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An assessment of antimicrobial resistance national action plans and their impact on antibiotic use

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ABSTRACT

Introduction By 2050, antimicrobial resistance (AMR) could lead to over 10 million deaths annually and $100 trillion in healthcare costs, making it one of the most urgent public health threats. The WHO recommends AMR National Action Plans (AMR NAPs) to address this threat, but the effectiveness of these plans is unknown.

Methods We estimate the impact of AMR NAPs on retail sales of all antibiotics across 68 countries from 2014 to 2023 using IQVIAs Multinational Integrated Data Analysis System dataset. We further examine the effect of AMR NAP adoption on the proportion of antibiotic sales by WHO AWaRe (Access, Watch, Reserve) classification. To account for differences in the quality of the AMR NAP, we also examine if countries with a better NAP have differential use of antibiotics following its adoption. Finally, we explore whether countries with higher quality NAPs make differential use of azithromycin during the COVID-19 pandemic.

Results The adoption of an AMR NAP did not have a significant impact on total retail antibiotic sales. But when accounting for the quality of the AMR NAP, as identified from an evaluation of NAP plans, we find that high-scoring AMR NAPs significantly increased the proportion of retail sales from Access-class agents (0.031; 95% CI 0.003 to 0.06), and significantly decreased the proportion of Watch-class antibiotics (−0.03; 95% CI −0.055 to −0.005) as compared with those with lower scoring or no NAPs. Countries with high-scoring NAPs also exhibited lower retail azithromycin sales per 1000 persons during the COVID-19 pandemic (−49.08; 95% CI −89 to −9.16).

Conclusions Countries with higher quality AMR NAPs exhibit more appropriate use of essential antibiotics overall and less inappropriate utilisation of azithromycin during the COVID-19 pandemic compared with those with no or low-scoring plans. Well-developed AMR NAPs may be a useful policy tool to promote more judicious antibiotic use globally.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Antimicrobial resistance National Action Plans (AMR NAPs) vary in quality and comprehensiveness, but there is a paucity of evidence to quantify their effects on AMR and AMR-related measures.

WHAT THIS STUDY ADDS

⇒ This is the first known observational study using quantitative methods to evaluate the impact of AMR NAP adoption on antibiotic sales across 68 countries. We find that countries with high-quality AMR NAPs use antibiotics more judiciously over time and during a healthcare shock such as the COVID-19 pandemic.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These results indicate that a high-quality AMR NAP is an effective policy tool to curb inappropriate antibiotic use and promote antimicrobial stewardship. Further work is needed to understand these effects at the country level.

INTRODUCTION

Antimicrobial resistance (AMR) is one of the most pressing challenges facing health systems globally. AMR threatens health system sustainability by reducing the effectiveness of antimicrobials, increasing healthcare costs and complicating disease control efforts.[1] By 2050, AMR is estimated to contribute to over 10 million annual deaths and $100 trillion in additional healthcare spending.[1 2] While AMR occurs naturally over time due to pathogen mutations and horizontal gene transfer, preventable antimicrobial misuse accelerates its emergence.[3] The COVID-19 pandemic provided conditions for further antibiotic misuse, given initial uncertainty regarding appropriate treatment regimens and disruptions to global supply chains.[4–6] Identifying practical policy tools that can promote improved antimicrobial stewardship within countries is an urgent priority.

In recognition of the pressing need to act on AMR, several governance tools have been created to assist health systems in providing effective stewardship. In 2015, 194 WHO member states committed to developing multisectoral AMR National Action Plans (NAPs).[7] AMR NAPs are the primary mechanism for guiding national strategy and action for AMR response. As of 2023, 115 publicly available AMR NAPs have been gradually implemented across countries.[8] Alongside these national strategies, the WHO introduced the AWaRe classification system (Access, Watch, Reserve) in 2017 to categorise antibiotics based on their importance in human medicine and their relation to AMR.[9] AWaRe classifies antibiotics into Access, Watch and Reserve groups. Access-class antibiotics consist of narrow-spectrum agents with the lowest potential for resistance generation.[9] Watch-class antibiotics require more caution and have a higher potential for AMR. Reserve-class antibiotics are agents of last resort for patients with confirmed multidrug-resistant infections.[9] AWaRe has been used for antibiotic monitoring and use targets across countries, with the WHO encouraging 60% of all countries' antibiotic use to be from the Access class. The current literature indicates that many countries fall below this WHO target, with most antibiotic use originating from the Watch class.[10]

Despite the continued exigency of AMR, limited literature assesses the effectiveness of AMR NAPs. While NAPs in other clinical areas are more robustly established and evaluated.[11] For example, national cancer control plans have been instituted in over 224 countries and have been shown to increase cancer screening strategies.[11–13] To address this gap in the literature, our study uses global antibiotic sales data from 68 countries to evaluate whether effective AMR NAPs promote more appropriate use of essential antibiotics. We aim to address three questions: (1) do countries make more responsible use of antibiotics, as outlined by the WHO AWaRe classification system, following the introduction of an AMR NAP? (2) Does the quality of an AMR NAP influence the use of antibiotics? (3) Did countries with high-scoring AMR NAPs exhibit different trends in the inappropriate use of azithromycin during the initial months of the COVID-19 pandemic?[14–17]

