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Evaluation of antibiotics returned for safe disposal during and after a community pharmacy antibiotic amnesty campaign

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Background: Community pharmacies in England offer convenient and safe disposal of unwanted medicines, including antimicrobials, and better uptake of this service could limit environmental antimicrobial resistance. However, there is limited information on the extent and nature of antibiotic returns to community pharmacies. The impact of an antibiotic amnesty campaign promoting antibiotic disposal through community pharmacies was evaluated with the intention of collecting detailed information on the antibiotics returned.

Methods: An antibiotic amnesty campaign was delivered by community pharmacies in the Midlands (England) with an audit of returned antibiotics conducted in 19 community pharmacies in Leicestershire. Detailed information on antibiotics returned for disposal was gathered during the month-long amnesty campaign and again 3 months later in the same pharmacies.

Results: Antibiotics accounted for 3.12%–3.35% of all returned medicines. The amnesty campaign led to a significant increase in defined daily doses of returned antibiotics compared to the post-amnesty period ($P = 0.0165$), but there was no difference in the overall number of returned medicines. Penicillins were the most commonly returned antibiotics in both periods (29.3% and 42.5% of packs, respectively), while solid oral dose formulations predominated. A total of 36.6% of antibiotics returned during the amnesty period were expired, increasing to 53.4% in the post-amnesty period. Amnesty conversations had a significant impact on the number of antibiotic returns but campaign posters did not.

Conclusions: Antibiotic conversations can increase the amount of antibiotics returned to community pharmacies for safe disposal, and passive campaign materials had limited impact. More research is needed to identify the most effective interventions to increase returns.

Introduction

Antimicrobial resistance (AMR) is a complex and multifaceted healthcare and societal challenge, and the presence of antimicrobials, or biologically active residues, in the environment is recognized as a driving factor for AMR. The United Nations Environment Programme[1] identified pharmaceutical pollution due to the discharge of antibiotics, disinfectants and heavy metals as a key risk factor for AMR. This has been echoed in subsequent reports.[2–4]

Recent environmental surveillance has reported concerning levels of antimicrobial compounds in many of the world's rivers and bodies-of-water.[5] Pharmaceutical manufacturing discharge, use in agriculture and aquaculture, runoff from landfill sites and the inability of water treatment plants to completely remove antimicrobial compounds from healthcare and household sewage allow these compounds to continue entering watercourses.[6]

Although human excreta are a source of these compounds entering waterways, data suggest that improper direct disposal via domestic waste and household sewage (e.g. in household bins or down sinks and toilets) is also a significant contributor. Evidence demonstrates that many patients do not complete the antibiotic course as prescribed,[7,8] and patients who have leftover antimicrobials report saving these for use at a later date, disposing of them in household waste, or sharing them with other people.[9] Raising awareness of AMR in the environment and encouraging the safe disposal of antimicrobials could reduce improper disposal and the resulting harms.

Community pharmacies in the UK are contracted, as part of the Community Pharmacy Essential Services Framework, to accept unused and unwanted medicines from patients for safe destruction.[10] Many patients are unaware of this service, yet appropriate information from healthcare professionals can change this.[11] The Midlands region of England has a population of approximately 10.8 million,[12] and 5.5 million antibiotic items were dispensed in primary care in the region in 2021,[13] emphasizing the scale of antimicrobial consumption and the potential for unsafe disposal practices.

In 2021, an Antibiotic Amnesty campaign was implemented in the Midlands region of England to improve public awareness of the issue and encourage members of the public to return unneeded antibiotics to community pharmacies for safe disposal. Two-hundred and thirty-nine participating community pharmacies undertook 7399 antibiotic amnesty conversations, with 126 unused full packs and 369 partially used packs of antibiotics returned.[14] One limitation of the 2021 campaign was an inability to capture detailed data on the types of antibiotics that were returned, and while some studies have reported on the proportion of antibiotics returned to community pharmacies for disposal,[15–17] there is a gap in our knowledge of which antibiotics are returned in England.

In November 2022, during World Antimicrobial Awareness Week, the Midlands Antibiotic Amnesty campaign was repeated. The aim of the present project was to gather more detail on the impact of the campaign and obtain more granular data regarding the types of antibiotics being returned to community pharmacies by the public.

