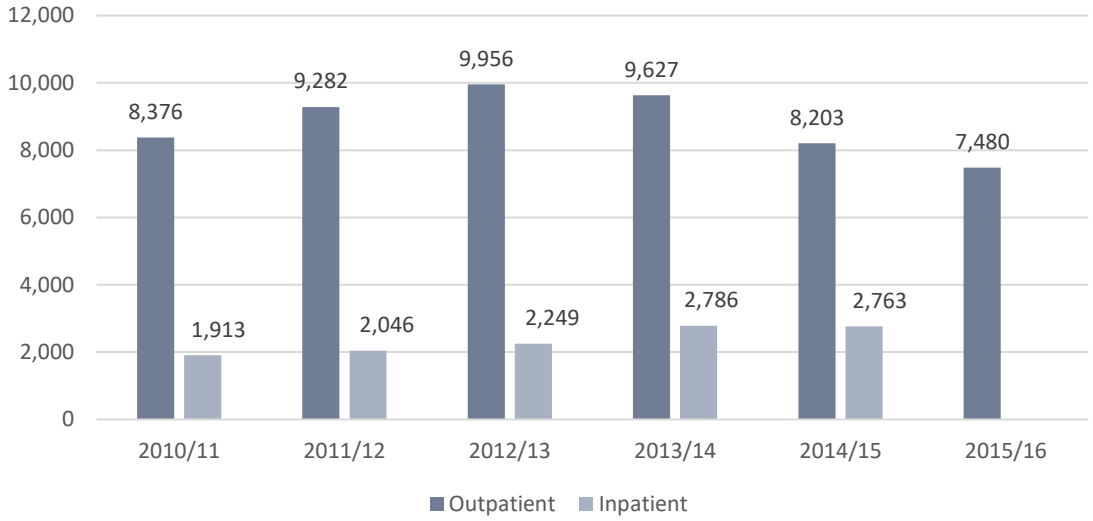
treatments, CBT and SFT, were significantly cheaper on a per-session basis - £136-£246 and £205-£246, respectively. While there is some uncertainty around these estimates, given that the information available for costing was adapted from data intended for a different purpose, the costing methods followed best practice, and these are the most comprehensive estimates of the costs of ED treatment in outpatient services to date.

While I was able to develop unit costs for a range of outpatient treatments (see Chapter 4), the lack of detail on the types of sessions provided, i.e. the nature of outpatient appointments for AN, and the lack of detailed data for community-based treatment, means that it was not possible to make good use of the new data available at this time. It is therefore uncertain whether my high estimate is too high or too low, pointing to a need for routine data collection in CAMHS.

The reliance of estimates of the costs of inpatient care, and more recently also the costs of outpatient care on HES data warrants a closer look at these data. The Hospital Episode Statistics (Herbert *et al.* 2017) provide information on admissions to NHS hospitals in England and outpatient treatment in hospitals. Classification is based on ICD-10 diagnostic codes. Summary data are publicly available by primary diagnosis, and since 2013/14 also by all diagnosis, i.e. including diagnoses in addition to the primary one. It includes non-residents treated in English hospitals and private patients treated in the NHS.

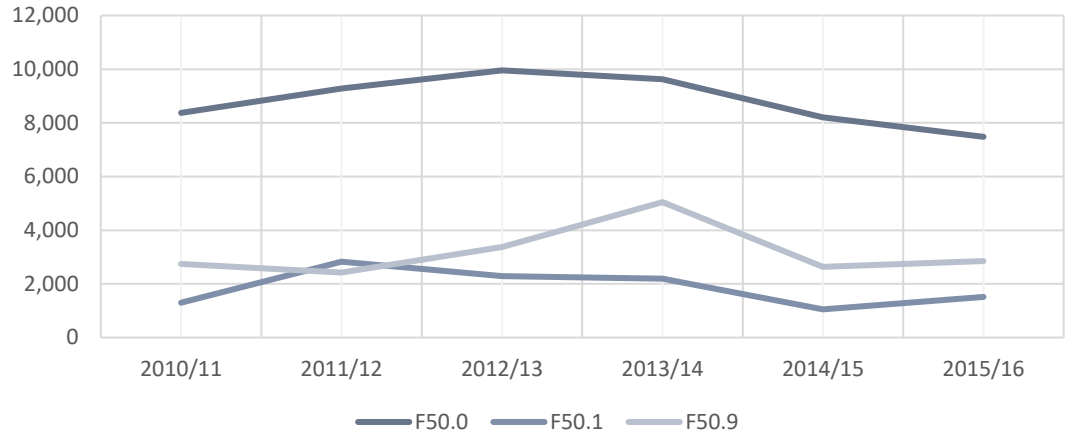
Figure 9-2 shows finished consultant episodes (FCEs) for a primary diagnosis of AN from 2010/11-2015/16. Note that inpatient data was not available for 2015/16 at the time of writing.

Figure 9-2: Inpatient and outpatient finished consultant episodes for primary diagnosis AN (F50.0), 2010/11-2015/16



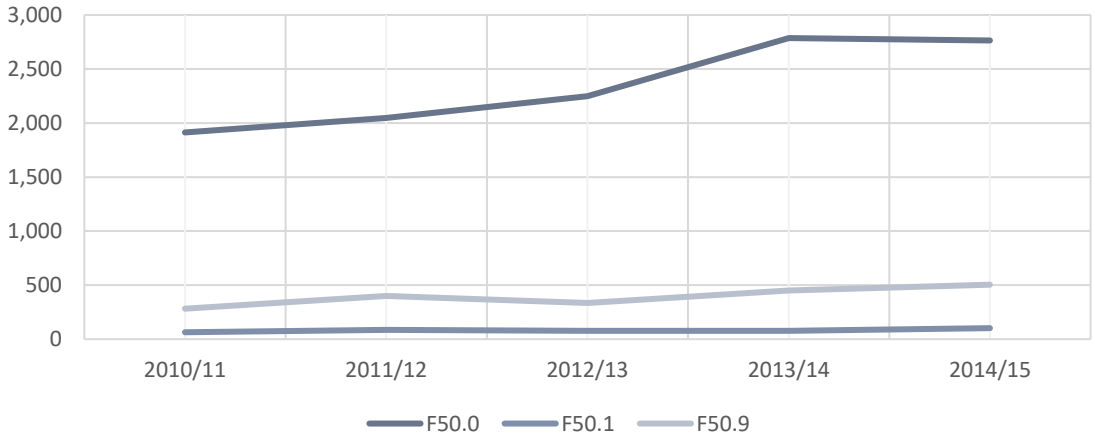
In 2010/11, there were 1,913 inpatient and 8,376 outpatient FCEs. However, data quality issues with the HES have long been recognised (Brennan *et al.* 2012), and a lack of clinician engagement with the data has been identified as a possible cause (Spencer & Davies 2012; Williams & Mann 2002). There is a particular issue with clinician-recorded diagnosis, with consistently over 95% of outpatient FCEs recorded without an ICD classification (ICD code R69.X). This can be illustrated by plotting the data on outpatient FCEs for full syndrome AN (F50.0), atypical AN (F50.1) and unspecified ED (F50.9). Figure 9-3 shows the trends for these categories: F50.9, the residual category, makes up a significant proportion of outpatient contacts for ED, and appears to increase over time, while visual inspection suggests a decreasing trend for outpatient appointments for full syndrome AN in recent years.

Figure 9-3: Outpatient finished consultant episodes for primary diagnosis AN, 2010/11-2015/16



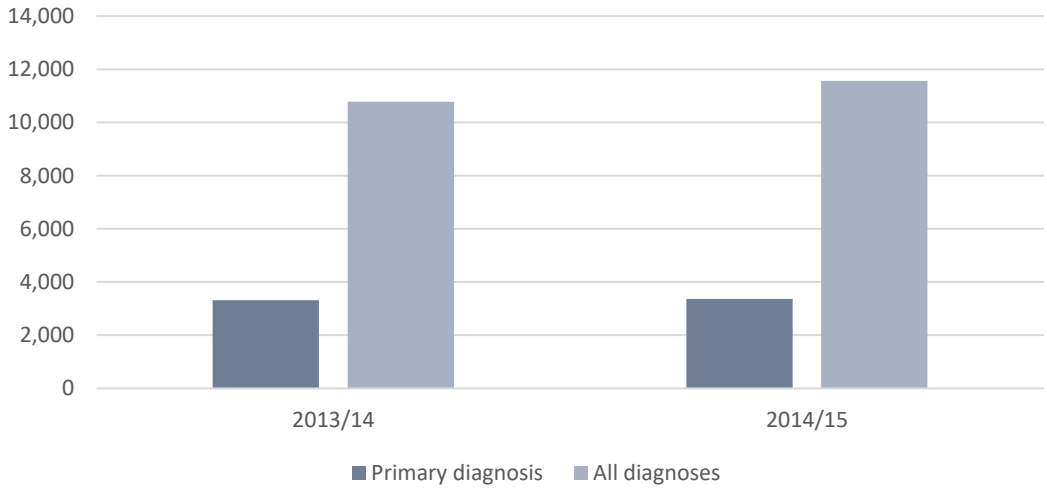
At the same time, there appears to have an uptick in admissions for both full syndrome AN and unspecified ED in 2013/14 (see Figure 9-4), which corresponds to the implementation of DSM-V criteria. As discussed above (Chapter 2), this tends to increase the likelihood of full syndrome AN being identified. However, these broad trends do not seem to reflect the shifting focus from inpatient towards outpatient treatment, at least not in a hospital setting. It is possible that overall demand for ED care increased, but data on activity in community-based services would be required to assess this claim.

Figure 9-4: Time trends in admissions for AN, atypical AN and unspecified, 2010/11 - 2014/2015



Summary data on FCEs for AN including additional diagnoses show that these are 2.6 times as high as admissions for the primary diagnosis (see Figure 9-5), and appeared to increase – although only data for two years can be shown.

Figure 9-5: FCEs for AN (inpatient), primary diagnosis vs all diagnoses



The increase in ED admissions was reported widely (Health and Social Care Information Centre 2014), and prompted a £150 million investment in service transformation over five years (Deputy Prime Minister's Office *et al.* 2014).

This brief analysis shows that HES data may not be entirely reliable. The general difficulties with data quality may be exacerbated by the fact that AN is a "disorder in transition" (Micali & Hebebrand 2015). At the same time, HES data are very influential, and in practice they are widely used in estimating CoI.

PRIMARY CARE SERVICES

Looking beyond HES data, there is a dearth of information on service use in AN. Previous estimates of the cost of AN have sometimes included primary care costs (Office of Health Economics 1994; ProBono Economics 2012), ostensibly both building the estimate from the 3rd National Survey of Morbidity in General Practice from the 1980s.

While for my conservative scenario, I use the same assumption of three GP consultation per prevalent case of AN (ProBono Economics 2012), while my high cost estimate uses

new information from my analysis of trial data (see Chapter 5, part 2), which allows me to include the costs of GP consultations as well as contacts with accident and emergency departments, nurses and dieticians, who play a prominent role in treating ED. I am also able to begin to look at the service use by patients in the time before entering different care pathways (inpatient vs outpatient treatment).

Patients later admitted to inpatient care (CASIS trial) reported on average 8.9 GP contacts, while those later commencing treatments on an outpatient basis reported 6.2 contacts. This is in line with the data presented by Byford and colleagues (Byford *et al.* 2007a), who reported six to seven contacts for their participants. This provides further evidence that the consultation rate for patients with AN may be higher than previous cost estimates have assumed – at least for adolescents in the year prior to commencing treatment in higher tier services. The finding is also in line with previous work showing that people with AN consult their GP significantly more than others in the 5 years prior to diagnosis (Ogg *et al.* 1997), and a single consultation about eating or weight and shape concerns strongly predicts the subsequent emergence of AN (Lask *et al.* 2005)..

While research into the service use and costs of people with AN has moved on considerably since the initial OHE estimate, and data availability for hospital-based services has improved, information is still lacking on community-based psychological treatment and primary care. The studies presented in this thesis represent a first step in addressing some of these data issues. The clinical trials providing data for the estimates of service use in primary care are some of the first larger-scale RCTs in AN, employed rigorous standards and were highly successful in collecting service use data from participants (Schmidt *et al.* 2017). While it is difficult to assess the representativeness of the trial population in the absence of good knowledge on the population with AN as a whole, the strength of the underlying data and the application of best practice in economic costing are strengths of the studies informing these cost estimates.

WIDER SERVICE COSTS

One limitation that I am unable to overcome with the available data is the inclusion of a robust estimate of the costs of service use beyond health care.

As presented in Chapter 5, part 2, there is some evidence that people with AN do use services such as self-help and support groups (14% in the CASIS trial and 9% in the MOSAIC trial), CAB (8% in CASIS and 6% in MOSAIC) and helplines (10% in CASIS and 11% in MOSAIC), and that some are in touch with social workers (12% in CASIS and 6% in MOSAIC). Costs associated with self-help and advice services were calculated at £32 per participant (SD £99) for CASIS and at £59 (SD £394) for MOSAIC. The costs associated with social work were £95 (SD £397) and £70 (SD £383) for CASIS and MOSAIC, respectively.

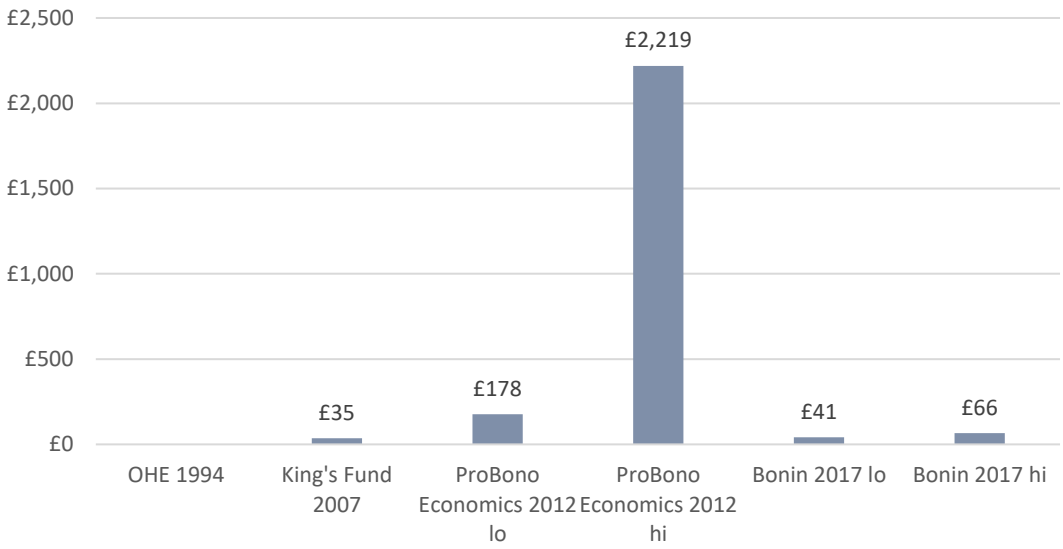
In order to include these figures in an estimate of the societal costs associated with AN, we would need to be able to establish causality between AN and service use, for example by comparing these figures to population norms. We would also need to establish whether these figures – calculated based on a 6-month period – should be 'scaled up' to an annual figure, i.e. whether the 6-month period is representative of any given 6-month period, or whether the period prior to commencing treatment for AN is qualitatively different in terms of contact with self-help services and social care. In addition, we would need to determine to what extent these figures are representative of the population with AN more generally, and how we could arrive at an average (or weighted average). Given that Byford and colleagues (2007a) find little evidence of contact with social care services in a younger cohort (aged 12-18), it is reasonable to assume some variation with age.