METHODS

Data

We first obtained information on medication sales in 70 high-income and middle-income countries (online supplemental appendix 1a) from the IQVIA Multinational Integrated Data Analysis System (MIDAS) dataset. IQVIA is a healthcare analytics company that collects data on prescription drug use in different countries. IQVIA MIDAS data are widely used in peer-reviewed studies to compare the volumes and prices of medicines including the Lancet Commission's Report on Essential Medicines and by international organisations including in the WHO's World Medicines Situation Report.[18–20] While IQVIA data report sales for retail and hospital sectors across countries, only 45 of the countries reported hospital sales. For this reason, we restrict all our primary analyses to the retail setting.

Using the 22nd version of the WHO Essential Medicines List (EML, online supplemental appendix 2a), we identified a basket of 41 antibiotics.[21] As the WHO outlines, these agents should always be available in functioning health systems to satisfy the population's needs. 95% of total antibiotic sales globally are from the antibiotics listed on the EML.[21] We group antibiotics into Access, Watch and Reserve classes based on the 2021 WHO AWaRe.[9] We obtained sales data for each antibiotic at the quarter level from 2014 to quarter 2 of 2023. Sales were recorded in terms of volume and monetary value. Volumes were measured in the number of 'standard units' (SUs), an IQVIA designation representing a single-dose unit. We further distinguished volumes sold by distribution channel. Of all antibiotic sales in each country, 7% were missing less than 30% of values over the study period. We applied a linear interpolation method to impute missing values based on existing sales. For those sales with over 30% missingness, we assumed there was no reported quarterly sale for an individual antibiotic in that country. In these cases, we filled missing values to 0, accounting for approximately 16.5% of the sales records.

To evaluate the effect of an AMR NAP on antibiotic sales, we first group countries by the year their AMR NAP is adopted, given the staggered roll-out (table 1). We further group countries based on their quality using previously published AMR NAP governance scores generated by Patel *et al* based on a previously published governance framework (online supplemental table 1a).[22] In their study, Patel *et al* systematically reviewed the contents of publicly available AMR NAPs across three domains: *policy design*, *implementation tools*, and *monitoring and evaluation* to generate an overall composite governance score between 0 (worst) and 100 (best) governance (online supplemental table 2a).[8] Patel *et al* drew on several data sources to generate scores, including publicly available AMR NAPs, the WHO Tripartite AMR Country Self-Assessment Survey (TrACSS), the WHO Global AMR and Use Surveillance System, the Global AMR Research and Development Hub, the WHO 2018 South-East Asia Region Situational Analysis and the WHO 2020 Immunisation Dashboard.[8 23] We removed New Zealand's AMR NAP from our analysis as it was not scored in Patel *et al*'s review since it is not included in TrACSS. We further excluded France from our analyses as it is the only country to implement the AMR NAP in 2022, which prevents the estimation of group treatment effects, resulting in a final sample of 68 countries.

We define AMR NAPs as 'high-scoring' and categorised them as part of the treatment group if their NAP's overall governance score was greater than or equal to the mean score (≥ 51, n=37) and define AMR NAPs as 'low-scoring' and part of the control group if the governance score was below the mean (≤ 50, n=21) (online supplemental figure 1a). We later vary the score thresholds as a sensitivity analysis (online supplemental figure 1a). We define the initial treatment quarter as the first quarter of the year of AMR NAP adoption (online supplemental table

Table 1 Groupings of countries by Antimicrobial Stewardship NAP enactment year, 2013–2022

AMR NAP enactment year	Countries
Any score AMR NAPs (n=60)	
2013	Vietnam
2015	Argentina, Germany and Switzerland
2016	China, Japan, Norway and Poland
2017	Bangladesh, Canada, Croatia, Finland, India *, Indonesia, Italy, Lithuania, Malaysia, New Zealand† Pakistan, Peru*, Saudi Arabia, Singapore, Sri Lanka* and Thailand
2018	Brazil, Colombia, Egypt, Jordan*, Korea, Luxembourg, Mexico*, South Africa, Turkey and Uruguay*
2019	Czech Republic, Ecuador, Greece*, Lebanon, Latvia, Morocco†, Philippines, Portugal, Russia, Serbia, Slovakia, Slovenia†, Spain, Tunisia, UAE and UK
2020	Australia, Belgium and USA
2021	Austria, Chile, Estonia*, Ireland, Netherlands and Sweden
2022	France
No AMR NAPs (n=10)	
Algeria‡, Belarus‡, Bosnia‡*, Bulgaria‡, Dominican Republic‡*, Hungary‡*, Kazakhstan‡, Kuwait‡*, Romania‡* and Venezuela‡*	

*Country does not report hospital data.
†Plan not reported in TrACSS.
‡Plan not developed or implemented.
AMR, antimicrobial resistance; NAP, National Action Plan; TrACSS, Tripartite AMR Country Self-Assessment Survey.