Methods

An observational study was undertaken that consisted of measuring the activities and antibiotic returns during an antibiotic amnesty campaign, followed by measuring baseline activity several months after the amnesty campaign in a selected group of pharmacies.

The amnesty campaign was run through community pharmacies across the Midlands, utilizing assets developed previously.[18] Community pharmacy participation in the amnesty was voluntary. All community pharmacies from across the Midlands region were contacted for expressions of interest in participating in the amnesty campaign and contributing to data collection and research. Pharmacies that agreed to take part in the amnesty campaign were able to record on the PharmOutcomes platform the number of conversations they had with people about the amnesty, and the number of full or part packs of antibiotics returned.

Twenty-seven pharmacies from across Leicestershire expressed interest in participating in the research project. A convenience sample of 19 pharmacies was enrolled in the in-depth audit of medicines returns. During the data collection periods, each pharmacy retained all patient-returned medicines, except for controlled drugs. Pharmacies were required to do this for both the amnesty period (November 2022) and the post-amnesty period (February or March 2023). Data collectors (Masters in Pharmacy students) visited the pharmacies regularly during these periods to audit patient-returned medicines, using a standardized audit form that captured the overall volume of returned medicines. Medical devices that did not contain drugs, multi-compartment compliance aids and dietetic products were excluded.

The primary outcome measures were the number and proportion (in relation to total medicines returned) of antimicrobial medicines returned during and after the amnesty period and the impact of displaying amnesty materials and undertaking amnesty conversations. Secondary outcome measures were the volume and proportion (in relation to the amount initially dispensed) of antimicrobial returns, during and after the amnesty period, with regard to: drug, formulation, dosing regimen, expiry date and whether dispensed from primary care (e.g. GP and urgent care) or secondary care (e.g. hospitals) locations.

Some of the secondary measures required data to be extracted from the dispensing label, secondary and/or primary packaging. As this was not always available (e.g. through patients disposing of the secondary packaging without the dispensing label attached), these returns were excluded from some analyses. Topical antimicrobial products returned were excluded from analyses of the defined daily doses (DDDs, a technical unit of measurement of consumption for systemic medicines[19]) and mass of antibiotics returned (expressed as active pharmaceutical ingredient, API). Outcome measures were all analysed using descriptive statistics.

Correlations and OLS regression models were computed in Stata to explore the associations between the number of amnesty conversations and the number and types of antibiotics returned. With regard to the secondary outcomes, continuous data were compared through *t*-tests assuming unequal variance, as returns data were not normally distributed. For categorical data, *F*-tests and ANOVA were used for comparing two or multiple categories, respectively. These tests were undertaken with Excel Data Analysis Toolpak. All statistical test results were considered significant for *P*-values of 0.05 or lower.

Ethical approval was granted by De Montfort University (Ethics Committee Reference: 509166). Participating pharmacies were provided with a participant information sheet that linked to the full study protocol. They gave informed and explicit consent by signing a consent form. No patient-identifiable information was collected during the audit, and all medicines were disposed of as per pharmacy standard operating procedures after data collection.

Results

Three hundred and forty-three community pharmacies in the Midlands expressed interest in participating in the antibiotic amnesty campaign, and 181 pharmacies returned data via the PharmOutcomes platform. Overall, there were 4678 amnesty conversations held with members of the public, with 883 packs of antibiotics (253 full packs and 630 part packs) returned for safe disposal. There was a positive correlation between the number of amnesty conversations and the number of full packs ($P = 0.0000$) and part packs ($P = 0.0000$) returned (Figure S1, available as Supplementary data at *JAC-AMR* Online and Table S1). Nineteen pharmacies in the Leicestershire region returned data through PharmOutcomes. They undertook 713 amnesty conversations and received a total of 122 packs of antibiotic medicines (38 full packs, 84 part packs).