There was little evidence in the data collected from the trials presented in Chapter 5 that people with AN are in contact with other services, such as the police.

INDIRECT COSTS

Comparing estimates of indirect costs, I find a wide range from £35 million to £2.2 billion. Both my estimates are significantly below the ProBono Economics estimates.

Figure 9-6: Comparison of estimates of indirect costs of AN, 2010/11 prices (£million)



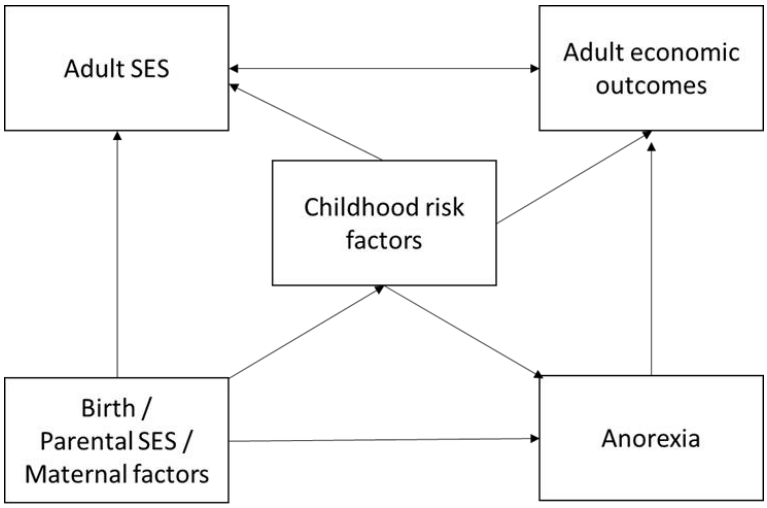
In my study using BCS-70 data (Chapter 6), I found no impact of AN on the likelihood of being in employment, education attainment or on wages. Similarly, my study of ALSPAC data did not show an effect of AN on GCSE-attainment. For this reason, I only include productivity losses based on the number of women with AN who received certain types of benefits, based on DWP data. This was justified because the BCS-70 analysis showed a significantly higher chance of being sick or disabled in terms of economic activity status.

I was unable to explore questions related to under-employment, i.e. whether women with AN were more likely to be in an occupational class that was lower than expected, given their level of education. However, women with AN were more likely than those without an ED to be in occupational classes I or II, if they were employed.

In addition, it is possible that there are weaknesses in the analysis approach beyond what has already been discussed: the amount of missing data with the possibility that these are not missing at random, the small sample size and the uncertainty about the predictor variable. Note that these limitations apply to both the analysis of ALSPAC and the BCS-70.

Conceptually, the underlying relationships are perhaps better represented by Figure 9-7, as there are likely complex relationships between the variables entered into the regression models.

Figure 9-7: Path model



In addition to the question whether productivity losses in terms of lost employment should be included at all, there is an issue around valuation of productivity losses. As discussed in Chapter 2, the primary productivity-based approach (the human capital approach) has been criticised for bias against those with lower market wages.

To avoid this pitfall at least in part, I used the median wage for women. Other acceptable choices would have been the average wage for women, the overall average or median, the minimum wage or the living wage. I did not assume that income would increase over time in line with long-term productivity growth, and did not make any assumptions that are often made in a human capital context regarding the inclusion of salary oncosts.

In contrast, the ProBono Economics calculation drew on an estimate of the impact of emotional disorders in childhood on earnings, included 2% real wage growth, adjusted for the probability of being employed and then discounted to present value, which yielded a present value of lifetime earnings of £0.64 million per person. The alternative calculation was a 7% reduction in earnings, which then came to £45,000 per person (excluding any

additional overheads). Differences in the total estimate also arise from assumptions about prevalence, which I discuss below.

INTANGIBLE COSTS

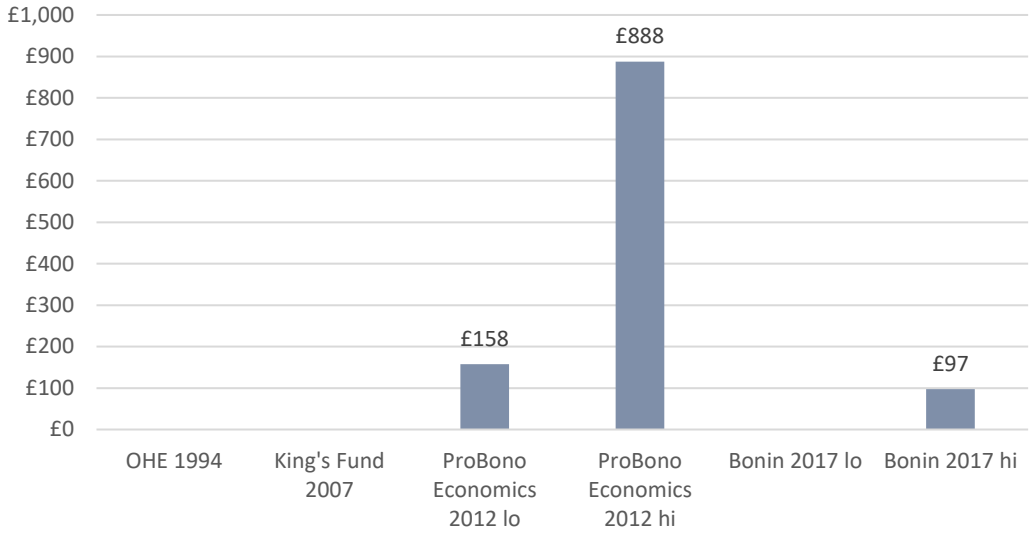
Intangible costs make up the largest proportion of costs, both in my high estimate and in the ProBono Economics estimates. As with indirect costs, my high estimate is lower than the lower ProBono Economics estimate.

I discussed the main approaches to valuing life years lost in Chapter 1. Several approaches are available, and I decided to base my estimate on the NICE WTP threshold for one quality-adjusted life year (£30,000; with sensitivity analyses using alternative estimates of £15,000 and £20,000) to ensure a better fit of the estimate within a health care context. I then adjusted for a disability weight for depression.

The ProBono Economics study is based on the Value of Preventing Fatality of around £1.8 million and calculated the number of excess fatalities based on a rate of fatalities per inpatient. This results in an estimate that is around eight times as high as mine.

My method for calculating the number of fatalities is based on a disease modelling study (see Chapter 7) that combines population data for England with parameters on excess mortality, duration of illness and relapse for AN. This resulted in an estimate of ca. 2,000 new cases per year, and a total of ca. 13,000 cases, with 69 fatalities from AN per year. The total present value of YPLL was around 6,000. Notably, the King's Fund estimates prevalence at almost 27,000.

Figure 9-8: Comparison of estimates of intangible costs of AN, 2010/11 prices (£million)



The question has been raised whether intangible costs should be included in CoI estimates at all, facing again the criticism that their inclusion discriminates against those receiving lower incomes. A striking recent example of such a bias is the fund compensating families of victims of the terrorist acts on 09/11/2001 in the USA, which, it has been reported, primarily bases compensation on lost future earnings, thus explicitly valuing loss of life differentially by income (Finkelstein & Corso 2014). A common recommendation is therefore first presenting a 'neutral' quantity (e.g. hours of work lost), which is then valued using a more equitable measure, such as average wages (Zhang *et al.* 2011, citing Drummond *et al.* 2005), and I have applied this recommendation to the estimate presented here.

WHY DO COSTS VARY?

While it was not possible to relate the societal costs associated with AN to individual characteristics, some progress can be reported on the question of whether and why costs may vary.

Chapter 5 discusses this in more detail with respect to direct costs. Costs appeared to be driven by care pathway and the associated risk of an inpatient admission, although it is unclear whether this is causal, or whether patients (to an extent) 'self-select' into care pathways owing to their clinical needs. Costs also vary based on some indicators of severity and some demographic characteristics.

At the individual level, costs were positively associated with

- Age and duration of illness in the CPS;
- English as a first language, WHO health rating and DASS stress scale in CASIS.

Costs were negatively associated with

- Vomiting and a co-morbid medical condition in the CPS
- The specialist-specialist pathway compared to the non-specialist-non-specialist pathway in the CPS;
- Lowest ever BMI in CASIS;
- Age and a diagnosis of AN (vs EDNOS-AN) in MOSAIC.

These findings are broadly in line with the existing literature, which finds that:

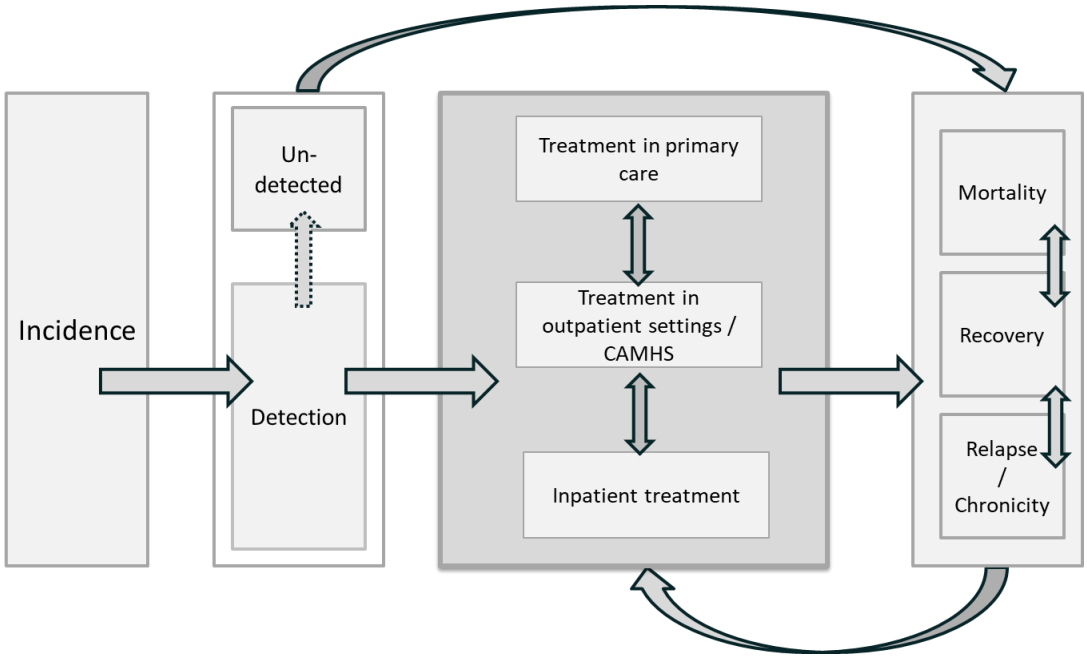
- Health care costs are higher for those with ED than for those without ED (Samnaliev *et al.* 2015);
- Hospital costs associated with AN are higher than those associated with other ED (Haas *et al.* 2012a);
- The presence of bingeing/purging behaviours is associated with higher outpatient costs (Stuhldreher *et al.* 2015);
- Longer duration of illness is associated with higher outpatient care costs (Stuhldreher *et al.* 2015);

- Lower BMI at admission is associated with higher costs in AN and vice versa (Haas *et al.* 2012b, 2012a; Toulany *et al.* 2015);
- Higher BMI following hospitalization is associated with higher retrospective costs, i.e. a longer inpatient stay is associated with a higher BMI (Stuhldreher *et al.* 2015);
- Co-morbid mental health problems and conditions may be associated with higher costs in inpatients (Haas *et al.* 2012b, 2012a) and outpatients (Stuhldreher *et al.* 2015), although some studies do not find this effect.

The 'missing link' needed to be able to reflect these cost variations in a 'bottom-up' estimate of the societal costs of AN is a model showing receipt of treatment over the course of the illness. This can be illustrated using the simplified model shown as Figure 9-9:

An incident case of AN is either detected or not detected. A detected case will (presumably) receive treatment. Both detected and un-detected cases will have an outcome (or an intermediate outcome) of recovery, relapse/chronic course of illness or mortality. What is missing in terms of data for an individual-level CoI estimate is information on a) course of illness and transitions between outcome states over a longer period of time (including number of relapses) and b) the link between this course of illness and treatment, including treatment settings (by 'stage' of illness) and transitions between settings of care.

Figure 9-9: Schematic model of course of illness and treatment of AN



STRENGTHS AND LIMITATIONS OF THE STUDY

The study of the cost of illness associated with AN has clear strengths and weaknesses. The study addresses a major gap in the literature. There is no other CoI estimate for England that provides the level of detail available here, and builds on such a breadth of data.

And the strength of the study is in the quality of the data. The clinical trials providing data for the study were robustly run and returned data of a high standard. The two cohort studies, BCS-70 and ALSPAC, are well established data sources, representative of the British population, and have been widely used to inform policy and practice – but they have not been interrogated with regard to the link between AN and productivity-related outcomes.

The studies on the costs of outpatient treatments, service use, costs and variations are among the first in England to provide this kind of information. Robust methods and best practices in economic costing were applied.

But there are limitations as well. Currently, the CoI estimate only covers treatment seeking individuals – although an effort has been made to include assumptions about additional service use, especially in primary care. This is an important consideration, given that it is people with AN may be reluctant to seek help – and specifically help for their ED (Hart *et al.* 2011).

Other methodological considerations highlight further gaps. While the current estimate covers a range of services beyond inpatient care, there are many potential cost categories that remain unexplored:

- Carer time and distress;
- Personal expenditure on food, medicines and other items;
- Medications;
- Presenteeism and;
- The value of non-market production foregone.