1a). Online supplemental figure 2a shows AMR NAP adoption over time by quality of the NAP.

Key variables

Our primary outcome variable is quarterly retail sales of antibiotics on the EML list, standardised per 1000 people in each country, using population estimates from the World Bank DataBank. Our secondary outcome variable is the proportion of antibiotic sales in each AWaRe class per quarter per country. Our third outcome is quarterly azithromycin sales per 1000 people per country per quarter. We obtained the baseline (2014) country-level on population (millions), country income classifications, median age and percentage of children immunised by 24 months with diphtheria, tetanus and acellular pertussis (DPT) vaccine from the World Bank DataBank and the WHO Global Health Observatory to control for country characteristics that may influence antibiotic uptake.[24 25]

To examine antibiotic use following the introduction of an AMR NAP, we plot median SUs of antibiotic sales by AMR NAP adoption from 2014 to 2023 (figure 1). As sales data are quarterly, we assign the first quarter of each year as the policy start date. We also plot the proportion of sales in each AWaRe class by AMR NAP scores (online supplemental Figure 3a). Each trend line is smoothed by a four-period moving average to adjust for seasonality in sales.

Statistical analysis

Due to the staggered-entry nature of the data, we used the Callaway and Sant'Anna (CS) multiple time period difference-in-difference to quantify the impact of AMR NAP adoption on total antibiotic sales and the proportion of sales by AWaRe class. We estimate the average treatment effect of AMR NAPs using the doubly robust estimator, adjusting for the 2014 country-level income classification. We follow the recommended bootstrapping procedure for inference and report simultaneous robust confidence bands with clustered errors at the country level.[26] In all our primary analyses, we observe the parallel trends in antibiotic sales in the pre-enactment period, with all CIs crossing zero (figures 2 and 3).

Next, we estimate the same model but grouping AMR NAPs by their governance score to examine whether the adoption of a high-scoring AMR NAP is significantly associated with a change in antibiotic sales relative to adopters of a low-scoring or no NAP. Finally, we examine whether countries with a high-scoring AMR NAP during the initial year of the COVID-19 pandemic had differential prescribing of azithromycin relative to countries with a low-scoring or no NAP, using the CS estimator to evaluate differences in total quarterly sales of azithromycin per 1000 people between treatment and control groups. We aggregate the observed effects from Q1 2020 to Q1 2021, during the acute period of the COVID-19 pandemic.

All analyses were conducted in R (V.4.3.2, R Project for Statistical Computing).

Robustness checks and sensitivity analysis

We estimate a set of alternative specifications: adding country-level income classification, comparing countries with high-scoring and low-scoring AMR NAPs and removing those without AMR NAPs. We further investigate alternative definitions of 'high-scoring' NAPs: 1 SD above the mean total score (online supplemental figure 1a), one SD below the mean total score (online supplemental figure 1a), mean domain scores for *implementation tools*, *policy design* and *monitoring and evaluation* (online supplemental tables 3a–5a).

RESULTS

AMR NAP adoption varies across countries. Vietnam was the first country to adopt an AMR NAP, in 2013, and France was the last, in 2022 (table 1). When we apply the mean governance score by Patel *et al* as the cut-off for a high-scoring NAP, we find that 21 countries have low-scoring NAPs and 37 have high-scoring NAPs. 10 countries have no AMR NAP. Countries with higher scoring NAPs are more populous, richer, have older populations and have a marginally higher percentage of children who

