Analysis

Patient-centredness, not personal responsibility, should drive adherence monitoring in outcomes-based pharmaceutical contracts

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KEY MESSAGES

- Outcomes-based pharmaceutical contracts (OBPCs) seek to align payments for drugs with their real-world outcomes and are gaining traction worldwide, including in the UK
- OBPCs raise novel issues for patients as medication adherence may affect the revenues of manufacturers and costs to the health system
- Adherence however is a highly complex issue, and OBPCs can create tensions between patients and financial outcomes which may be exacerbated further by adherence monitoring technologies
- Patient-centredness and transparency must be prioritised in the development of OBPCs and adherence monitoring technologies, and in their potential combination

Contributors and sources

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HN is an Associate Professor of Health Policy at the London School of Economics (UK). He conducts research and teaches on pharmaceutical policy. He has written extensively on pharmaceutical economics, policy, and regulation.

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The idea for the article was conceived by HS. TB wrote the first draft and led all subsequent revisions. TB, HN and HS contributed to all subsequent drafts. ER contributed to later drafts, providing critical patient perspective to the article. All have read and agreed to the final version. TB is guarantor of the article.

Patient involvement

ER was introduced to TB, HN and HS by the BMJ editors. First and foremost a cancer patient, ER has been a patient representative on the CRUK and Greater Manchester Health and Social Care Partnership project researching OBPCs since its initiation. ER has a range of PPI experience across multiple organisations.

Conflicts of Interest

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None.

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Standfirst

Outcomes-based pharmaceutical contracts and digital health technologies that monitor adherence might harm patients' interests, argue Theodore Bartholomew and colleagues.

Multiple outcomes-based pharmaceutical contracts (OBPCs) have been agreed by NHS England in recent years,[1] in which payment for drugs is tied to real-world effectiveness instead of a fixed price per unit.[2] A drug manufacturer in an OBPC may, for example, refund drug costs if a patient has not responded to treatment. Challenges with OBPCs include how to measure outcomes (and the availability of infrastructure to do so) as well as political and commercial conflicts of interest.[2–4]

Patients' adherence to medications attains new importance in OBPCs. While reasons are complex and not all well understood, medication nonadherence is widespread with rates of up to 50% reported in hypertension, diabetes, asthma and cancer.[5–7] To secure financial advantage, manufacturers may argue that poor outcomes are not due to the drug but to suboptimal adherence. Payers like NHS England meanwhile may be inclined to argue the opposite. One solution to address such tensions may lie in tying OBPCs with a requirement for adherence monitoring. This presents clear measurement advantages for both manufacturer and payer, but whether it is in the interests of patients is unclear.

Here, we consider how OBPCs – and their potential combination with adherence monitoring – might affect patients within a nationalised health system such as the NHS. We argue that OBPCs must put patients first and emphasise the need for transparency.

OBPCs overview

The confidential manner in which OBPCs are negotiated[8] means that their emergence globally has been somewhat surreptitious in nature. The first publicly disclosed OBPCs emerged in the USA in the mid-1990s.[9] In one example, Merck refunded up to six months of prescription costs (to both patient and payer) if simvastatin plus diet did not lower cholesterol to target levels.[4] In England, North Staffordshire Health Authority agreed a similar contract with Parke-Davis (Pfizer) in 2000.[10] The first national UK OBPC was for four multiple sclerosis drugs where patients were monitored using a clinical disability score. Price adjustments were then made to achieve a cost per quality-adjusted life-year (QALY) of £36,000 or less, effectively leveraging the OBPC to close data gaps.[11] More recently, NHS

England has implemented a 'pay-per-cure' OBPC for hepatitis C in which the manufacturer is only paid if the patient is cured (see Table 1).[12] NHS England has stated that a 'series' of OBPCs have been agreed in recent years, although few have been publicly-disclosed.[1] Greater Manchester Health and Social Care Partnership have also stated their intent to introduce OBPCs, focusing on cancer drugs for which the NHS and manufacturers struggle to agree a price.[13] Across Europe and the USA, OBPC use has increased and is expected to increase further.[9,14] Selected UK examples of OBPCs are listed in Table 1.

Table 1: Selected UK examples of OBPCs

Therapeutic Area	Manufacturer(s)	Drug(s)	Year	Outcome Agreement
Hypercholesterolaemia	Parke-Davis (Pfizer)	Lipitor (atorvastatin)	2000	Manufacturer agreed to rebate North Staffordshire Health Authority if threshold percentages of defined patient cohorts did not achieve target cholesterol levels.[10]
Multiple Sclerosis	Biogen Bayer EMD Serono Teva	Avonex (beta-interferon) Betaferon (beta-interferon) Rebif (beta-interferon) Copaxone (glatiramer acetate)	2003	Price adjustments made at intervals to achieve an agreed cost per QALY of £36,000 or less.[11]
Multiple Myeloma	Johnson & Johnson	Velcade (bortezomib)	2006	Manufacturer reimburses NHS for the first four cycles if there is no response to treatment (response defined as 50% decrease in serum M protein).[4]
Psoriasis	Novartis	Cosentyx (secukinumab)	2017	Participating NHS trusts are provided with an (undisclosed) rebate if a patient fails to achieve a reduction in Psoriasis Area Severity Index score >90% after 16 weeks of treatment.[15]