Missing data presents a potential problem, especially when it is likely that assumptions about the missing data mechanism may be violated – although I found no evidence for this. In addition, the analysis approach can be critiqued. Slightly different approaches were taken

for the analysis of ALSPAC and the BCS-70. To an extent, this reflects different conceptual models underpinning the analyses I used to build these studies, but it also reflects the large amount of time that has passed between the beginning and completion of this project.

IMPLICATIONS FOR POLICY AND PRACTICE

POLICY DEVELOPMENTS FOLLOWING 'NO HEALTH WITHOUT MENTAL HEALTH'

Since the publication of No Health Without Mental Health in 2011, there has been a lot of activity in the mental health policy field. A brief overview of major policy documents and events and the implication for mental health services generally or, where applicable, for ED specifically. Following the publication of statistics showing that ED inpatient admissions rose by 8% from 2013 (Health and Social Care Information Centre 2014), this figure has been quoted widely and can be found in many of the policy documents that referenced ED.

The implementation of a waiting time standard for ED, backed by substantial funding commitments, is driving service development. The stated aim is to meet the standard by 2020/21, i.e. that 95% of children receive treatment within one week or four weeks for urgent and routine cases, respectively. Baseline data collection is taking place in 2016/17.

While the evidence base is still in development, recent developments following the publication of the Five Year Forward View in 2014 have seen £30 million annual funding was announced in 2014 to support capacity building for evidence-based Community Eating Disorders Services for Children and Young People (CEDS-CYP). The aim is to provide specialist care to release capacity in general CAMHS and to support the implementation of the waiting time standard for ED.

Another aim, originating in the Five Year Forward View for Mental Health, is to reduce the number and duration of inpatient stays and end out-of-area placements. It envisioned that the use of inpatient beds overall will reduce, with potential larger reductions in specialist beds – and much of this reduction is expected to come from a reduction in bed days required by ED patients.

The evidence cited for CEDS-CYP is limited to the TOuCAN trial and the CPS (National Collaborating Centre for Mental Health 2015, p. 21), indicating that there is still a need for developing the economic case for the two strategies for reducing waiting times and improving access to services: A shift from inpatient to outpatient services, and a shift from

general to specialist community-based services. The proposed CEDS-CYP therefore reflects the debates in the ED literature that were outlined in Chapter 2.

THE ECONOMIC ARGUMENT FOR A SHIFT FROM INPATIENT TO OUTPATIENT SERVICES

As highlighted in Chapter 2, treatment of AN needs to be considered in the broader context of deinstitutionalisation, as there is a shift from inpatient to outpatient treatment driven by both cost pressures and clinical considerations. The problems arising from this process that have been identified for mental health services generally, such as restrictive access and limited capacity, geographic clustering of inpatient beds, problems in the interplay between different service tiers (such as recognition in and referral onwards from primary care) and staff confidence and skill in providing treatment, are mirrored in the service landscape for ED.

There is a consensus that treatment provision for ED needs to be improved, and this is reflected in the new waiting time standard for ED (National Collaborating Centre for Mental Health 2015). Assuming that existing services currently operate at (or above) capacity, and that there is no desire to see a 're-institutionalisation' of ED treatment[3], the economic question arising is whether it is 'worth' trying to improve provision by expanding outpatient services.

Economic evaluation is concerned with both costs and outcomes, so to start answering this question, we need to look at the evidence relating to both:

- How effective is outpatient treatment, compared to the alternative?
- What is its cost, compared to the alternative?

The question of effectiveness needs to be answered in the clinical realm. Evaluating service models in ED is difficult, as the experience from the TOuCAN trial (Gowers *et al.* 2010) has demonstrated, but there is a clinical consensus that inpatient admission should be reserved for the most severe and critical cases (National Institute for Health and Care

[3] Interestingly, some European countries appear to be seeing an increase in available beds (Thornicroft & Tansella 2013).

Excellence 2017a). What is clear is that preventing hospitalisation will address the cost-effectiveness question from both ends.

But what are the costs? The King's Fund (2008) estimated that, assuming that currently, 34.6% of people with ED are accessing services, a 100% coverage by 2026 could be achieved at a cost of £6.6 million. Given that NICE estimates the costs of specialist ED services in 2015/16 to be in the region of £83 million (National Institute for Health and Care Excellence 2017b), it is likely that this was an underestimate. Assuming the same current coverage, a rough estimate would be in the region of £240 million.

On the face of it, outpatient treatment is cheaper. The resource impact report accompanying the recently updated NICE guidance (National Institute for Health and Care Excellence 2017b), for example, cites NHS reference costs for 2015/16 that show the unit cost of an inpatient day for children to be £510, compared to £262 for an outpatient appointment and £191 for a community contact. The estimates presented in this thesis are even more favourable, with costs for the most commonly provided treatments ranging from £136-£246 per session (see Chapter 4, part 2). If these costs are accurate, expanding outpatient services would be cost saving (assuming equal outcomes) if twice the number of contacts per patient were required than if they had been admitted as inpatients. However, Knapp and colleagues (2011) find that deinstitutionalisation does not lead to cost savings. Thornicroft and Tansella (2013) confirm this finding and elaborate that quality of care is linked to expenditure, i.e. better acre is more expensive, and overall, community-based models are as expensive as institutional care. This finding is often replicated e.g. (Mansell *et al.* 2007). The TOuCAN trial (Byford *et al.* 2007a) seems to indicate that there is no difference in costs between inpatient and outpatient treatment overall, given the fact that inpatient admissions may be inevitable for some.

The lack of cost savings overall, despite arguably lower unit costs of services may be explained by the need to – at least initially – build up community-based and outpatient capacity while still retaining inpatient capacity to continue treating existing cases (Gilburt & Peck 2014).

So while the overall cost impact is unclear, these costs do not take into account a potential additional burden placed on carers. It is well established that the caregiving burden and carer distress in AN are high (Anastasiadou *et al.* 2014; Zabala *et al.* 2009), and the

Department of Health has explicitly acknowledged the role of caregivers in the 2014 document 'Closing the Gap: Priorities for Essential Change in Mental Health'. Raenker and colleagues (2013) found that carers spent most time providing emotional support, and more time spent caregiving was associated with higher distress. Social support, both from services and from informal sources, was found to alleviate distress. While we may not yet be able to quantify caregiving burden in AN for England, it is clear that in developing the economic argument for a shift towards outpatient treatment, the impact on carers needs to be considered, and it may be necessary to put in place services to in turn support caring for people with AN. Some interventions have been developed, and shown to have a positive effect (Treasure & Nazar 2016).

THE ECONOMIC ARGUMENT FOR SERVICE SPECIALISATION

Another current debate in ED is whether a higher degree of service specialisation in outpatient treatment is beneficial overall because highly specialist services may be more effective and better able to prevent hospitalisation, with the potential of treating between 70%-90% of patients on an outpatient basis (House *et al.* 2012).

Developing the economic argument for service specialisation again requires consideration of outcomes and costs.

While it could be expected that treatment provision in non-specialist services would be cheaper, unit costs were similar across service types, and CBT was in fact cheaper in specialist ED services (see Chapter 4).

Another argument might be that generic services provide more flexible capacity. Given that the prevalence of ED is low, specialist services need to cover larger catchment areas than general services with equivalent overall resources. This means that the argument for specialisation needs to consider how geographic distribution of services affects the cost of attending for treatment. A recent study estimated that the median productivity loss for caregivers was $673 and the value of lost leisure time associated with caregiving and travel to the hospital was $2,565 (Toulany *et al.* 2015). It is of course possible that an expansion of specialist services reduces the average travel time, but any economic argument needs to take this into account.

The CPS showed that the specialist pathway was associated with lower rates of admission and greater consistency of care (House *et al.* 2012). My analysis of showed that the S-S pathway had the lowest average cost (although differences in total costs were not significant), and inpatient costs contributed less than 50% to total costs, compared to over 70% in the other pathways. This information seems to point towards lower costs due to lower hospitalisation rates, and better outcomes as indicated by these lower hospitalisation rates.

The main limitations of the CPS were the small sample size and a bias towards specialist outpatient services, especially at the individual level – 63% of participants with economic data were on the S-S pathway. Moreover, as this was an observational study, it is difficult to establish causality between pathways and outcomes. This is an especially relevant point in this study, because it is possible that care pathways was determined by treatment success, e.g. those deteriorating or presenting with complex problems in non-specialist services may have been referred on to specialist services or admitted for inpatient care.

The findings from the only RCT of inpatient vs outpatient care in the UK, the TOuCAN trial (Byford *et al.* 2007a), seem to support an economic argument for service specialisation to an extent: There was no significant difference in outcome nor in costs, but given the favourable trends in the data, specialist outpatient treatment had a higher probability of being considered cost-effective – at least at lower values of WTP (Byford *et al.* 2007a).

IMPROVING DATA QUALITY IN CAMHS

The Children and Young People's Improving Access to Psychological Therapies programme (CYP IAPT) started in 2011. No new services are created, but the programme seeks to improve CAMHS by incorporating principles of outcomes monitoring. Linked initiatives are the CAMHS quality network and the support for data interpretation from CORC. While this has enabled some services to demonstrate their efficiency, funding cuts have been cited as a cause of limiting capacity for treatment but also capacity for implementing these principles (House of Commons Health Committee 2014, pp. 37-38). These principles are intended to underpin the development of the new ED community services from the start. As this thesis has demonstrated, there is still a dearth of detailed

information on CAMHS. Capacity for evaluation (and to be evaluated) will be key for achieving improvements in services.

RECOMMENDATIONS FOR FUTURE RESEARCH

TOWARDS AN INCIDENCE-BASED ESTIMATE OF THE COSTS OF ANOREXIA NERVOSA

The discussion of the usefulness of CoI estimates above concludes, they are most relevant when they are incidence-based and reflect variations between individuals, as this can be used to in scenario modelling and cost-effectiveness analysis. How far away are we from a robust incidence-based estimate for AN?

A decision-analytic model, used to combine evidence from different sources, would require information on the course of illness, including the probability of remission, relapse, recovery and mortality over the life course. While some information on these parameters is available, difficulty arises from a lack of data on individual patterns of remission and recovery.

In addition, these patterns would need to be matched with appropriate cost data. The present study has advanced the evidence base somewhat, but the challenge remains to match the available unit cost data to robust service use data that reflect actual rather than estimated service use at the individual level. This is particularly true for service use beyond inpatient care, and treatment within private sector services.

While some progress has been made in this study in exploring variations in costs, there are still some gaps that are difficult to fill. In particular, a difficulty arises from the low prevalence of AN, and especially the low prevalence in males that makes it unlikely that statistical testing of differences can succeed, and this is true to an even greater extent for formal sub-group analysis within males with AN.

One strategy to increase sample size might be to follow the shift in thinking about ED in terms of behaviours discussed in Chapter 2, as individual behaviours are more common than any full syndrome or diagnostic category. However, this is still a relatively new concept and little research is available on life course, service use and costs. Issues around service use and costs rely on the implementation of principles and strategies that facilitate data collection and ultimately, service evaluation. While there are some promising efforts, such

as the children's IAPT programme, it is unclear whether this will result in better and more data being publicly available down the line.

CONSIDERATIONS FOR ECONOMIC EVALUATION OF INTERVENTIONS

The findings from this study provide some implications for future economic evaluations of interventions for AN.

If the finding from the studies using ALSPAC and BCS-70 data holds, namely that no effect of AN on education attainment or economic activity could be found, any economic argument focussing on investment in the present to be offset by savings later will need to focus on service costs alone because the increased costs of service provisions cannot be offset by increased future income – except from avoidable mortality. At the moment, the little evidence we have available suggests that changes in treatment models are unlikely to result in savings from lower direct costs. However, all else being equal, cost-effectiveness could be improved by increasing effectiveness of new interventions.

As discussed above, the inclusion of the carer perspective in any cost-effectiveness study, especially of interventions for younger people, is crucial to avoid shifting costs from one element of society (e.g. the health service) to another (the individual).

Similarly, the inclusion of travel costs is likely to be relevant given the current distribution of services. With the development and roll-out of group-based therapies, where the number of families attending each session is relevant not just in terms of unit costs but also in terms of clinical effectiveness (Eisler *et al.* 2016), recruitment and retention become even more important. The unit cost estimate for MCTAAN (see Chapter 4) does not include travel costs because this was considered a research cost, related to the requirements of the RCT. However, but with limited local availability of ED services, travel is – for the time being – a factor that needs to be acknowledged.[4]

[4] It is worth mentioning that one strategy for improving access to therapies has been to develop online interventions. At this point, this for the most part offers alternative treatments for BN (Shingleton *et al.* 2013), which tend to be CBT-based, and support for carers (Hibbs *et al.* 2015). However, an online version of the MANTRA intervention – now recommended by NICE – has been piloted to enhance relapse

Finally, there is a need for relevant outcome data, including utility data, that can be used together with cost data in economic evaluations of interventions and service models. The QALY is commonly measured using the EQ-5D (The EuroQol Group 1990), a generic measure of quality of life for which utility weights (needed to convert EQ-5D scores into QALYs) are readily available. However, it is generally accepted that generic measures of quality of life such as the are unlikely to be sensitive to changes in specific conditions, and in particular to changes in mental health problems (Adair *et al.* 2007; Chisholm *et al.* 1997). A factor that has arisen in the literature on quality of life in ED is that some people with ED may respond in 'ego-syntonic' ways, i.e. ways that are consistent with how they see themselves. This may lead to reporting of higher QoL than is actually experienced (de la Rie *et al.* 2005a). In a comparison with physical health conditions and healthy controls, an early study (Keilen *et al.* 1994) found the QoL profile for AN (measured on the Nottingham Health Profile, Hunt *et al.* 1981) to be quite different, especially when it came to ratings for mobility and broadly defined social functioning, drawing into question whether treatments for different conditions with very different needs profiles can be usefully compared on a single measure. In response to these concerns, a quality of life scale specific to ED (Eating Disorder Quality of Life Scale, EDQLS) was developed (Adair *et al.* 2007). The instrument consists of 40 self-report items in 12 domains rated on 5-point Likert scales. While changes in QoL can therefore be measured, there is no associated 'utility tariff' available that would allow for conversion of EDQLS scores into QALYs. This currently limits the usefulness of the EDQLS when it comes to comparison between interventions for different conditions, which is facilitated by the use of QALYs.

Given the wide-ranging changes that can be expected in the landscape of ED services following implementation of CEDS-CYP, and the need to develop the evidence base for these services, presents an opportunity to build evaluation capacity into the service from the start, including data collection that can facilitate economic evaluation. The experience with the children's IAPT programme can serve as a potential model, and the adoption of core models is recommended in the commissioning guidelines (National Collaborating Centre for Mental Health 2015).