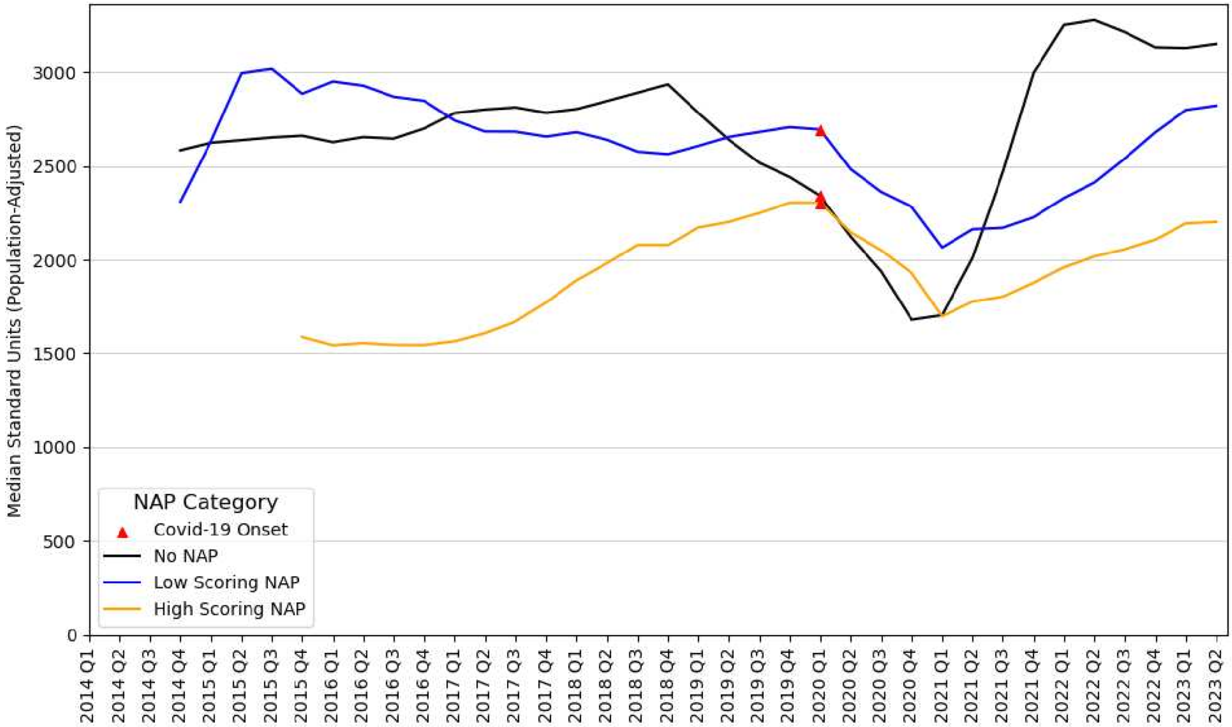

Figure 1 Median standard units of antibiotics sold over time by AMR NAP adoption in the retail sector. Sales volume is measured in the number of 'standard units' an IQVIA designation representing a single-dose unit. Red triangles indicate the onset of the COVID-19 pandemic. Blue: countries with high-scoring AMR NAPs (n=37); Yellow: countries with low-scoring AMR NAPs (n=21); Black: countries with no AMR NAPs (n=10). AMR, antimicrobial resistance; NAP, National Action Plan.

receive DPT immunisations relative to countries with no NAP or lower scoring NAPs (online supplemental table 6a).

Countries with a high-scoring AMR NAP have lower total median antibiotic sales compared with countries with low-scoring or no AMR NAP (figure 1). All countries see volatility in sales around the COVID-19 pandemic, with initial drops in sales and then accelerations. This volatility is most pronounced in the no-NAP group. We also present these trends differentiated by AMR NAP adoption year (online supplemental figure 4a). The proportion of sales of antibiotics by AWaRe class also varies by AMR adoption (online supplemental figure 3a). The high-scoring AMR NAP countries have a growing proportion of access-class antibiotic sales towards the end of the period, and a decrease in the watch-class antibiotic sales. We observe the opposite trend for the no-NAP group and the low-scoring NAP group. Trends are stable in the median proportion of Reserve-class antibiotics among all groups except for a spike between 2014 and 2017 in countries with a high-scoring AMR NAP, during the time two new Reserve-class antibiotics were added to the market.

Our first analyses explore the impact of AMR NAP adoption on antibiotic sales. We observe parallel trends in antibiotic sales in the pre-enactment period, with all CIs crossing zero between treatment and control countries. Total antibiotic sales per 1000 persons do not significantly decrease following the adoption of a NAP (408.19; 95% CI −68.61 to 884.98) (online supplemental figure 5a). When we evaluate the proportion of antibiotics consumed by AWaRe class, we observe an increase in the relative proportion of Access-class antibiotics consumed after NAP adoption (0.038; 95% CI −0.01 to 0.08) and a decrease in the relative proportion of Watch-class antibiotics (−0.037; 95% CI −0.08 to 0.006) but these changes are not statistically significant (figure 2). These models are further evaluated for calendar-level and group-level effects (online supplemental figures 6a–9a).

The adoption of a high-scoring NAP is associated with a statistically significant increase in the sales of Access-class antibiotics and a decrease in Watch-class antibiotics relative to countries with no NAP or the adoption of a low-scoring NAP (Access 0.031; 95% CI 0.003 to 0.058, Watch −0.03; 95% CI −0.055–−0.005) (figure 3). There is no significant change in total antibiotic sales across the two groups (4.54; 95% CI −202.63 to 211.71) (online supplemental figure 10a) and no significant effect on the proportion of Reserve-class retail sales (−0.0008; 95% CI −0.0028 to 0.0013). These models are evaluated for calendar-level and group-level effects (online supplemental figures 11a–14a), indicating that the effect is driven by the first adopters of a high-quality NAP (Germany and Switzerland), and the effect occurs approximately 7 years after NAP adoption.