Multiple Sclerosis	Merck	Mavenclad (cladribine)	2017	Undisclosed.[1]
Hepatitis C	Gilead Merck, Sharpe & Dohme (MSD) AbbVie	Harvoni (ledipasvir/ sofosbuvir) Epcusa (sofosbuvir/ velpatasvir) Zepatier (elbasvir/ grazoprevir) Maviret (glecaprevir) Viekirax (ombitasvir/ paritaprevir/ ritonavir) Exviera (dasabuvir)	2018	NHS only pays for medication if a patient is cured (defined as sustained virologic response at 12 weeks or longer after treatment completion).[12]

Payers such as NHS England are primarily interested in using OBPCs to provide access to high-cost drugs in situations where there is uncertainty over effectiveness and budgetary impact.[8,13] OBPCs in theory provide the opportunity for additional outcomes data to be gathered so that the drug can be priced according to its real-world value.[13]

For manufacturers, one attraction of OBPCs is that they can help demonstrate their product's effectiveness over competitors.[8] There are concerns however about being held accountable for outcomes given they lack control over how a medication is prescribed or taken,[8] which appear to have manifested in contractual terms. In one publicly-disclosed OBPC in the USA, a payer was given additional discounts if administrative data demonstrated that diabetic patients had been adherent, although specific stipulations were not disclosed.[2] Due to their oft-confidential nature, the prevalence of tying adherence to payment is not known but this OBPC is unlikely to be the only one of its kind.

Adherence monitoring

Adherence has previously been defined as "the extent to which patients take medications as prescribed by their health care providers".[16] Newer conceptualisations of adherence however more aptly recognise its complexity by appreciating the need for both a multilevel (i.e. regimen, patient, provider, health system) and multidimensional (i.e. initiation, implementation and persistence) approach.[6,16,17] There is no single ideal measure of adherence, and no universally accepted threshold for defining adherence.[16,18] A combination

approach using both subjective measures (i.e. those that evaluate a patient's beliefs and explanations) and objective measures (i.e. those that capture a record of medication use) however is recognised to be the most appropriate method for capturing the barriers, including patient preferences, to adherence.[18]

Many metrics (e.g. blood pressure, obesity) are routinely measured by health systems,[19] yet adherence is not and may only be informally checked by clinicians. Recently, multiple technologies have emerged that monitor adherence remotely (see Table 2).[20] Evidence supporting adherence monitoring technologies is typically poor and depends on the modality employed, the disease area studied and the resources allocated.[21–25] While it is currently not possible to make conclusive statements about their utility or cost-effectiveness, these technologies are of particular relevance to OBPCs.[26,27] Remote adherence monitoring may provide greater accuracy than pharmacy dispensing reports which are, for example, currently in use within the NHS to monitor treatment completion for hepatitis C patients.[28]

Table 2: Types of remote adherence monitoring technologies (conceptual overview)

Adherence Monitoring Type	Description
Text messages / Electronic diary	● Provider prompts patient via text message / electronic diary ● Patient reports adherence via text message / electronic diary
Signalling bottle	● Pill bottle flashes light when pill should be taken ● Pill bottle automatically sends a message to a computer/smartphone each time the cap is removed ● Computer/smartphone records whether/when pill bottle was opened
Video check (with healthcare professional)	● Professional calls and observes patient taking pill using video platform ● Professional records whether/when pill was taken
Video check (automated)	● App with facial and pill recognition capability analyses patient through smartphone camera ● App records whether/when pill was taken
Signalling pill	● Sensor is embedded within a pill ● Smartphone app reminds patient when pill should be taken ● When pill reaches stomach, signal is sent to a receiver which relays information to a smartphone recording whether/when pill was taken

Measurement of physiological/ biochemical marker	● Measurement of physiological markers (e.g. heart rate or blood pressure) ● Measurement of biochemical markers (e.g. blood glucose monitoring)

Adherence monitoring can go against patient interests

Patients have clear interests in their health. Whether a patient wishes or is able to be adherent depends on a vast array of complex factors, many of which may depend upon the relationships they have built with their medical teams and the communication between those teams.[6,17] Patients however often cite forgetfulness as a factor, and find adherence more challenging the more frequently a medication has to be taken.[6,26] Typically adherence is also higher for patients with acute conditions but with chronic conditions drops dramatically after six months of treatment.[26] Consequently, if patients voluntarily choose to use adherence monitoring as part of a shared decision making process, its use may support patients to act autonomously.[29] Conversely, it is possible that monitoring (particularly objective monitoring alone) may increase responsibility placed onto patients in ways that offer no or marginal additional benefit, and undermine, rather than support their interests.

Patients have many reasons for not taking their medications.[6,17] Side effects, for example, are a major predictor of nonadherence due to the impact they have on quality of life.[26] Adherence may also depend on the drug's perceived benefit. While adherence monitoring may help improve understanding of side effects[30] its use may still be resisted as patients may feel uncomfortable if it causes them to be labelled in an unqualified manner as 'non-adherent'.