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prevention in AN (Schmidt *et al.* 2017), and a multi-national RCT is underway to test the effectiveness of the everybody intervention (ICare Consortium 2017).

THE IMPACT OF SPECIALISATION ON SKILLS, CONFIDENCE AND QUALITY OF CARE

The study of CPS data (Chapter 5, part 1) generated hypotheses with regard to the impact of service specialisation. The literature on primary care (Currin 2006; Currin *et al.* 2007a) (Currin *et al.* 2006) suggests that confidence and experience play a role in choices about treatment and referral. The CPS (House 2011) found that the specialist – specialist (S-S) pathway was associated with greater continuity of care, while my study found that specialist services offered a wider range of ED treatments, and there was a trend for staff other than consultants to be involved in treatment, and it is hypothesised that this is due to greater specialist skills in all staff. The link between service specialisation, skills, confidence and quality of care should be explored, especially to support the evidence base for the new CEDS-CYP model.

CONCLUSIONS

In this thesis, I have presented the costs of Anorexia nervosa to society in England:

- Direct costs ranged from £40.1 million to £89 million.
- Indirect costs ranged from £40.7 million to £65.7 million.
- Intangible costs in the high cost scenario were calculated at £49 to £97.1 million.
- Transfer payments were estimated from £4.9 million to £10.4 million.
- Total societal costs ranged from £80.8 million to £251.8 million.

While my approach was conservative, the fact remains that the costs of AN are high, and much of it may not be borne by the health service or indeed the public purse. For the time being, these remain as 'blind spots' within the CoI of Anorexia.

Since the publication of 'No Health Without Mental Health', there have been significant policy developments that specifically affect the ED services landscape. In particular, the imminent introduction of community-based specialist ED services – aiming to improve access to treatment and relieve capacity in general CAMHS – means that going forward, there will be a need to improve the evidence base for ED treatment, and this will include economic evaluations. It will become even more important, then, that adequate and meaningful data are collected.

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APPENDICES

APPENDIX 1: SERVICE INFORMATION SCHEDULE FOR MULTI-FAMILY DAY TREATMENT

Design Stage

How much staff time was spent in tailoring your existing intervention to suit this specific client group? Please include any secretarial/admin support and volunteer time.

Staff identifier (e.g. initials)	**Profession**	**Grade**	**No hours/days**

Were any special materials used in this design stage? YES NO

If YES, please describe below.

Preparing to hold the intervention

For each activity listed below, please give hours of staff time absorbed, including volunteer time. Also list the identifier, profession and grade of staff not included in the table above. Please also describe materials used (or an approximate cost) and give one-off costs.

Staff training

Staff identifier (e.g. initials)	**Profession**	**Grade**	**No hours/days**

Any other resources/materials?

The intervention

Preparation and/or purchase of intervention materials

Staff travel time to and from the intervention venue (if applicable)

Staff mileage to and from the intervention venue (if applicable)

Staff time for giving the intervention

Staff identifier (e.g. initials)	**Profession**	**Grade**	**No hours/days**

Details on intervention

Length of sessions (start & end times)

Intensive programme	
One-day meetings	
Individual family meetings	

Number of participants at each session

Intensive programme	
One-day meetings	
Individual family meetings	

Any other resources not mentioned above?

APPENDIX 2: SERVICE-LEVEL QUESTIONNAIRE FOR SERVICE MANAGERS

ONE: STAFFING

(a) What medical staff work in your service, and how much of their time is dedicated to working with adolescent* eating disorders?

Level	**Total Whole Time Equivalents (WTE)**	**Clinical sessions/programmed activities* dedicated to adolescent eating disorders**
Consultant		
Staff grade		
ST4-6		
ST1-3		
F1-F2		
Other (please specify)		
Other (please specify)		

*Please specify

*Adolescent: 13 up to 18th birthday

(b) What nursing staff work in your service, and how much of their time is dedicated to working with adolescent eating disorders?

Agenda for Change Band	**Total Whole Time Equivalents (WTE)**	**Time dedicated to adolescent eating disorders (WTE)**
1		
2		
3		
4		
5		
6		
7		
8a		

8b		
8c		
8d		
9		

(c)

What other staff work in your service, and how much of their time is dedicated to working with adolescent eating disorders?

Staff	**Agenda for Change Band**	**Total Whole Time Equivalents**	**Clinical sessions/WTE* dedicated to adolescent eating disorders**
Clinical/counselling psychologist			
Psychotherapist			
Family therapist			
Dietician			
Social worker			
Primary Mental Health Worker			
Administrative and clerical staff			
Other (please specify)			
Other (please specify)			

*Please specify

TWO: REFERRALS, ASSESSMENT AND TREATMENT

(a) How many referrals of adolescents with a primary diagnosis of an eating disorder did your service receive during the financial year 2007-2008?

(b) How many of these were for cases of anorexia nervosa (and related eating disorders) and how many were for bulimia nervosa (and related eating disorders)?

AN-TYPE EATING DISORDERS:

BN-TYPE EATING DISORDERS:

_____(c)

During the financial year 2007-2008, what was the total number of adolescents seen by your service (i.e. overall, not just eating disorders)?

Number assessed:

Number treated:

Total number seen (assessed and/or treated):

THREE: EXPENDITURE

Please attach a copy of your cost centre accounts or complete the table below to let us know a bit about your expenditure during the 2007-2008 financial year.

Please be assured that any information provided in this questionnaire will be treated with the strictest confidence and all data will be anonymised.

Category	**Expenditure 2007-2008**	**Notes/comments**
Medical staff (doctors, consultants) (salaries and on-costs)		
Nursing staff (salaries and on-costs)		
Managers (salaries and on-costs)		
Clerical/domestic staff (salaries and on-costs)		
TOTAL STAFF (salaries and on-costs)		
Expenditure on sessional staff		
Other staff/user expenditure (e.g. travel, subsistence)		
Clinical expenditure/consumables (e.g. drugs, tests, patient supplies)		

Office expenses (e.g. stationery, computers)		
Other costs (please describe)		
Building-related costs (e.g. power, cleaning, laundry, maintenance)		
Rent/capital charges		
Overhead costs/charges for managing agency		

AGENDA FOR CHANGE BANDS

£13,233 – £13, 944

Administration, catering, domestic, portering staff

£13,233 – £16, 588

Administration, catering, clinical support worker, patient transport, pharmacy assistant

£15, 190 – £18, 157

Microbiology assistant, secretary, security

£17,732 – £21,318

Mortuary, radiography or occupational therapy assistant, operating department practitioner (during training or entry level), assistant psychologists, nursing auxiliaries and nursery nurses

£20,710 – £26,839

Nurse and midwife (old D and E grades), dental technician (entry level), Diagnostic/Therapeutic Radiographers, dietician, occupational therapist, paramedic, senior pharmacy technician, physiotherapist, assistant psychologists (higher grade), Clinical Psychologists, operating department practitioner (qualified)

£24,831 – £33,436

Junior Sister/specialist senior staff nurse, Senior II Radiographer (diagnostic/therapeutic), Art therapist, specialist dental technician, health visitor, nurse specialist, trainee clinical psychologist, pharmacist, Senior Clinical Physiologists

£29,789 – £39,273

Senior sister, Senior I Radiographer (diagnostic/therapeutic team leader), Chief dental technician, management – clinical and administrative, qualified psychologist, specialist pharmacist, Chief Clinical Psychologists

(a) £37,996 – £45,596

(b) £44,258 – £54-714

(c) £53,256 – £65,657

(d) £63,833 – £79,031
Advanced pharmacists, nurse and midwife consultants, Superintendent Radiographers (diagnostic/therapeutic), higher management, psychologists, senior therapists (divided into 4 bands – a, b, c, d), Senior Chief Clinical Psychologists

£75,383 – £95,333

Consultant Psychologists who run large services

APPENDIX 3: SERVICE-LEVEL QUESTIONNAIRE FOR CLINICIANS

QUESTIONNAIRE FOR CLINICIANS

ONE: TYPE OF SERVICE

(a) How would you describe your service?

Outpatient:

General child and adolescent mental health service

Specialist child and adolescent eating disorder service

Specialist adult eating disorder service

Other (please specify)

Inpatient:

General child and adolescent mental health service

Specialist child and adolescent eating disorder service

Specialist adult eating disorder service

Other (please specify)

(b) Which Tier does your service come under?

Tier 3

Tier 4

N/A

(c) Where is your service located?

Community building

Hospital building

Other (please specify)

(d) What is the age range of patients seen by your service?

(e) Please provide a general description of your service:

(f) Does your service specialise in treatment eating disorders?

Yes (child and adolescent eating disorders)

Yes (adult eating disorders)

No

(g) How would you describe the level of specialisation in adolescent* eating disorders within your service?

*Adolescent: Aged 13 years up to 18th birthday

Service is entirely dedicated to the treatment of (child and) adolescent eating disorders

Service is dedicated to the treatment of adult eating disorders but has specialisation in adolescent eating disorders within it

Service is dedicated to general adolescent mental health but has specialisation in adolescent eating disorders within it

Service is dedicated to general adolescent mental health and has no specialisation in adolescent eating disorders within it

Notes:

TWO:REFERRALS

(a) Who can refer to your service?

Patients (self-referrals)

Schools

Voluntary sector organisations (e.g. charities)

Primary care (e.g. GPs)

Hospitals (e.g. paediatric departments)

Tier 2 mental health services

Tier 3 mental health services

Tier 4 mental health services

Private/Independent services

- Other (please specify)

_____

(b) Which of the following statements best describes your usual practice with adolescent eating disorder referrals?

AN-TYPE EATING DISORDERS:

Referred for assessment and treatment elsewhere (referral not accepted by your service)

Assessed in your service and referred elsewhere for treatment if eating disorder is diagnosed

Assessed and treated within your service in the first instance (may be referred elsewhere if initial treatment is unsuccessful)

BN-TYPE EATING DISORDERS:

Referred for assessment and treatment elsewhere (referral not accepted by your service)

Assessed in your service and referred elsewhere for treatment if eating disorder is diagnosed

Assessed and treated within your service in the first instance (may be referred elsewhere if initial treatment is unsuccessful)

(d) If you refer adolescent eating disorder cases elsewhere, please outline below where and under what circumstances you do this:

For example: Cases of anorexia nervosa are treated within our general child and adolescent mental health service but are referred on for inpatient care in a specialist child and adolescent eating disorder unit if they drop below 70% weight for height.

AN-TYPE EATING DISORDERS:

BN-TYPE EATING DISORDERS:

THREE: ASSESSMENT AND TREATMENT

(a) In your service, who are adolescents with eating disorders typically assessed by?

Individual clinicians

A number of clinicians (as a team)

N/A

(b) In your service, who are adolescents with eating disorders typically treated by?

Individual clinicians

A number of clinicians (as a team)

A combination of individual and team work

N/A

(c) What services do you offer for adolescents with eating disorders?

Inpatient programme

Outpatient programme

Day programme

Outreach programme

(d) What is the average length of each type of programme (in weeks)?

Inpatient programme

Outpatient programme

Day programme

Outreach programme

(e) Please fill in the spaces below to give us an idea of your assessment procedure and treatment provided for adolescents with eating disorders in your service:

FOR AN-TYPE EATING DISORDERS

Typical length of assessment:

Professional(s) typically involved in assessment:

FOR BN-TYPE EATING DISORDERS

Typical length of assessment:

Professional(s) typically involved in assessment:

FOR AN-TYPE EATING DISORDERS:

Type of treatment	**Typical length of one session**	**Professional(s) typically responsible for providing the treatment**
CBT		
Interpersonal therapy		
Psychodynamic psychotherapy		
Family therapy		
Multi-family group therapy		
Group therapy (w/o families)		
Dietary regime		
Nurse counselling		
Medical monitoring		
Other (please specify)		
Other (please specify)		

FOR BN-TYPE EATING DISORDERS

Type of treatment	Typical length of one session	Professional(s) typically responsible for providing the treatment
CBT		
Interpersonal therapy		
Psychodynamic psychotherapy		
Family therapy		
Multi-family group therapy		
Group therapy (w/o families)		
Dietary regime		
Nurse counselling		
Medical monitoring		
Other (please specify)		
Other (please specify)		

APPENDIX 4: FULL MODELS FOR ALSPAC ANALYSIS

1) Variable coding

Variable name	*Level and meaning*
eb_ed_ed	Categorical variable: ED status
0	No ED
1	AN
2	Other ED
eb_bp_ed	Binary: bingeing/purging; no vs yes
eb_fh5312_abs	Scale: Days of absence in last two weeks
int1	Interaction term: eb_ed_ed * eb_bp_ed
int2	Interaction term: eb_ed_ed * eb_fh5312_abs
int3	Interaction term: eb_ed_ed * eb_bp_ed* eb_fh5312_abs
sex	Binary: female vs male
soclass_set1_pred	Categorical: Parental social class
II	Class II
III NM	Class III non-manual
III M	Class III manual
IV	Class IV
V	Class V
eb_ptlbw	Binary: pre-term or low birth weigt; no vs yes
mz028b_set1_pred	Scale: Maternal age at delivery
c645a_set1_pred	Categorical: parental qualifications
Vocational	Vocational qualification
O level	O-level qualification
A level	A-level qualification
Degree	Degrees-level qualification
paritybi_set1_pred	Binary: parity; no vs yes
eb_b650_set1_pred	Binary: Mother ever smoked; no vs yes
eb_c804_set1_pred	Binary: Child ethnic background; white vs other background
eb_marital_set1_pred	Categorical: Maternal marital status
0	Never married
1	Married
2	No longer married
ks4_fsm_set2_pred	Binary: eligible for free school meals; no vs yes
ks4_idaci_set2_pred	Scale: deprivation indicator
ccxa180_set2_pred	Categorical: YP expectation of obtaining 5+ good GCSEs
Fairly likely	Fairly likely
Not very likely	Not very likely
Not at all likely	Not at all likely
eb_se033a_set2_pred	Binary: emotional and behavioural difficulties: no vs yes
eb_a006_set2_pred	Categorical: Housing tenure

Variable name	*Level and meaning*
Social housing	Social housing
Privately rented	Privately rented
Other	Other accommodation
eb_sen_set2_pred	Binary: School Action or School Action Plus (KS4); no vs yes
eb_children_set2_pred	Scale: Number of children in household

2) Full sample. Outcome: GCSE total score

Model 1

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ks4_ptstne~t	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	.4486387	14.02945	0.03	0.975	-27.4988	28.39608
2	-13.21774	5.167365	-2.56	0.012	-23.48491	-2.950566
_cons	411.7639	2.890248	142.47	0.000	406.059	417.4687