Finally, we evaluate whether countries adopting high-scoring AMR NAPs experienced differential sales of the antibiotic azithromycin during the acute phase of the COVID-19 pandemic. Figure 4 illustrates that countries with effective AMR NAPs have significantly lower retail

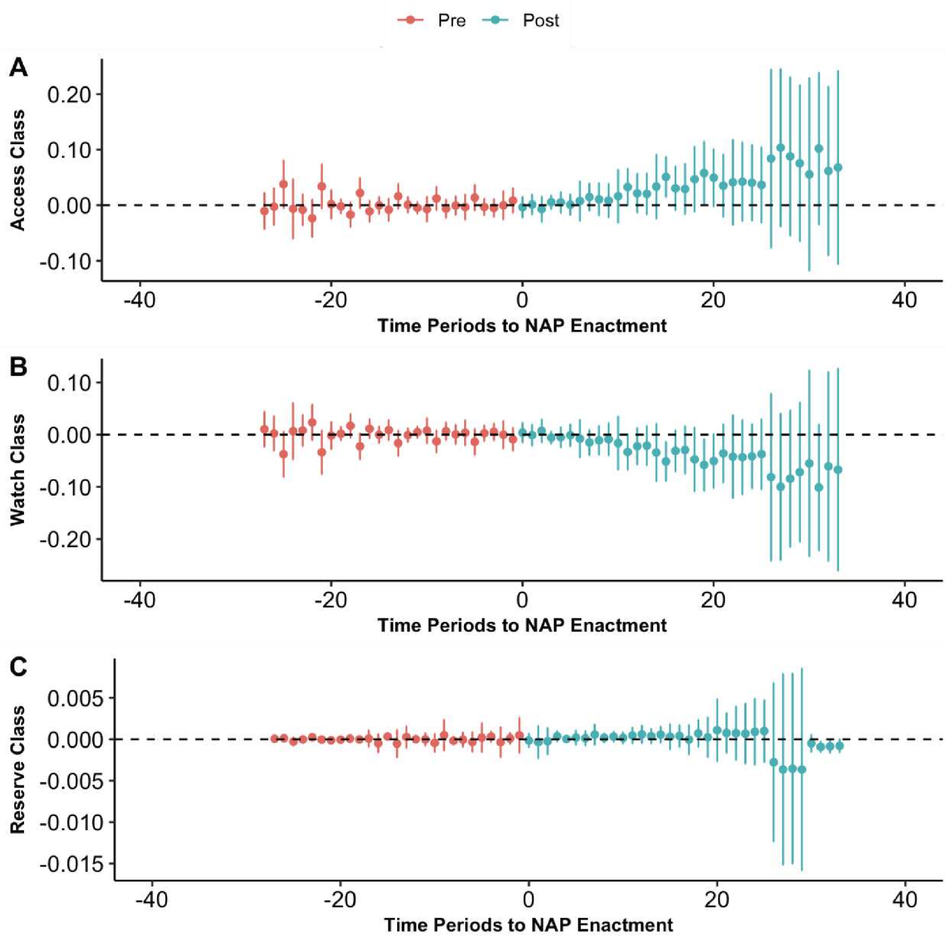

Figure 2 (A–C) Average effect of any AMR NAP enactment on changes in the proportion of AWaRe (Access, Watch, Reserve) Class sales in the retail sector by the length of exposure. 2014 baseline country income classification used to estimate propensity score model. (A) Proportion of Access Class sales. (B) Proportion of Watch Class sales. (C) Proportion of Reserve Class sales. Time periods are reported as quarters. AMR, antimicrobial resistance; NAP, National Action Plan.

sales of azithromycin (−49.08; 95% CI −89 to −9.16) as compared with countries with low-scoring or no AMR NAPs. When evaluating group-level effects, we see that countries who adopted a high-scoring AMR NAP in 2015 (−252.06; 95% CI −454.64 to −49.47), 2016 (−488.23; 95% CI −722.57 to −253.88), 2018 (−338.27; 95% CI −567.61 to −108.94) and 2019 (−269.73; 95% CI −499.63 to −39.84) had significantly less total volume of azithromycin compared with others.

We perform several robustness checks, which confirm our main findings. First, we observe no differences in our primary analyses or changes in parallel trends when exchanging the baseline covariates in our models. Second, we run a model excluding countries with no AMR NAPs (high-scoring vs low-scoring), we observe similar effects as our primary analysis with a smaller effect size in the change of the proportion of Access-class and Watch-class agents (Access 0.029; 95% CI 0.002 to 0.056 and Watch −0.029; 95% CI −0.053 to −0.004) (online supplemental figure 15a). Third, we observe a stronger and weaker effect when modifying the score of an effective AMR NAP to higher and lower cut-offs, respectively (online supplemental figures 16a–19a).

To better understand what part of the NAP might be driving the effect on sales, we run the model using different domains of evaluation scores to group countries as high or low-scoring. Using the *implementation tools, monitoring and evaluation* and *policy design* domain scores to delineate effective AMR NAPs produces similar results but smaller than the primary analysis with the *implementation tools* and *monitoring and evaluation* domains associated with a statistically significant increase in relative Access-class retail sales and decrease in Watch-class retail sales (online supplemental figures 20a–25a).