Six of these Leicestershire pharmacies also participated in the detailed audit of returns, with an additional 13 pharmacies recruited through the university. During the amnesty period, a total of 3170 packs of medicines were returned across the 19 audited Leicestershire pharmacies, of which 99 packs were antibiotics, equating to 3.12% of the total returned medicines. In the post-amnesty period, out of 4000 returned packs of medicines, 134 were antibacterial medicines, equating to 3.35% of total returns (Table S2). Of the enteral formulations returned, a total of 733.1 DDDs of antibacterial therapy were returned during the amnesty period and 658.4 DDDs were returned during the post-amnesty period. There was no significant difference in the overall number of antibiotic packs returned between the two audit periods (*t*-test, $P=0.183$, dF = 16) but there was a significant difference in DDDs returned between the amnesty and post-amnesty periods (*t*-test, $P=0.0165$, dF = 116).

Of the pharmacies with auditable returns, approximately one-third ($n=7/19$, 36.8%) were clearly displaying antibiotic amnesty campaign materials to their service users. Comparing pharmacies that were displaying campaign materials to those that were not, there was no significant difference in antibiotic return rates during the amnesty period (*t*-test, $P=0.084$, dF = 7) or post-amnesty period (*t*-test, $P=0.979$, dF = 12).

Table 1 provides an overview of the granular data obtained during the amnesty and post-amnesty periods. A large proportion of the returned antibiotics (39.06% overall; $n=27$ in the amnesty period, $n=64$ in the post-amnesty period) had the dispensing label and/or secondary (outer) packaging removed, so it was not possible to obtain all of the desired data.

Figure 1 illustrates the number of packs returned for each antibiotic type during the amnesty and post-amnesty periods. Large increases in the number of items of amoxicillin and phenoxymethylpenicillin returned in the post-amnesty period compared to the amnesty period were observed, whereas the opposite was observed for doxycycline. When considering the returns in DDDs, more DDDs of clarithromycin and phenoxymethylpenicillin were returned post-amnesty, compared to the small differences observed for amoxicillin. The lower number of doxycycline DDDs returned in the post-amnesty period represented the largest difference in DDDs observed of all drugs audited (Figure S2). The drug or class did not impact the proportion of the dispensed course returned to the pharmacy (Figure S3).

Most returns were oral enteral formulations (76% overall: 71.7% amnesty period, 79.1% post-amnesty period). When converted to DDDs, 1366.7 DDDs of solid enteral dosage forms (721.6 DDDs during amnesty period, 645.1 DDDs during post-amnesty) and 24.8 DDDs of enteral liquids were returned (11.5 DDDs during amnesty period, 13.3 DDDs during post-amnesty) (see Figures S4 and S5).

Overall, the proportion of courses returned unused was found to be significantly greater (*t*-test, $P=0.00898$, dF = 11) for solid enteral formulations (mean 76.54% ± 29.8%) compared to liquid enteral formulations (mean 49.18% ± 26.1%) (Figure S6).

The proportion of courses returned by dosing regimen was assessable for 54 returns during the amnesty period and 50 returns in the post-amnesty period. Antibiotics prescribed twice daily were returned more than other dosing regimens across both the amnesty and post-amnesty periods (Figure S7). This difference was more pronounced when looking at DDDs returned (Figure 2a), with 550.9 DDDs returned from twice-daily dosing regimens across both amnesty and post-amnesty periods, compared to 111.7 DDDs returned from once-daily, 107.3 DDDs returned from three-times daily and 139.4 DDDs returned from four-times daily regimens.

Table 1. Number of packs of antibiotics returned to community pharmacies

	Amnesty period		Post-amnesty period	
	N	%[a]	*N*	%[a]
Antibiotic class				
Penicillin	29	29.3	57	42.5
Penicillin-β-lactamase inhibitor	18	18.2	11	8.2
Tetracycline	9	9.1	11	8.2
Macrolide	9	9.1	11	8.2
Sulphonamides/trimethoprim	5	5.1	5	3.7
Formulations returned for disposal				
Solid oral (tablets/capsules)	71	71.7	106	79.1
Liquid oral	6	60.6	10	7.5
Topical preparations	22	22.2	18	13.4
Dosing regimen				
Once daily	6	8.6	8	11.8
Twice daily[b]	33	47.1	21	30.9
Three times daily	9	12.9	21	30.9
Four times daily	22	31.4	18	26.5
Unknown[c]	29[a]	—	66[a]	—
Antibiotics returned in date or expired				
In date	59	63.4	55	46.6
Expired	34	36.6	63	53.4
Unknown[c]	6[a]	—	16[a]	—
Place of original dispensing				
Community	61	89.7	56	83.6
Hospital	7	10.3	11	16.4
Unknown[c]	31[a]	—	67[a]	—