Model 2

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-9.377248	11.4054	-0.82	0.413	-32.02071	13.26621
2	-19.15454	4.622817	-4.14	0.000	-28.32096	-9.988126
soclass_set1_pred						
II	16.31491	7.79965	2.09	0.037	1.003082	31.62674
III NM	28.03363	7.513879	3.73	0.000	13.28079	42.78647
III M	57.67176	7.689045	7.50	0.000	42.57815	72.76537
IV	58.30731	8.085116	7.21	0.000	42.4367	74.17792
V	74.95699	11.87594	6.31	0.000	51.66939	98.24459
sex	-41.23698	3.01941	-13.66	0.000	-47.15798	-35.31598
eb_ptlbw	-.567181	6.40443	-0.09	0.929	-13.12132	11.98696
mz028b_set1_pred	3.154462	.3387753	9.31	0.000	2.490379	3.818544
c645a_set1_pred						
Vocational	28.69391	5.403997	5.31	0.000	18.09933	39.28849
O level	52.83203	4.04281	13.07	0.000	44.90546	60.7586
A level	80.77058	4.628879	17.45	0.000	71.69612	89.84503
Degree	115.5552	6.125826	18.86	0.000	103.5458	127.5645
paritybi_set1_pred	-35.6744	2.993219	-11.92	0.000	-41.54217	-29.80663
eb_b650_set1_pred	18.16031	2.929352	6.20	0.000	12.4175	23.90312
eb_c804_set1_pred	-3.916237	7.248526	-0.54	0.589	-18.13292	10.30045
eb_marital_set1_pred						
1	35.36353	4.103855	8.62	0.000	27.31816	43.4089
2	-5.367522	7.025783	-0.76	0.445	-19.14056	8.405518
_cons	240.6363	12.75982	18.86	0.000	215.6146	265.6581

Model 3

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-1.660911	7.79531	-0.21	0.832	-17.07639	13.75457
2	-9.206543	3.433771	-2.68	0.008	-16.00554	-2.40755
soclass_set1_pred						
II	-6.598743	8.227468	-0.80	0.424	-22.89572	9.698237
III NM	-4.380838	7.899853	-0.55	0.580	-20.02821	11.26654
III M	8.461112	7.897974	1.07	0.286	-7.162472	24.0847
IV	6.015526	7.978099	0.75	0.452	-9.745846	21.7769
V	9.012674	11.33189	0.80	0.427	-13.31167	31.33702
sex	-22.73634	2.963921	-7.67	0.000	-28.57985	-16.89283
eb_ptlbw	-3.888842	5.63249	-0.69	0.490	-14.94892	7.171237
mz028b_set1_pred	1.228402	.3456006	3.55	0.000	.5479326	1.908871
c645a_set1_pred						
Vocational	9.609157	5.764857	1.67	0.098	-1.780953	20.99927
O level	12.53278	4.370387	2.87	0.005	3.89796	21.16759
A level	25.54579	4.98123	5.13	0.000	15.71237	35.37921
Degree	51.01751	5.90405	8.64	0.000	39.39755	62.63747
paritybi_set1_pred	-12.26779	2.967311	-4.13	0.000	-18.10419	-6.431381
eb_b650_set1_pred	12.56395	2.824627	4.45	0.000	7.001007	18.12689
eb_c804_set1_pred	-4.738713	7.224236	-0.66	0.513	-18.99778	9.52035
eb_marital_set1_pred						
1	7.355795	4.342512	1.69	0.092	-1.2108	15.92239
2	-10.96303	7.114998	-1.54	0.125	-24.99589	3.06983
ks4_fsm_set2_pred	-18.54203	7.522272	-2.46	0.015	-33.43168	-3.652389
ks4_idaci_set2_pred	34.90874	11.55954	3.02	0.003	12.07429	57.74318
ccxa180_set2_pred						
Fairly likely	-98.06653	3.257391	-30.11	0.000	-104.4906	-91.64246
Not very likely	-193.9128	6.360782	-30.49	0.000	-206.5251	-181.3004
Not at all likely	-254.2649	8.501742	-29.91	0.000	-271.1597	-237.3701
eb_se033a_set2_pred	-54.65698	9.13019	-5.99	0.000	-72.87904	-36.43491
eb_a006_set2_pred						
Social housing	-32.00247	5.761247	-5.55	0.000	-43.42406	-20.58087
Privately rented	-18.00279	6.130533	-2.94	0.004	-30.09254	-5.913044
Other	2.669588	9.131321	0.29	0.770	-15.39055	20.72973
eb_sen_set2_pred	-55.04573	5.217229	-10.55	0.000	-65.37898	-44.71248
eb_children_set2_pred	1.114781	1.96222	0.57	0.571	-2.769274	4.998836
_cons	452.1144	14.15474	31.94	0.000	424.2483	479.9805

Model 4

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-1.180544	7.970206	-0.15	0.883	-16.97524	14.61416
2	-9.132773	3.503705	-2.61	0.011	-16.08281	-2.182731
soclass_set1_pred						
II	-5.612258	8.004182	-0.70	0.485	-21.53141	10.30689
III NM	-3.614319	7.697142	-0.47	0.640	-18.91673	11.6881
III M	9.203509	7.84822	1.17	0.244	-6.362926	24.76994
IV	6.459784	8.135769	0.79	0.429	-9.638907	22.55848
V	8.93445	12.58738	0.71	0.479	-15.86678	33.73568
sex	-22.11813	3.95051	-5.60	0.000	-29.88872	-14.34753
eb_ptlbw	-3.914354	6.012663	-0.65	0.515	-15.7376	7.908887
mz028b_set1_pred	1.189282	.3767858	3.16	0.002	.4469191	1.931645
c645a_set1_pred						
Vocational	9.433634	5.77808	1.63	0.105	-2.013969	20.88124
O level	12.68875	4.278345	2.97	0.004	4.207442	21.17005
A level	25.12888	5.289733	4.75	0.000	14.67459	35.58317
Degree	50.70585	5.940991	8.53	0.000	38.98786	62.42385
paritybi_set1_pred	-11.38923	2.983939	-3.82	0.000	-17.26603	-5.512436
eb_b650_set1_pred	12.29416	2.914126	4.22	0.000	6.549611	18.03872
eb_c804_set1_pred	-4.643236	8.176179	-0.57	0.571	-20.78036	11.49389
eb_marital_set1_pred						
1	7.23652	4.310878	1.68	0.095	-1.286945	15.75999
2	-10.78241	7.290355	-1.48	0.141	-25.18447	3.619652
ks4_fsm_set2_pred	-18.32861	8.0511	-2.28	0.025	-34.27379	-2.383425
ks4_idaci_set2_pred	40.13563	16.72687	2.40	0.017	7.227814	73.04345
ccxa180_set2_pred						
Fairly likely	-96.61238	4.30568	-22.44	0.000	-105.0884	-88.13637
Not very likely	-190.9634	8.464997	-22.56	0.000	-207.6713	-174.2556
Not at all likely	-250.4803	11.60364	-21.59	0.000	-273.4038	-227.5569
eb_se033a_set2_pred	-54.75443	9.556401	-5.73	0.000	-73.86458	-35.64428
eb_a006_set2_pred						
Social housing	-32.42906	6.706045	-4.84	0.000	-45.69102	-19.16709
Privately rented	-17.55614	5.987716	-2.93	0.004	-29.39775	-5.714532
Other	2.383843	9.463971	0.25	0.802	-16.35227	21.11995
eb_sen_set2_pred	-55.10529	6.52516	-8.45	0.000	-67.97471	-42.23588
eb_children_set2_pred	1.045885	1.974849	0.53	0.598	-2.873225	4.964994
eb_txa110_set3_pred						
2	-6.805089	4.175226	-1.63	0.107	-15.10256	1.492385
3	-23.29834	8.789141	-2.65	0.010	-40.79644	-5.800244
4	-32.21571	26.85156	-1.20	0.235	-85.99136	21.55994
eb_ks4_asco005_set3_pred						
1	13.01698	13.48158	0.97	0.335	-13.45055	39.48451
_cons	455.3512	15.67704	29.05	0.000	424.4894	486.213

Model 3b

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-2.489117	8.468808	-0.29	0.769	-19.20074	14.2225
2	-8.496155	3.759459	-2.26	0.025	-15.92892	-1.063391
eb_bp_ed	-11.90053	18.10772	-0.66	0.512	-47.59017	23.78911
int1						
1	14.30126	22.86003	0.63	0.532	-30.7217	59.32423
2	9.751518	17.82524	0.55	0.585	-25.33886	44.8419
soclass_set1_pred						
II	-6.54325	8.213606	-0.80	0.427	-22.81176	9.72526
III NM	-4.326852	7.891599	-0.55	0.585	-19.95725	11.30355
III M	8.514455	7.879285	1.08	0.282	-7.070856	24.09977
IV	6.060566	7.949706	0.76	0.447	-9.642789	21.76392
V	8.996562	11.2935	0.80	0.426	-13.24978	31.2429
sex	-22.90575	3.012653	-7.60	0.000	-28.84718	-16.96431
eb_ptlbw	-3.859177	5.634699	-0.68	0.494	-14.92366	7.205301
mz028b_set1_pred	1.223929	.3472657	3.52	0.001	.5400919	1.907766
c645a_set1_pred						
Vocational	9.463961	5.756145	1.64	0.102	-1.908144	20.83607
O level	12.45498	4.348525	2.86	0.005	3.864839	21.04512
A level	25.54589	4.970919	5.14	0.000	15.73353	35.35826
Degree	50.97095	5.88554	8.66	0.000	39.3885	62.55339
paritybi_set1_pred	-12.21767	2.978188	-4.10	0.000	-18.07598	-6.359366
eb_b650_set1_pred	12.51076	2.840488	4.40	0.000	6.915732	18.10579
eb_c804_set1_pred	-4.649366	7.221786	-0.64	0.521	-18.90326	9.604529
eb_marital_set1_pred						
1	7.374027	4.346959	1.70	0.091	-1.20159	15.94964
2	-10.98092	7.123193	-1.54	0.125	-25.03036	3.068516
ks4_fsm_set2_pred	-18.5213	7.495449	-2.47	0.015	-33.35598	-3.686616
ks4_idaci_set2_pred	34.97848	11.53419	3.03	0.003	12.19593	57.76102
ccxa180_set2_pred						
Fairly likely	-98.01458	3.268898	-29.98	0.000	-104.462	-91.56716
Not very likely	-193.8023	6.383706	-30.36	0.000	-206.4612	-181.1434
Not at all likely	-254.1418	8.521254	-29.82	0.000	-271.076	-237.2075
eb_se033a_set2_pred	-54.45053	9.212693	-5.91	0.000	-72.84044	-36.06062
eb_a006_set2_pred						
Social housing	-31.96645	5.757993	-5.55	0.000	-43.38131	-20.5516
Privately rented	-17.98454	6.132576	-2.93	0.004	-30.07841	-5.890677
Other	2.672833	9.140851	0.29	0.770	-15.4065	20.75216
eb_sen_set2_pred	-55.09033	5.243505	-10.51	0.000	-65.47704	-44.70362
eb_children_set2_pred	1.101673	1.954381	0.56	0.574	-2.766329	4.969675
_cons	452.4309	14.14422	31.99	0.000	424.5866	480.2753

Model 3c

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-1.511382	7.761176	-0.19	0.846	-16.85788	13.83511
2	-8.707375	3.454444	-2.52	0.013	-15.54855	-1.866202
eb_fh5312_abs	-5.408233	2.254551	-2.40	0.018	-9.86586	-.9506072
int2	.4894067	1.360944	0.36	0.720	-2.198158	3.176971
soclass_set1_pred						
II	-6.031982	8.318115	-0.73	0.470	-22.51473	10.45077
III NM	-3.853974	7.994556	-0.48	0.631	-19.69538	11.98743
III M	8.820608	7.962029	1.11	0.270	-6.934347	24.57556
IV	6.46418	8.060697	0.80	0.424	-9.466209	22.39457
V	9.630144	11.43687	0.84	0.401	-12.9082	32.16849
sex	-22.90439	2.958155	-7.74	0.000	-28.7364	-17.07238
eb_ptlbw	-3.80014	5.611719	-0.68	0.499	-14.81885	7.218573
mz028b_set1_pred	1.224354	.3446222	3.55	0.000	.5458419	1.902866
c645a_set1_pred						
Vocational	9.833769	5.760774	1.71	0.090	-1.548469	21.21601
O level	12.80008	4.381667	2.92	0.004	4.141934	21.45822
A level	25.75592	5.008592	5.14	0.000	15.86637	35.64547
Degree	51.14481	5.908455	8.66	0.000	39.51548	62.77414
paritybi_set1_pred	-11.82545	2.972716	-3.98	0.000	-17.67291	-5.977992
eb_b650_set1_pred	12.76057	2.847062	4.48	0.000	7.151909	18.36922
eb_c804_set1_pred	-3.981806	7.174232	-0.56	0.580	-18.13948	10.17587
eb_marital_set1_pred						
1	7.118393	4.384177	1.62	0.106	-1.533314	15.7701
2	-10.58517	7.068628	-1.50	0.136	-24.52424	3.353897
ks4_fsm_set2_pred	-18.92079	7.563377	-2.50	0.014	-33.89491	-3.946677
ks4_idaci_set2_pred	35.81328	11.54564	3.10	0.002	13.00642	58.62014
ccxa180_set2_pred						
Fairly likely	-97.68473	3.262638	-29.94	0.000	-104.1197	-91.24981
Not very likely	-192.5858	6.424055	-29.98	0.000	-205.3272	-179.8445
Not at all likely	-251.9483	8.529112	-29.54	0.000	-268.8975	-234.9992
eb_se033a_set2_pred	-54.65436	9.059814	-6.03	0.000	-72.733	-36.57573
eb_a006_set2_pred						
Social housing	-32.43137	5.761075	-5.63	0.000	-43.85299	-21.00975
Privately rented	-18.03973	6.113132	-2.95	0.004	-30.09458	-5.984871
Other	2.54825	9.19729	0.28	0.782	-15.64725	20.74375
eb_sen_set2_pred	-54.28913	5.061412	-10.73	0.000	-64.30429	-44.27398
eb_children_set2_pred	1.046737	1.950613	0.54	0.592	-2.81377	4.907244
_cons	450.9699	14.19674	31.77	0.000	423.0177	478.9221