DISCUSSION

Our results offer insights for policymakers interested in promoting effective antimicrobial stewardship in their health systems using an AMR NAP. Countries with a higher quality AMR NAP, as determined by a prior evaluation of AMR NAPs, demonstrate more judicious antibiotic usage than those with no or a low-scoring NAP.[8] Specifically, following the adoption of a high-scoring AMR NAP, countries use a greater proportion of Access-class antibiotics—recommended as first-line therapy

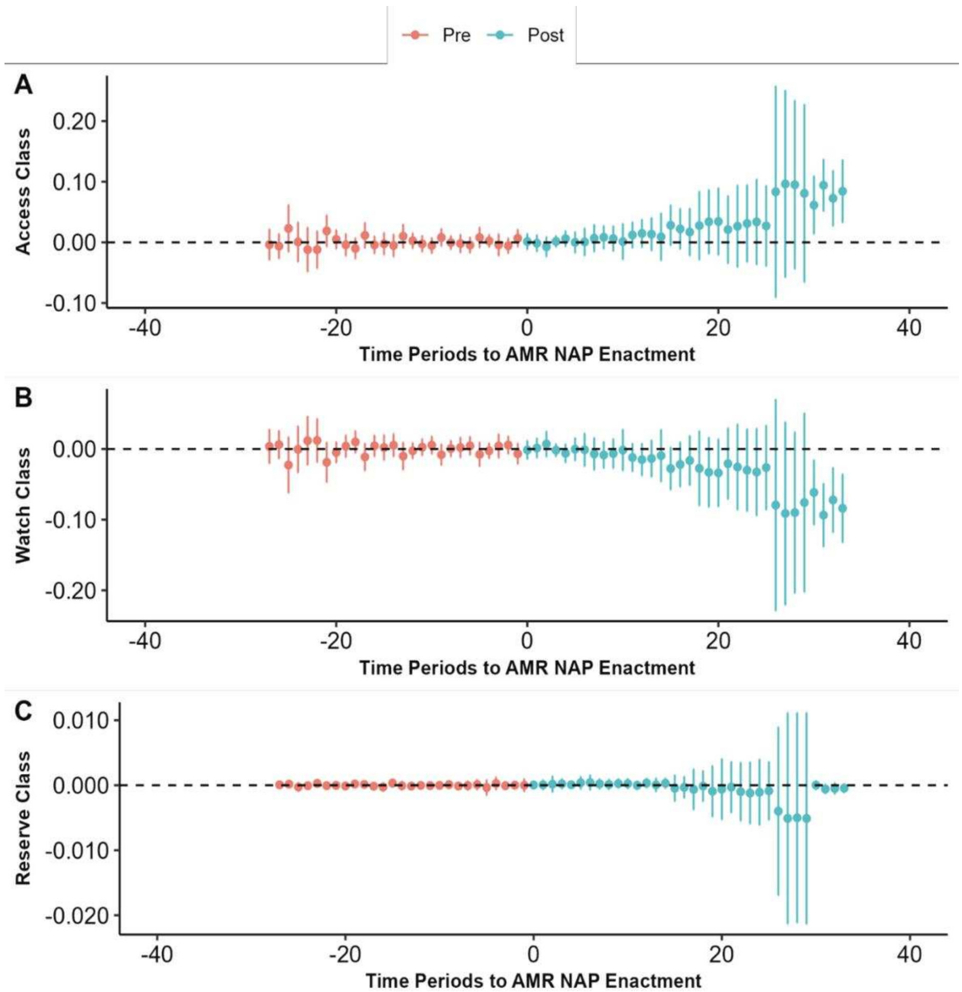

Figure 3 (A-C) Average effect of high-scoring AMR NAP adoption on changes in the proportion of AWaRe (Access, Watch, Reserve) Class sales in the retail sector by the length of exposure. 2014 baseline country income classification used to estimate propensity score model. (A) Proportion of Access Class sales. (B) Proportion of Watch Class sales. (C) Proportion of Reserve Class sales. Time periods are reported as quarters. AMR, antimicrobial resistance; NAP, National Action Plan.

by the WHO—and a smaller proportion of Watch-class antibiotics. We find that this effect is not immediate, and while there is a broader trend among NAP adopters to use a greater proportion of Aware class antibiotics, the effect is only statistically significant for the first adopters of a high-quality NAP, suggesting these policies may take time to achieve their intended effect. Finally, we also show that countries with high-scoring AMR NAPs in place during the acute phase of the COVID-19 pandemic made lower use of azithromycin, an antibiotic routinely misused to treat COVID-19, suggesting that AMR NAPs may also be useful in promoting judicious use of antibiotics during an epidemiological shock.