Additional concerns exist surrounding whether adherence monitoring may unduly restrict patient liberty and autonomy.[29,31] Expectations to use adherence monitoring could undermine voluntariness, or even become coercive for patients, for example, where a patient is concerned that non-use will negatively impact the relationship with their physician. Another concern stems from tying financial rewards or penalties to adherence. The NHS does not presently allow financial penalties but incentives have been trialled, for example, in smoking cessation and weight loss programs.[32,33] Providing financial incentives to patients entails the risk that consent may be compromised. This concern would be heightened with patients who come from marginalised groups, where incentives could have disproportionate leverage.[34] Others may have privacy-related concerns that their confidential information might be sold to third parties and potentially linked back to them.[30] While further testing in actual clinical practice is required to fully understand adherence monitoring acceptability, concerns relating

to how it may affect face-to-face contact time, confidentiality, and difficulties using the technologies have been raised by patients before.[35,36]

Societal perspective can influence personal responsibility

A key consideration from the societal perspective is the patient's moral (and in some cases, legal[37]) obligations to consider how non-adherence may affect the health of others. Public health risk, for example, is the justification for using directly-observed therapy in some patients with tuberculosis.[37] As evidenced by the international response to the COVID-19 pandemic, public health can motivate obligations that go far beyond the individual.[38] In principle, the case for using adherence monitoring on public-interest grounds can therefore increase as risk of harm to others increases. Yet, it also increases healthcare professionals' obligations to communicate with their patients about the reasons why adherence may be important, which can only be done well if they have sufficient time to do so.

Within a nationalised health system such as the NHS, there is a societal expectation that the public should use collective resources responsibly.[39,40] This typically manifests, for example, in the notion that patients should keep their appointments, as set out in the NHS Constitution, which also states "Please follow the course of treatment which you have agreed, and talk to your clinician if you find this difficult".[39,40] Yet, this appeal also extends the other way, leading citizens to hold expectations about their treatment and how, for example, their data should not be used for profit. Societal expectation could extend to medication non-adherence, given its opportunity cost (health gains foregone) is estimated to be more than £500 million annually in the UK alone.[41] This however must be considered carefully alongside the wide-ranging and legitimate reasons that patients may have for not taking their medications.[6,17]

Risks to the patient-provider relationship and health system

Critically, adherence monitoring seems likely to impact one of the fundamental tenets of healthcare: the patient-provider relationship. The interactions between professionals and patients are already highly variable, and trust can be majorly affected if medications do not have desired consequences, if professionals fail to communicate effectively and if the patients have concerns about being taken advantage of.[42] Combining OBPCs with adherence monitoring technologies is unlikely to have predictable consequences. Physicians, for example, may exert implicit or explicit pressure on patients to use adherence monitoring to gain insights into how they take their medications. Behaviours may also be influenced by the amount of public information available for each OBPC: for example if both patient and physician, or neither are aware of the potential financial implications of

nonadherence. Both NICE and the Association of the British Pharmaceutical Industry (ABPI) acknowledge that all relevant information about drugs being appraised should be put in the public domain.[43] Current redaction practices however demonstrate that clinical and economic data of importance to patients, clinicians and researchers is frequently concealed.[44] In OBPCs, contractual stipulations relating to adherence monitoring and the effect of nonadherence on reimbursement are of direct relevance to patients, the public and health system, and should therefore be in the public domain.

Conclusion

The use of OBPCs is increasing, with their emergence driven by the commercial interests of manufacturers and the economic interests of payers to limit the budgetary impact of high-cost drugs. Concurrently, interest in the use of adherence monitoring has expanded rapidly in an attempt to address the challenges presented by nonadherence.[20] Patient and public acceptability to both of these practices in isolation however remains limited, and the policy-technology combination of OBPCs and adherence monitoring is likely have many unpredictable consequences.

Patients, society and health providers – particularly in a nationalised system using collective resources – have a right to greater involvement in how OBPCs will develop and are negotiated. This process should begin with the creation of a new transparency agreement between ABPI and NICE that is co-developed with patients. Additionally, we echo calls for the regulation of data transparency in drug appraisals.[44]

The importance of using subjective and objective adherence monitoring in conjunction must be recognised, as well as a more nuanced appreciation of both the multilevel and multidimensional nature of nonadherence. The impact on patients who are reluctant to use adherence monitoring must also be considered.

Impacts on behaviour and patient-provider relationships are likely to vary considerably according to disease characteristics, patient population, and the transparency with which contracts have been negotiated. Patient and public expectations will also be different across nationalised, privatised and insurance-based health systems, and will vary according to cultural and societal contexts.

Wider debate and more qualitative research needs to be undertaken with patients, healthcare professionals and policy makers on OBPCs and adherence monitoring to understand acceptability and feasibility. Both adherence monitoring technologies and the

OBPCs that they may be designed to support will fail if they are not created in partnership with patients, and with patient-centredness as the overarching goal.

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