Model 3d

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-1.084685	7.830318	-0.14	0.890	-16.56771	14.39834
2	-8.050023	3.76778	-2.14	0.035	-15.50561	-.5944386
1.eb_bp_ed	-1.763856	4.956218	-0.36	0.723	-11.60389	8.07618
eb_fh5312_abs	-5.226734	1.806606	-2.89	0.005	-8.804365	-1.649103
int3	.5706085	1.319116	0.43	0.666	-2.033529	3.174746
soclass_set1_pred						
II	-6.027756	8.306995	-0.73	0.470	-22.48769	10.43218
III NM	-3.843772	7.993332	-0.48	0.632	-19.68261	11.99506
III M	8.833118	7.953274	1.11	0.269	-6.903882	24.57012
IV	6.477995	8.044909	0.81	0.422	-9.420117	22.37611
V	9.586235	11.40865	0.84	0.402	-12.89479	32.06726
sex	-23.04792	3.012547	-7.65	0.000	-28.98942	-17.10643
eb_ptlbw	-3.746085	5.60872	-0.67	0.504	-14.75876	7.266588
mz028b_set1_pred	1.22085	.3460397	3.53	0.000	.5394701	1.902229
c645a_set1_pred						
Vocational	9.729331	5.755353	1.69	0.093	-1.641644	21.10031
O level	12.7337	4.368434	2.91	0.004	4.102618	21.36477
A level	25.74073	4.98636	5.16	0.000	15.89648	35.58498
Degree	51.11033	5.888718	8.68	0.000	39.52098	62.69969
paritybi_set1_pred	-11.79502	2.983937	-3.95	0.000	-17.66511	-5.924934
eb_b650_set1_pred	12.71564	2.862277	4.44	0.000	7.076174	18.3551
eb_c804_set1_pred	-3.919757	7.166693	-0.55	0.585	-18.06196	10.22244
eb_marital_set1_pred						
1	7.132106	4.384002	1.63	0.106	-1.519246	15.78346
2	-10.57379	7.062855	-1.50	0.136	-24.50109	3.353514
ks4_fsm_set2_pred	-18.9219	7.529662	-2.51	0.013	-33.82707	-4.016724
ks4_idaci_set2_pred	35.84569	11.58256	3.09	0.002	12.96372	58.72765
ccxa180_set2_pred						
Fairly likely	-97.64494	3.263686	-29.92	0.000	-104.0819	-91.20794
Not very likely	-192.5281	6.442694	-29.88	0.000	-205.3073	-179.7489
Not at all likely	-251.8748	8.554441	-29.44	0.000	-268.8754	-234.8741
eb_se033a_set2_pred	-54.52518	9.109329	-5.99	0.000	-72.70431	-36.34604
eb_a006_set2_pred						
Social housing	-32.40942	5.772009	-5.61	0.000	-43.85334	-20.96551
Privately rented	-18.01815	6.10826	-2.95	0.004	-30.0631	-5.973207
Other	2.583306	9.189289	0.28	0.779	-15.59583	20.76244
eb_sen_set2_pred	-54.32107	5.121705	-10.61	0.000	-64.45914	-44.18299
eb_children_set2_pred	1.04331	1.947069	0.54	0.593	-2.809943	4.896563
_cons	451.1372	14.19397	31.78	0.000	423.1909	479.0835

3) Full sample. Outcome: 5 'good' GCSEs

Model 1

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.129574	.1873473	0.73	0.464	.8129095	1.569594
2	.9682226	.0535377	-0.58	0.560	.8681838	1.079789
_cons	1.154255	.038969	4.25	0.000	1.080161	1.233431

Model 2

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.024455	.1763122	0.14	0.889	.7288953	1.439861
2	.9075241	.0571763	-1.54	0.125	.8016095	1.027433
soclass_set1_pred						
II	1.448908	.188315	2.85	0.004	1.122968	1.869452
III NM	1.693189	.2126109	4.19	0.000	1.323636	2.16592
III M	2.950931	.38227	8.35	0.000	2.288901	3.804444
IV	2.916395	.3963791	7.88	0.000	2.234032	3.80718
V	3.438408	.7644681	5.55	0.000	2.223597	5.316902
sex	.6142169	.0304466	-9.83	0.000	.5573422	.6768954
eb_ptlbw	1.073891	.1151219	0.67	0.506	.8703835	1.324982
mz028b_set1_pred	1.049678	.0059324	8.58	0.000	1.038115	1.06137
c645a_set1_pred						
Vocational	1.312184	.1158793	3.08	0.002	1.103619	1.560164
O level	2.094662	.1393324	11.12	0.000	1.838579	2.386415
A level	3.415603	.2593144	16.18	0.000	2.943345	3.963635
Degree	4.698686	.5159494	14.09	0.000	3.788767	5.827134
paritybi_set1_pred	.6693046	.0333604	-8.06	0.000	.6070101	.737992
eb_b650_set1_pred	1.182147	.0564964	3.50	0.000	1.07644	1.298234
eb_c804_set1_pred	.8576129	.1026929	-1.28	0.200	.6781637	1.084546
eb_marital_set1_pred						
1	1.658995	.1133887	7.41	0.000	1.450989	1.89682
2	1.167298	.1363008	1.32	0.185	.9285113	1.467494
_cons	.0669174	.0143281	-12.63	0.000	.0439816	.1018138

Model 3

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.195428	.2530916	0.84	0.401	.7860389	1.818036
2	1.03075	.0770365	0.41	0.686	.8896204	1.194269
soclass_set1_pred						
II	1.073008	.1945831	0.39	0.698	.7508692	1.53335
III NM	1.152869	.1909103	0.86	0.391	.8325208	1.596486
III M	1.745584	.2934356	3.31	0.001	1.254492	2.428921
IV	1.565879	.2760251	2.54	0.011	1.107475	2.214023
V	1.318825	.3476558	1.05	0.294	.786362	2.211832
sex	.704227	.0460036	-5.37	0.000	.6194446	.8006133
eb_ptlbw	1.058154	.1431175	0.42	0.676	.811643	1.379534
mz028b_set1_pred	1.030532	.0084127	3.68	0.000	1.014137	1.047192
c645a_set1_pred						
Vocational	1.067875	.1290065	0.54	0.587	.8422295	1.353973
O level	1.398945	.1291834	3.64	0.000	1.166689	1.677435
A level	2.016017	.2180713	6.48	0.000	1.629813	2.493738
Degree	2.294323	.3339926	5.70	0.000	1.723881	3.053528
paritybi_set1_pred	.8770817	.0603977	-1.90	0.057	.7662112	1.003995
eb_b650_set1_pred	1.136291	.0731325	1.99	0.048	1.001372	1.289387
eb_c804_set1_pred	.8807082	.1410568	-0.79	0.428	.6428039	1.206662
eb_marital_set1_pred						
1	1.133565	.1096624	1.30	0.196	.9373581	1.370841
2	1.035689	.1675382	0.22	0.828	.7537074	1.423167
ks4_fsm_set2_pred	.6217299	.1085992	-2.72	0.007	.4410947	.876338
ks4_idaci_set2_pred	.5602566	.1401183	-2.32	0.021	.3427867	.9156933
ccxa180_set2_pred						
Fairly likely	.1931218	.0160504	-19.79	0.000	.1638531	.2276188
Not very likely	.0312948	.0068901	-15.73	0.000	.0202239	.0484261
Not at all likely	.0180193	.0060195	-12.02	0.000	.0093187	.0348434
eb_se033a_set2_pred	.3636334	.0831922	-4.42	0.000	.2310759	.5722331
eb_a006_set2_pred						
Social housing	.5912062	.0724303	-4.29	0.000	.4644414	.7525701
Privately rented	.7496083	.1059793	-2.04	0.042	.56765	.9898927
Other	.9840657	.1900353	-0.08	0.934	.6731779	1.438528
eb_sen_set2_pred	.3007159	.0370768	-9.75	0.000	.2359323	.3832882
eb_children_set2_pred	1.06664	.0486699	1.41	0.159	.9748118	1.167119
_cons	1.048262	.350304	0.14	0.888	.5438092	2.02066

Model 4

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.195762	.2545105	0.84	0.403	.7844842	1.822658
2	1.031002	.0776507	0.41	0.686	.8888394	1.195903
soclass_set1_pred						
II	1.079823	.1930851	0.43	0.668	.7593261	1.535595
III NM	1.15932	.1942107	0.88	0.378	.8340535	1.611435
III M	1.758941	.2789243	3.56	0.000	1.287742	2.402556
IV	1.573625	.2858196	2.50	0.013	1.101428	2.24826
V	1.317895	.4066244	0.89	0.371	.7196724	2.413387
sex	.707004	.0597144	-4.11	0.000	.5990777	.8343736
eb_ptlbw	1.054445	.1450695	0.39	0.700	.8051233	1.380974
mz028b_set1_pred	1.030133	.0090127	3.39	0.001	1.012589	1.047981
c645a_set1_pred						
Vocational	1.067437	.1346819	0.52	0.605	.8331201	1.367655
O level	1.400543	.1257164	3.75	0.000	1.173895	1.670951
A level	2.010954	.2399455	5.85	0.000	1.59082	2.542045
Degree	2.295046	.7309858	2.61	0.009	1.229293	4.284768
paritybi_set1_pred	.8837946	.063372	-1.72	0.085	.7678078	1.017303
eb_b650_set1_pred	1.133491	.0841316	1.69	0.092	.9798756	1.311188
eb_c804_set1_pred	.8841363	.1466375	-0.74	0.458	.6381727	1.224899
eb_marital_set1_pred						
1	1.131288	.1120904	1.24	0.214	.9312484	1.374298
2	1.035405	.1709998	0.21	0.833	.7485822	1.432125
ks4_fsm_set2_pred	.623311	.1124535	-2.62	0.009	.4372916	.8884613
ks4_idaci_set2_pred	.5890418	.2388345	-1.31	0.192	.2660046	1.304377
ccxa180_set2_pred						
Fairly likely	.194438	.0212522	-14.98	0.000	.1568316	.2410619
Not very likely	.0319545	.0073202	-15.03	0.000	.0202933	.0503165
Not at all likely	.0185607	.0062711	-11.80	0.000	.0095218	.0361801
eb_se033a_set2_pred	.3639436	.0865633	-4.25	0.000	.2273156	.5826919
eb_a006_set2_pred						
Social housing	.5898561	.0732172	-4.25	0.000	.461909	.753244
Privately rented	.7552856	.1079669	-1.96	0.050	.5701905	1.000466
Other	.9808986	.2077626	-0.09	0.927	.6470694	1.486953
eb_sen_set2_pred	.3010886	.0425698	-8.49	0.000	.228066	.3974917
eb_children_set2_pred	1.065837	.0485829	1.40	0.164	.9741558	1.166148
eb_txa110_set3_pred						
2	.9932623	.1210534	-0.06	0.956	.781832	1.26187
3	.6994673	.1494237	-1.67	0.096	.4589081	1.066128
4	.5561302	.3450422	-0.95	0.346	.1628598	1.899062
eb_ks4_asco005_set3_pred						
1	1.095193	.5624738	0.18	0.859	.400242	2.996809
_cons	1.061927	.3416875	0.19	0.852	.5644184	1.997965

Model 3b

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.210265	.2818147	0.82	0.414	.7638395	1.917605
2	1.055361	.0927875	0.61	0.541	.8873924	1.255124
eb_bp_ed	.7574413	.3690498	-0.57	0.569	.2897399	1.980111
int1						
1	1.245029	.7088668	0.38	0.701	.4063029	3.815128
2	1.233259	.6007401	0.43	0.667	.4721912	3.220999
soclass_set1_pred						
II	1.075093	.1952232	0.40	0.690	.7519617	1.537081
III NM	1.154357	.1915489	0.87	0.388	.8330271	1.599635
III M	1.749359	.2941987	3.33	0.001	1.257026	2.434522
IV	1.568811	.276751	2.55	0.011	1.109257	2.218753
V	1.321004	.3483956	1.06	0.291	.7874693	2.216026
sex	.7000965	.0464723	-5.37	0.000	.6145195	.7975909
eb_ptlbw	1.060042	.1434576	0.43	0.667	.8129648	1.382212
mz028b_set1_pred	1.030332	.0084892	3.63	0.000	1.013785	1.047149
c645a_set1_pred						
Vocational	1.064278	.1289921	0.51	0.607	.8387307	1.350479
O level	1.397006	.1290363	3.62	0.000	1.165023	1.675182
A level	2.017353	.2176651	6.50	0.000	1.631797	2.494007
Degree	2.291784	.3330881	5.71	0.000	1.722785	3.04871
paritybi_set1_pred	.8785584	.0607441	-1.87	0.061	.767075	1.006244
eb_b650_set1_pred	1.13462	.0734244	1.95	0.051	.999195	1.288399
eb_c804_set1_pred	.8835688	.1421083	-0.77	0.442	.6440236	1.212213
eb_marital_set1_pred						
1	1.133691	.1094401	1.30	0.194	.9378543	1.370421
2	1.035764	.1678548	0.22	0.828	.7533189	1.424106
ks4_fsm_set2_pred	.6210934	.1086677	-2.72	0.007	.4403895	.8759452
ks4_idaci_set2_pred	.5622846	.1407137	-2.30	0.022	.3439222	.9192894
ccxa180_set2_pred						
Fairly likely	.1931888	.0160802	-19.75	0.000	.1638687	.227755
Not very likely	.0313688	.0069031	-15.73	0.000	.0202762	.0485299
Not at all likely	.0180678	.0060355	-12.02	0.000	.0093441	.0349358
eb_se033a_set2_pred	.3661036	.0842173	-4.37	0.000	.2320548	.577587
eb_a006_set2_pred						
Social housing	.5919163	.0725373	-4.28	0.000	.4649696	.7535221
Privately rented	.7503123	.1061412	-2.03	0.043	.568089	.9909865
Other	.9857017	.1905782	-0.07	0.941	.6739899	1.441576
eb_sen_set2_pred	.3000781	.0370038	-9.76	0.000	.2354241	.3824879
eb_children_set2_pred	1.06627	.0488736	1.40	0.163	.9740654	1.167203
_cons	1.058155	.3574647	0.17	0.867	.5449425	2.054696