These findings have important implications for policymakers interested in learning more about the effect of NAP adoption on antibiotic use. Importantly, we do not find that every country adopting a NAP experiences a relative increase in the use of Access class antibiotics, but only those with a high-scoring NAP. Furthermore, we observe a dose-response effect, with higher-scoring AMR NAPs impacting sales more than lower-scoring AMR NAPs. Thus, there are likely attributes of the NAP themselves that make NAPs more or less likely to be successful. To further understand the role of a country's AMR NAP attributes, we undertake several robustness analyses examining the relationship between different dimensions of a NAP and sales. We find that the *implementation tools* and *monitoring and evaluation* components of the NAP drive the effect. These two domains include indicators that evaluate areas of antimicrobial stewardship, medicine regulations and feedback mechanisms, which may contribute to their stronger impact on antibiotic consumption. Our findings suggest that focusing on strengthening the *implementation tools* and *monitoring and evaluation* components of AMR NAPs may enhance their overall effectiveness, especially in countries with low-quality AMR NAPs or those seeking to establish a NAP.

Importantly, we do not find an association between a high-scoring NAP and a change in total retail antibiotic sales. It is unclear whether a change in total sales would be desirable, as total sales likely reflect differences in underlying disease burden in relation to AMR, gross domestic product and cultural and behaviour attitudes.[27–30] Since antimicrobial stewardship efforts cannot always avoid

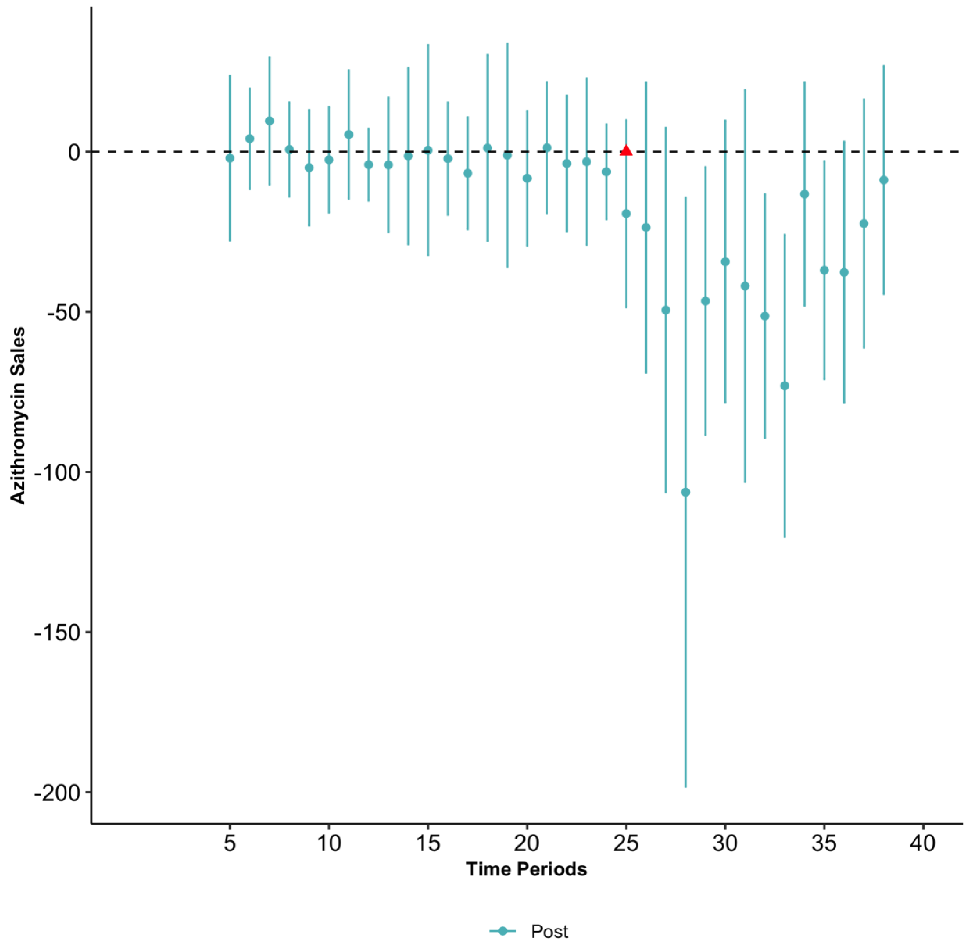

Figure 4 Average effect of a high-scoring AMR NAP on total Azithromycin sales by calendar time in the retail sector. Time period 25 represents quarter 1 in year 2020 and signifies the onset of the COVID-19 pandemic. Sales volume is measured in the number of 'standard units', an IQVIA designation representing a single-dose unit. Time periods are reported as quarters. Red triangle indicates the onset of the COVID-19 pandemic.

antibiotic usage altogether due to the inability to obtain culture, laboratory and diagnostic data, the judicious use of empiric antibiotics is a powerful component of antimicrobial stewardship in situations where antibiotics cannot be stopped. In these cases, determining the appropriate empiric regimen can sometimes be a more fitting outcome of these efforts, influencing the relative use of antibiotic type.[31–34] For this reason, the proportion of antibiotics sold by AWaRe class is a more suitable outcome. When we examine the proportion of antibiotics by AWaRe class, we find that countries that adopt effective AMR NAPs use more Access-class antibiotics and fewer Watch-class antibiotics. We do not find significant effects regarding the relative use of Reserve-class antibiotics. Reserve-class antibiotics are typically withheld until a definitive diagnosis is made; they are more expensive and tend to be used in the most critically ill patients; this may explain why adopting an effective AMR NAP does not significantly change their relative use in the retail sector.