Model 3c

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.198996	.2527061	0.86	0.391	.7899223	1.819914
2	1.037643	.0770927	0.50	0.619	.89638	1.201167
eb_fh5312_abs	.9151465	.0533787	-1.52	0.130	.8157495	1.026655
int2	1.014925	.0384479	0.39	0.696	.9418597	1.093657
soclass_set1_pred						
II	1.07891	.1961779	0.42	0.676	.7542614	1.543293
III NM	1.159287	.1926103	0.89	0.374	.8362312	1.607148
III M	1.74858	.2945715	3.32	0.001	1.255735	2.434854
IV	1.572511	.2781375	2.56	0.011	1.110828	2.226079
V	1.326211	.3503196	1.07	0.285	.7899187	2.226603
sex	.7019101	.0459183	-5.41	0.000	.6172916	.7981281
eb_ptlbw	1.059442	.1434725	0.43	0.670	.8123574	1.381678
mz028b_set1_pred	1.030496	.0084347	3.67	0.000	1.014057	1.047201
c645a_set1_pred						
Vocational	1.069602	.1290696	0.56	0.577	.8438265	1.355786
O level	1.404236	.1296869	3.68	0.000	1.171082	1.683809
A level	2.02251	.2193957	6.49	0.000	1.634054	2.503312
Degree	2.302148	.3357167	5.72	0.000	1.728887	3.065488
paritybi_set1_pred	.8819744	.0609255	-1.82	0.069	.770154	1.01003
eb_b650_set1_pred	1.138919	.0736614	2.01	0.045	1.003054	1.293187
eb_c804_set1_pred	.8911326	.1423593	-0.72	0.471	.6509651	1.219908
eb_marital_set1_pred						
1	1.129559	.1097476	1.25	0.210	.9332629	1.367144
2	1.04054	.1682443	0.25	0.806	.7573596	1.429602
ks4_fsm_set2_pred	.618969	.108325	-2.74	0.006	.4388408	.8730334
ks4_idaci_set2_pred	.5644371	.1412633	-2.29	0.023	.345225	.9228451
ccxa180_set2_pred						
Fairly likely	.1939193	.0161431	-19.70	0.000	.1644847	.2286211
Not very likely	.0317003	.0069748	-15.69	0.000	.0204922	.0490385
Not at all likely	.0184734	.0061762	-11.94	0.000	.0095486	.0357402
eb_se033a_set2_pred	.3634199	.0830286	-4.43	0.000	.2310903	.5715256
eb_a006_set2_pred						
Social housing	.5874385	.072	-4.34	0.000	.4614351	.7478496
Privately rented	.7495736	.1057689	-2.04	0.042	.5679425	.9892913
Other	.9837906	.1911521	-0.08	0.933	.6713829	1.441568
eb_sen_set2_pred	.3033921	.0372848	-9.71	0.000	.2382279	.3863812
eb_children_set2_pred	1.06622	.0484937	1.41	0.160	.974721	1.166307
_cons	1.034665	.3471246	0.10	0.919	.5353412	1.99972

Model 3d

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.220266	.2621313	0.93	0.356	.7974229	1.867327
2	1.065785	.0931713	0.73	0.467	.896963	1.266381
1.eb_bp_ed	.9311954	.1077551	-0.62	0.539	.7405657	1.170895
eb_fh5312_abs	.9252961	.0379935	-1.89	0.059	.8535141	1.003115
int3	1.010667	.0365009	0.29	0.769	.941297	1.08515
soclass_set1_pred						
II	1.080201	.196431	0.42	0.672	.75514	1.545188
III NM	1.160503	.1927856	0.90	0.371	.8371492	1.608754
III M	1.75128	.2944728	3.33	0.001	1.25848	2.437054
IV	1.574938	.2780814	2.57	0.010	1.113237	2.228124
V	1.328119	.3506128	1.07	0.283	.7913093	2.22909
sex	.6978023	.0463273	-5.42	0.000	.6124936	.7949929
eb_ptlbw	1.062022	.1437374	0.44	0.657	.8144663	1.384823
mz028b_set1_pred	1.030278	.0084894	3.62	0.000	1.013731	1.047095
c645a_set1_pred						
Vocational	1.065868	.1289175	0.53	0.598	.8404102	1.351809
O level	1.401383	.1293676	3.66	0.000	1.1688	1.680249
A level	2.022753	.2187625	6.51	0.000	1.635328	2.501962
Degree	2.298609	.3343005	5.72	0.000	1.727589	3.058368
paritybi_set1_pred	.8831688	.0611842	-1.79	0.073	.77089	1.011801
eb_b650_set1_pred	1.137314	.0738366	1.98	0.048	1.001148	1.292
eb_c804_set1_pred	.8938381	.1435791	-0.70	0.485	.6517847	1.225783
eb_marital_set1_pred						
1	1.129918	.1098396	1.26	0.210	.9334641	1.367716
2	1.04237	.1690734	0.26	0.798	.7579134	1.433588
ks4_fsm_set2_pred	.6182521	.108288	-2.75	0.006	.4382086	.8722689
ks4_idaci_set2_pred	.5659835	.1419951	-2.27	0.024	.3457492	.926502
ccxa180_set2_pred						
Fairly likely	.1940574	.0161775	-19.67	0.000	.1645626	.2288386
Not very likely	.0317941	.0069939	-15.68	0.000	.020555	.0491785
Not at all likely	.0185127	.0061778	-11.95	0.000	.009581	.0357706
eb_se033a_set2_pred	.3657131	.0838413	-4.39	0.000	.2321779	.5760498
eb_a006_set2_pred						
Social housing	.5879018	.0720777	-4.33	0.000	.4617669	.7484914
Privately rented	.7500874	.1058382	-2.04	0.042	.5683371	.9899603
Other	.9844864	.191149	-0.08	0.936	.6720513	1.442172
eb_sen_set2_pred	.3027475	.0372185	-9.72	0.000	.2377017	.3855927
eb_children_set2_pred	1.065902	.0485996	1.40	0.163	.9742077	1.166226
_cons	1.042897	.3526074	0.12	0.901	.5367806	2.026216

4) Females only. Outcome: GCSE total score

Model 3

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-.6479159	9.269097	-0.07	0.944	-18.92657	17.63074
2	-11.59456	4.401383	-2.63	0.009	-20.28097	-2.908152
soclass_set1_pred						
II	-5.702831	10.13482	-0.56	0.574	-25.69373	14.28807
III NM	-5.698794	9.8232	-0.58	0.563	-25.07796	13.68038
III M	10.65555	9.771635	1.09	0.277	-8.593611	29.90471
IV	3.245698	10.06953	0.32	0.747	-16.57771	23.06911
V	11.50411	14.92548	0.77	0.441	-17.84431	40.85253
eb_ptlbw	-7.205994	8.273514	-0.87	0.384	-23.45303	9.041038
mz028b_set1_pred	1.280821	.4708134	2.72	0.007	.3552205	2.206422
c645a_set1_pred						
Vocational	6.344878	7.071043	0.90	0.370	-7.561973	20.25173
O level	6.395173	5.401123	1.18	0.237	-4.229284	17.01963
A level	18.98935	6.307415	3.01	0.003	6.584513	31.39418
Degree	51.05121	7.90515	6.46	0.000	35.52096	66.58146
paritybi_set1_pred	-13.14667	3.889867	-3.38	0.001	-20.78251	-5.510829
eb_b650_set1_pred	13.74677	3.706023	3.71	0.000	6.46542	21.02813
eb_c804_set1_pred	-5.440013	9.401308	-0.58	0.563	-23.94575	13.06572
eb_marital_set1_pred						
1	10.89722	5.815106	1.87	0.062	-.5521737	22.34662
2	1.009031	9.737115	0.10	0.918	-18.16345	20.18151
ks4_fsm_set2_pred	-16.59601	9.882429	-1.68	0.095	-36.09987	2.907844
ks4_idaci_set2_pred	26.55515	14.33156	1.85	0.065	-1.645469	54.75577
ccxa180_set2_pred						
Fairly likely	-97.98427	4.370334	-22.42	0.000	-106.5894	-89.3791
Not very likely	-197.9369	8.142801	-24.31	0.000	-214.0141	-181.8597
Not at all likely	-260.7641	10.60248	-24.59	0.000	-281.7351	-239.7931
eb_se033a_set2_pred	-60.33303	13.97636	-4.32	0.000	-87.99311	-32.67295
eb_a006_set2_pred						
Social housing	-35.15847	7.083176	-4.96	0.000	-49.13363	-21.1833
Privately rented	-15.48568	8.154331	-1.90	0.058	-31.53097	.5596015
Other	8.769146	10.39887	0.84	0.400	-11.67942	29.21771
eb_sen_set2_pred	-61.9397	7.85336	-7.89	0.000	-77.44608	-46.43333
eb_children_set2_pred	2.639637	2.610286	1.01	0.313	-2.51336	7.792634
_cons	454.9203	19.02782	23.91	0.000	417.5269	492.3138

Model 3b

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-1.506546	10.79677	-0.14	0.889	-22.78016	19.76707
2	-11.34834	5.150399	-2.20	0.029	-21.51706	-1.179622
eb_bp_ed	-11.55356	32.09577	-0.36	0.719	-74.94359	51.83647
int1						
1	13.72134	36.3738	0.38	0.706	-58.05469	85.49737
2	10.6759	31.80106	0.34	0.737	-52.08614	73.43794
soclass_set1_pred						
II	-5.660843	10.12199	-0.56	0.577	-25.62536	14.30367
III NM	-5.645379	9.797722	-0.58	0.565	-24.97247	13.68172
III M	10.69004	9.732123	1.10	0.273	-8.478694	29.85877
IV	3.275707	10.03027	0.33	0.744	-16.46786	23.01928
V	11.50394	14.88397	0.77	0.440	-17.76046	40.76834
eb_ptlbw	-7.206352	8.299586	-0.87	0.386	-23.5056	9.0929
mz028b_set1_pred	1.279689	.4725954	2.71	0.007	.3504997	2.208879
c645a_set1_pred						
Vocational	6.25728	7.06782	0.89	0.377	-7.642641	20.1572
O level	6.350366	5.387611	1.18	0.239	-4.246568	16.9473
A level	18.99079	6.29858	3.02	0.003	6.603926	31.37765
Degree	51.02244	7.903965	6.46	0.000	35.4947	66.55017
paritybi_set1_pred	-13.13448	3.900449	-3.37	0.001	-20.79141	-5.477543
eb_b650_set1_pred	13.70519	3.726601	3.68	0.000	6.382626	21.02775
eb_c804_set1_pred	-5.402763	9.392625	-0.58	0.566	-23.89042	13.0849
eb_marital_set1_pred						
1	10.89718	5.812911	1.87	0.062	-.5476693	22.34204
2	.9633887	9.754596	0.10	0.921	-18.24428	20.17106
ks4_fsm_set2_pred	-16.58241	9.863287	-1.68	0.094	-36.04689	2.882074
ks4_idaci_set2_pred	26.56412	14.34667	1.85	0.065	-1.666659	54.7949
ccxa180_set2_pred						
Fairly likely	-97.97217	4.36366	-22.45	0.000	-106.5637	-89.38065
Not very likely	-197.8666	8.127353	-24.35	0.000	-213.9117	-181.8215
Not at all likely	-260.7009	10.60663	-24.58	0.000	-281.6794	-239.7223
eb_se033a_set2_pred	-60.20014	14.11703	-4.26	0.000	-88.14587	-32.2544
eb_a006_set2_pred						
Social housing	-35.13963	7.096869	-4.95	0.000	-49.14245	-21.1368
Privately rented	-15.47061	8.129777	-1.90	0.058	-31.46607	.5248404
Other	8.712531	10.40434	0.84	0.403	-11.74652	29.17158
eb_sen_set2_pred	-61.98151	7.848969	-7.90	0.000	-77.47853	-46.4845
eb_children_set2_pred	2.636461	2.603818	1.01	0.313	-2.503235	7.776157
_cons	455.1293	19.02994	23.92	0.000	417.7322	492.5264

Model 3c

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-.6115731	9.222929	-0.07	0.947	-18.79706	17.57391
2	-11.03081	4.415298	-2.50	0.013	-19.74553	-2.316093
eb_fh5312_abs	-4.797223	3.735762	-1.28	0.201	-12.16667	2.572223
int2	.0717871	2.163231	0.03	0.974	-4.198518	4.342092
soclass_set1_pred						
II	-5.136796	10.28049	-0.50	0.618	-25.42488	15.15129
III NM	-5.171362	9.911008	-0.52	0.602	-24.72991	14.38719
III M	10.92266	9.843916	1.11	0.268	-8.473967	30.31928
IV	3.613261	10.12505	0.36	0.721	-16.32337	23.54989
V	12.2135	14.98557	0.82	0.416	-17.25725	41.68425
eb_ptlbw	-7.101053	8.224118	-0.86	0.388	-23.24938	9.047278
mz028b_set1_pred	1.273593	.4671578	2.73	0.007	.3553367	2.191849
c645a_set1_pred						
Vocational	6.581664	7.038156	0.94	0.350	-7.259173	20.4225
O level	6.886867	5.420987	1.27	0.205	-3.778016	17.55175
A level	19.45565	6.338278	3.07	0.002	6.988065	31.92323
Degree	51.11548	7.927781	6.45	0.000	35.53918	66.69178
paritybi_set1_pred	-12.67638	3.907619	-3.24	0.001	-20.3479	-5.004861
eb_b650_set1_pred	13.97745	3.730515	3.75	0.000	6.646592	21.30831
eb_c804_set1_pred	-4.507899	9.414326	-0.48	0.632	-23.04035	14.02455
eb_marital_set1_pred						
1	10.4459	5.823583	1.79	0.074	-1.020963	21.91276
2	1.497926	9.701977	0.15	0.877	-17.6039	20.59975
ks4_fsm_set2_pred	-17.09057	9.975215	-1.71	0.089	-36.78403	2.602901
ks4_idaci_set2_pred	27.70193	14.30603	1.94	0.054	-.4477055	55.85157
ccxa180_set2_pred						
Fairly likely	-97.63815	4.37154	-22.33	0.000	-106.246	-89.03031
Not very likely	-196.6634	8.185988	-24.02	0.000	-212.8282	-180.4985
Not at all likely	-258.5446	10.76216	-24.02	0.000	-279.8396	-237.2496
eb_se033a_set2_pred	-59.95002	13.87379	-4.32	0.000	-87.40134	-32.4987
eb_a006_set2_pred						
Social housing	-35.51966	7.070298	-5.02	0.000	-49.46907	-21.57024
Privately rented	-15.60172	8.154832	-1.91	0.057	-31.64853	.4450867
Other	8.565181	10.457	0.82	0.413	-12.00144	29.1318
eb_sen_set2_pred	-61.06861	7.747587	-7.88	0.000	-76.3595	-45.77771
eb_children_set2_pred	2.628274	2.58729	1.02	0.311	-2.47807	7.734618
_cons	453.6899	18.98727	23.89	0.000	416.3772	491.0026