One effect of AMR governance on antibiotic prescribing may be how well this is maintained during a health system shock, such as the COVID-19 pandemic. Our results show that countries with a high-quality NAP had significantly lower azithromycin sales. Azithromycin was the most used antibiotic for treating COVID-19 during this period, though it was established that it was not appropriate to use in this instance.[17] AMR NAPs may have strengthened health systems during the pandemic, making them more resistant to overuse of this antibiotic. We compared the group-level effects of azithromycin sales to TraCSS 2023 COVID-19-related AMR NAP questions. We found that most countries still reported COVID-19 as having a negative impact on AMR NAP governance and operations despite seeing lower total volume of azithromycin sales.[35] Further research is needed to understand how AMR NAPs may promote health system resilience.

As research moves toward exploring how to evaluate AMR NAPs, our study provides novel insight for future quantitative evaluations. The CS estimator allows us to evaluate different groups of countries separately and over time, which are reported in the supplementary material. We see that Germany and Switzerland, the first to adopt an effective NAP in 2015, appear to be driving the effect. It is unclear if this reflects either country-specific policies or the fact that they were the earliest implementers with the longest observation period. Further research and intracounty analysis is necessary to evaluate and understand this observed effect and any specific policies that may be driving it.

As far as we know, this is the first quantitative study to examine the impact of AMR NAP implementation on the appropriate use of antibiotics across countries globally. This study contributes to and extends the work of Patel *et al*, who assessed and scored AMR NAPs across 115 countries in 2023.[8] In addition to this, we contribute to the work by Charani *et al*, who identified strategic gaps in AMR NAP objectives, such as the development and monitoring of antibiotic policies.[36] Our results align with a similar study by Ya and colleagues showing that increased AMR governance in low-and-middle-income countries was associated with reduced overall antibiotic consumption in children at the country level.[37] Our work also adds to the broader literature examining the effect of NAPs on improving and standardising care for clinical areas such as cancer, mental health and health literacy. Finally, this study contributes to understanding the differential response to the COVID-19 pandemic by demonstrating variations in the use of antibiotics to treat COVID-19 in the early months of the pandemic.

This study has limitations. First, we rely on antibiotic sales data from IQVIA as a proxy for antibiotic use, although use cannot be entirely ascertained from sales. However, IQVIA data are widely published in antibiotic use studies and are the only provider of global antibiotic sales.[18–20] Second, IQVIA data do not capture hospital-level pharmaceutical sales for 23 countries. For this reason, we focus our primary analyses at the retail level. As antimicrobial stewardship efforts are more easily enacted in the hospital sector, we believe this restriction means we are likely underestimating the effect of AMR NAP adoption. Hospital prescribing practices are shown to influence retail-sector antibiotic usage on patients' discharge, as many hospital antimicrobial stewardship programmes focus on ensuring appropriate discharge antibiotics.[31 38 39] Third, we use a binary assessment of a composite score to delineate an AMR NAP as high-scoring or low-scoring in relation to antibiotic usage. However, other country-level policies or measures may influence the results. To mitigate this, we run multiple sensitivity analyses to explore the impact of the individual domain scores, increased and decreased composite scores and exclusion of countries with no AMR NAPs on antibiotic use. However, we acknowledge that this may not fully capture AMR NAP effectiveness. Still, we believe adopting an AMR NAP signals the country's willingness to tackle AMR and may be related to more judicious use. Finally, we do not have the exact date of the AMR NAP enactment. As our sales data are quarterly, we assign the first quarter of each year as the policy start date; this assumption may not reflect the actual start date of the AMR NAP and may lead to a slight overlap of effects. However, this is likely to bias the results towards a null finding.

CONCLUSION

Identifying successful mechanisms to slow the spread of AMR is essential to all health systems, yet there is limited evidence to support which policy tools are practical. Our results indicate effective NAPs can be a valuable tool to promote the appropriate use of antibiotics, particularly in the retail sector. Further research is needed at the country level to understand these effects and continue to improve and tailor AMR NAPs.

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Contributors EO participated in conceiving the study, literature search, data analysis, interpretation of the data, writing and critical revision of the manuscript for important intellectual content and final approval of the manuscript submitted. IP participated in conceiving the study, interpretation of the data, critical revision of the manuscript for important intellectual content and final approval of the manuscript submitted. IP serves as the guarantor of this study. JW and SM participated in data analysis, interpretation of the data, critical revision of the manuscript for important intellectual content and final approval of the manuscript submitted. OG participated in interpreting results, providing critical revisions and final approval of the manuscript.

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Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study does not involve human participants and did not require ethics approval.

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