Model 3d

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ks4_ptstnewe_out	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	-.4849142	9.375611	-0.05	0.959	-18.97278	18.00296
2	-10.88028	4.926403	-2.21	0.028	-20.60011	-1.160458
1.eb_bp_ed	-.3714487	5.514523	-0.07	0.946	-11.28285	10.53995
eb_fh5312_abs	-5.00313	2.877041	-1.74	0.085	-10.70604	.6997758
int3	.273007	1.899187	0.14	0.886	-3.485523	4.031537
soclass_set1_pred						
II	-5.154467	10.26224	-0.50	0.616	-25.40527	15.09633
III NM	-5.194643	9.907087	-0.52	0.601	-24.74513	14.35584
III M	10.90948	9.815801	1.11	0.268	-8.42992	30.24889
IV	3.595181	10.09381	0.36	0.722	-16.278	23.46837
V	12.12602	14.98562	0.81	0.419	-17.34473	41.59676
eb_ptlbw	-7.070654	8.233669	-0.86	0.391	-23.23811	9.096801
mz028b_set1_pred	1.272802	.4671931	2.72	0.007	.354478	2.191126
c645a_set1_pred						
Vocational	6.533565	7.029154	0.93	0.353	-7.288768	20.3559
O level	6.850471	5.411848	1.27	0.206	-3.795799	17.49674
A level	19.44113	6.332136	3.07	0.002	6.985997	31.89626
Degree	51.08354	7.921916	6.45	0.000	35.51906	66.64802
paritybi_set1_pred	-12.67944	3.923412	-3.23	0.001	-20.38256	-4.976325
eb_b650_set1_pred	13.95188	3.75366	3.72	0.000	6.574579	21.32918
eb_c804_set1_pred	-4.479122	9.383914	-0.48	0.634	-22.94961	13.99137
eb_marital_set1_pred						
1	10.46163	5.80374	1.80	0.073	-.965003	21.88827
2	1.457302	9.65889	0.15	0.880	-17.5571	20.47171
ks4_fsm_set2_pred	-17.09896	9.966636	-1.72	0.088	-36.77481	2.576895
ks4_idaci_set2_pred	27.62827	14.32761	1.93	0.055	-.5648064	55.82136
ccxa180_set2_pred						
Fairly likely	-97.63459	4.369117	-22.35	0.000	-106.2374	-89.03176
Not very likely	-196.6622	8.170047	-24.07	0.000	-212.794	-180.5303
Not at all likely	-258.5512	10.77587	-23.99	0.000	-279.8736	-237.2288
eb_se033a_set2_pred	-59.91093	14.00397	-4.28	0.000	-87.62668	-32.19517
eb_a006_set2_pred						
Social housing	-35.52106	7.079392	-5.02	0.000	-49.48891	-21.55321
Privately rented	-15.61008	8.151812	-1.91	0.056	-31.65079	.4306341
Other	8.584377	10.43869	0.82	0.411	-11.94521	29.11397
eb_sen_set2_pred	-61.04913	7.774175	-7.85	0.000	-76.39393	-45.70433
eb_children_set2_pred	2.630429	2.584455	1.02	0.310	-2.470084	7.730941
_cons	453.7484	18.99201	23.89	0.000	416.4263	491.0706

5) Females only. Outcome: 5 'good' GCSEs

Model 3/3a

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.227312	.3314719	0.76	0.450	.7191122	2.094659
2	1.073214	.1107276	0.68	0.494	.8759719	1.314869
soclass_set1_pred						
II	1.139873	.2634547	0.57	0.571	.7238096	1.795099
III NM	1.153093	.2530001	0.65	0.516	.7493621	1.774341
III M	1.740984	.3852012	2.51	0.012	1.127621	2.687983
IV	1.775638	.4153089	2.45	0.014	1.12199	2.810088
V	1.881568	.7928675	1.50	0.134	.8231678	4.300824
eb_ptlbw	1.155551	.2322123	0.72	0.472	.7790977	1.713904
mz028b_set1_pred	1.022138	.011466	1.95	0.051	.9998814	1.044889
c645a_set1_pred						
Vocational	1.160069	.1795525	0.96	0.338	.8562689	1.571657
O level	1.435747	.1726184	3.01	0.003	1.133934	1.817893
A level	1.976235	.2828801	4.76	0.000	1.492189	2.617298
Degree	3.139941	.6794659	5.29	0.000	2.053824	4.800426
paritybi_set1_pred	.9639028	.0939317	-0.38	0.706	.7961664	1.166978
eb_b650_set1_pred	1.31906	.1186217	3.08	0.002	1.105637	1.573679
eb_c804_set1_pred	.9210092	.2034149	-0.37	0.710	.5969124	1.421076
eb_marital_set1_pred						
1	1.03058	.1395927	0.22	0.824	.789865	1.344653
2	.9266107	.2091658	-0.34	0.736	.5947663	1.443605
ks4_fsm_set2_pred	.5227826	.1242425	-2.73	0.007	.3277945	.8337591
ks4_idaci_set2_pred	.5597807	.1842088	-1.76	0.078	.2934997	1.067648
ccxa180_set2_pred						
Fairly likely	.179004	.0196559	-15.67	0.000	.1441611	.2222682
Not very likely	.0258646	.0070877	-13.34	0.000	.0150541	.0444382
Not at all likely	.0161644	.007469	-8.93	0.000	.0064884	.0402699
eb_se033a_set2_pred	.3330453	.1437147	-2.55	0.012	.142162	.7802309
eb_a006_set2_pred						
Social housing	.57511	.0897336	-3.55	0.000	.4232157	.7815201
Privately rented	.6747322	.1303266	-2.04	0.042	.4616909	.9860784
Other	.9908625	.24682	-0.04	0.971	.6077194	1.615562
eb_sen_set2_pred	.2659282	.0513998	-6.85	0.000	.1819484	.3886695
eb_children_set2_pred	1.07812	.0688101	1.18	0.240	.9507181	1.222594
_cons	1.100383	.5073046	0.21	0.836	.4452253	2.719618

Model 3b

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.258821	.4067208	0.71	0.477	.6642841	2.385472
2	1.092755	.1311233	0.74	0.460	.8628507	1.383916
eb_bp_ed	.8068297	.6332137	-0.27	0.785	.1717579	3.790068
int1						
1	1.143093	1.011473	0.15	0.880	.2001004	6.530029
2	1.186134	.9457544	0.21	0.831	.2463203	5.71173
soclass_set1_pred						
II	1.141012	.2646571	0.57	0.570	.7233384	1.799862
III NM	1.15406	.2542074	0.65	0.516	.7486947	1.778901
III M	1.744031	.3871654	2.51	0.012	1.127927	2.696667
IV	1.778551	.417128	2.46	0.014	1.122399	2.81829
V	1.884664	.794632	1.50	0.133	.8241343	4.309925
eb_ptlbw	1.157365	.2331323	0.73	0.468	.7795797	1.718225
mz028b_set1_pred	1.022067	.0115482	1.93	0.054	.9996499	1.044986
c645a_set1_pred						
Vocational	1.156952	.179319	0.94	0.347	.8536075	1.568096
O level	1.433731	.1726005	2.99	0.003	1.131992	1.8159
A level	1.976852	.2823936	4.77	0.000	1.493533	2.616576
Degree	3.135973	.6792667	5.28	0.000	2.050378	4.796351
paritybi_set1_pred	.9647241	.0940587	-0.37	0.713	.7967706	1.168081
eb_b650_set1_pred	1.316763	.1190651	3.04	0.002	1.102628	1.572484
eb_c804_set1_pred	.9248673	.2052275	-0.35	0.725	.5981733	1.429986
eb_marital_set1_pred						
1	1.02993	.1393356	0.22	0.828	.7896311	1.343356
2	.9267938	.2097695	-0.34	0.737	.5941657	1.445635
ks4_fsm_set2_pred	.5215457	.1238531	-2.74	0.006	.3271431	.8314706
ks4_idaci_set2_pred	.5611358	.1843804	-1.76	0.079	.2945021	1.069172
ccxa180_set2_pred						
Fairly likely	.1788641	.0196324	-15.68	0.000	.1440626	.2220727
Not very likely	.0258839	.0070897	-13.34	0.000	.0150695	.0444592
Not at all likely	.0161837	.0074834	-8.92	0.000	.0064918	.0403453
eb_se033a_set2_pred	.3350838	.1459919	-2.51	0.013	.141831	.7916542
eb_a006_set2_pred						
Social housing	.5760823	.0900707	-3.53	0.000	.4236593	.7833437
Privately rented	.6749466	.1302045	-2.04	0.042	.4620654	.9859057
Other	.9927222	.2477096	-0.03	0.977	.6083452	1.619964
eb_sen_set2_pred	.265141	.0515284	-6.83	0.000	.1810261	.3883406
eb_children_set2_pred	1.077561	.0689823	1.17	0.244	.9498577	1.222433
_cons	1.105954	.5127126	0.22	0.828	.445193	2.747424

Model 3c

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.228844	.3311221	0.76	0.446	.7209349	2.094582
2	1.081828	.1110301	0.77	0.444	.8839828	1.323954
eb_fh5312_abs	.9396748	.0910778	-0.64	0.522	.7763374	1.137377
int2	.9938983	.0563638	-0.11	0.914	.8887999	1.111424
soclass_set1_pred						
II	1.146959	.2659675	0.59	0.555	.727198	1.809019
III NM	1.159948	.2548952	0.68	0.500	.7533109	1.786088
III M	1.744852	.3865798	2.51	0.012	1.129453	2.69556
IV	1.783797	.4175414	2.47	0.014	1.126742	2.824011
V	1.898867	.802487	1.52	0.129	.8287188	4.35093
eb_ptlbw	1.157925	.2324535	0.73	0.465	.7810191	1.716719
mz028b_set1_pred	1.021955	.0114615	1.94	0.053	.9997082	1.044697
c645a_set1_pred						
Vocational	1.162467	.1793885	0.98	0.329	.8588325	1.57345
O level	1.444861	.1738472	3.06	0.002	1.140929	1.829758
A level	1.988861	.2855655	4.79	0.000	1.500407	2.636331
Degree	3.137655	.6798753	5.28	0.000	2.051161	4.799659
paritybi_set1_pred	.9702791	.0950105	-0.31	0.758	.8006839	1.175797
eb_b650_set1_pred	1.323761	.1196672	3.10	0.002	1.108538	1.580769
eb_c804_set1_pred	.9357813	.2065254	-0.30	0.764	.6066974	1.443367
eb_marital_set1_pred						
1	1.022353	.1387909	0.16	0.871	.7830865	1.334726
2	.9317942	.2103011	-0.31	0.754	.598153	1.451536
ks4_fsm_set2_pred	.5190773	.1239795	-2.75	0.006	.324698	.8298212
ks4_idaci_set2_pred	.5656776	.1865454	-1.73	0.084	.2961819	1.080387
ccxa180_set2_pred						
Fairly likely	.1795145	.0196609	-15.68	0.000	.1446567	.222772
Not very likely	.0261651	.0071591	-13.32	0.000	.0152423	.0449152
Not at all likely	.0165129	.0076449	-8.86	0.000	.0066164	.0412123
eb_se033a_set2_pred	.3336707	.1437259	-2.55	0.012	.1426534	.7804659
eb_a006_set2_pred						
Social housing	.570631	.0890225	-3.60	0.000	.4199433	.7753897
Privately rented	.6727449	.1299471	-2.05	0.041	.4603311	.9831745
Other	.9886553	.2478143	-0.05	0.964	.6044784	1.616996
eb_sen_set2_pred	.2690692	.0519447	-6.80	0.000	.1841854	.3930727
eb_children_set2_pred	1.078545	.0686356	1.19	0.236	.9514577	1.222608
_cons	1.088595	.5026909	0.18	0.854	.4397992	2.6945

Model 3d

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ks4_level2_em_out	Odds Ratio	Std. Err.	t	P>|t|	[95% Conf.	Interval]
eb_ed_ed						
1	1.248328	.3455652	0.80	0.425	.72164	2.159419
2	1.103588	.1308476	0.83	0.407	.8738045	1.393799
1.eb_bp_ed	.9554229	.1246506	-0.35	0.727	.7385659	1.235953
eb_fh5312_abs	.9204033	.0607633	-1.26	0.210	.8081141	1.048295
int3	1.01205	.0477294	0.25	0.800	.9222629	1.110579
soclass_set1_pred						
II	1.147839	.2664261	0.59	0.553	.7274313	1.811214
III NM	1.159845	.2551761	0.67	0.501	.7528483	1.786868
III M	1.744956	.3870801	2.51	0.012	1.128903	2.697196
IV	1.785433	.4181104	2.48	0.014	1.127541	2.827187
V	1.897735	.8018669	1.52	0.130	.8283598	4.347624
eb_ptlbw	1.159986	.2327676	0.74	0.460	.7825468	1.719471
mz028b_set1_pred	1.021878	.0114832	1.93	0.054	.9995881	1.044664
c645a_set1_pred						
Vocational	1.15961	.1791379	0.96	0.338	.8564449	1.570089
O level	1.442914	.1735954	3.05	0.002	1.139422	1.827242
A level	1.991471	.2850967	4.81	0.000	1.503654	2.637545
Degree	3.135914	.6784522	5.28	0.000	2.051391	4.793797
paritybi_set1_pred	.9716154	.0952774	-0.29	0.769	.8015641	1.177743
eb_b650_set1_pred	1.321653	.1198539	3.08	0.002	1.106145	1.579148
eb_c804_set1_pred	.9397908	.2083563	-0.28	0.779	.6080747	1.452464
eb_marital_set1_pred						
1	1.022532	.1387841	0.16	0.870	.7832718	1.334876
2	.9344403	.2111171	-0.30	0.764	.5995727	1.456335
ks4_fsm_set2_pred	.517918	.1237273	-2.75	0.006	.3239438	.828042
ks4_idaci_set2_pred	.5661682	.1863969	-1.73	0.084	.296766	1.080132
ccxa180_set2_pred						
Fairly likely	.1796228	.0196754	-15.67	0.000	.1447401	.2229123
Not very likely	.0262089	.0071665	-13.32	0.000	.0152735	.0449738
Not at all likely	.0165157	.0076496	-8.86	0.000	.0066148	.0412362
eb_se033a_set2_pred	.3355035	.1448725	-2.53	0.012	.1431295	.7864384
eb_a006_set2_pred						
Social housing	.5712103	.0891528	-3.59	0.000	.4203115	.7762843
Privately rented	.67332	.129932	-2.05	0.041	.4608982	.9836442
Other	.9907236	.2476795	-0.04	0.970	.6065463	1.618233
eb_sen_set2_pred	.2684731	.0519547	-6.80	0.000	.1836064	.3925671
eb_children_set2_pred	1.07797	.0687915	1.18	0.241	.9506075	1.222396
_cons	1.090349	.5037676	0.19	0.852	.440295	2.700145