[a]For percentage calculation, the ‘unknown’ values were excluded.
[b]Combines standard ‘Twice daily’ and ‘Twice daily on Mondays, Wednesday, and Fridays’ regimens (see Section 3.2.3).
[c]Unknown = unable to obtain this data as no label and/or outer packaging, or information, could not be extracted from the label (e.g. dispensing location).

Overall, the dosing regimen had no significant impact on the proportion of courses returned (ANOVA, $F=1.388$, $P=0.2435$, dF = 4). There was a trend towards greater proportions of courses being returned for antimicrobials prescribed once daily (overall mean 93.2% ± 20.4%) compared to four times a day (overall mean 67.9% ± 30.5%) (Figure S8).

The expiry date was assessable for 93 returns in the amnesty period and 118 returns in the post-amnesty period. During the amnesty period, 63.4% of returned antibiotics were in date (equivalent to 538.3 DDDs in date and 164.8 DDDs expired) compared to the post-amnesty period, where 46.6% of returned antibiotics were in date (equivalent to 231.6 DDDs in date and 360.9 DDDs expired) (Figure 2b and Figure S9).

The longest dates since expiry were 12.8 years and 17.5 years, both returned during the amnesty period (Figure S10). There was no significant difference in the proportion of courses returned across the amnesty and post-amnesty periods when comparing expired against non-expired products (*t*-test, $P=0.7752$,

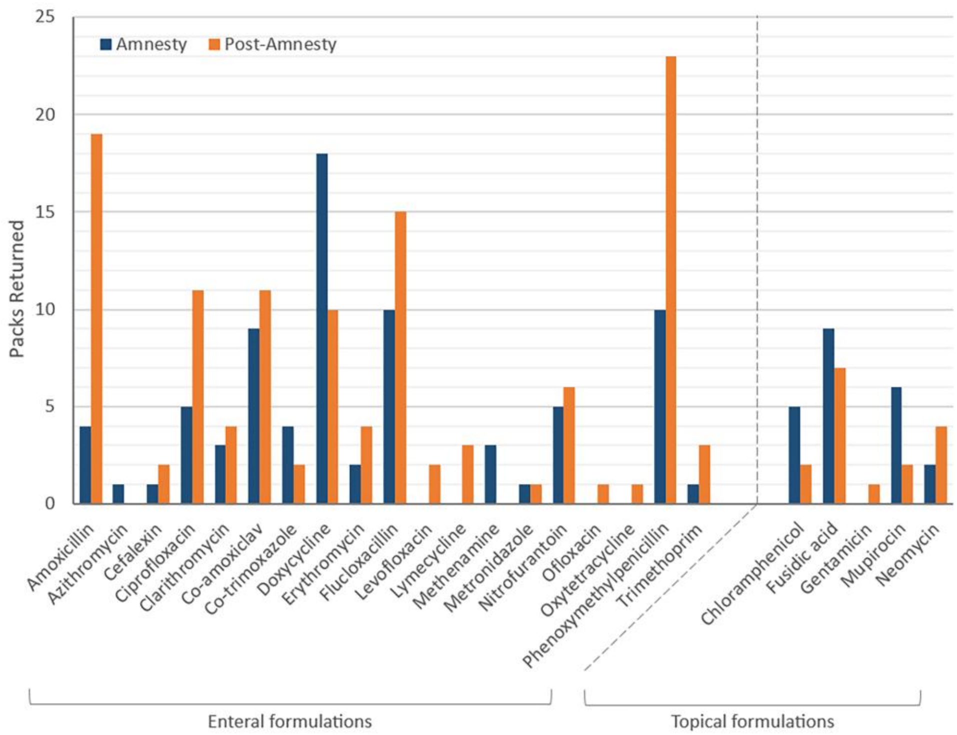

Figure 1. Number of packs (full and part packs) returned to audited pharmacies in the amnesty and post-amnesty periods.

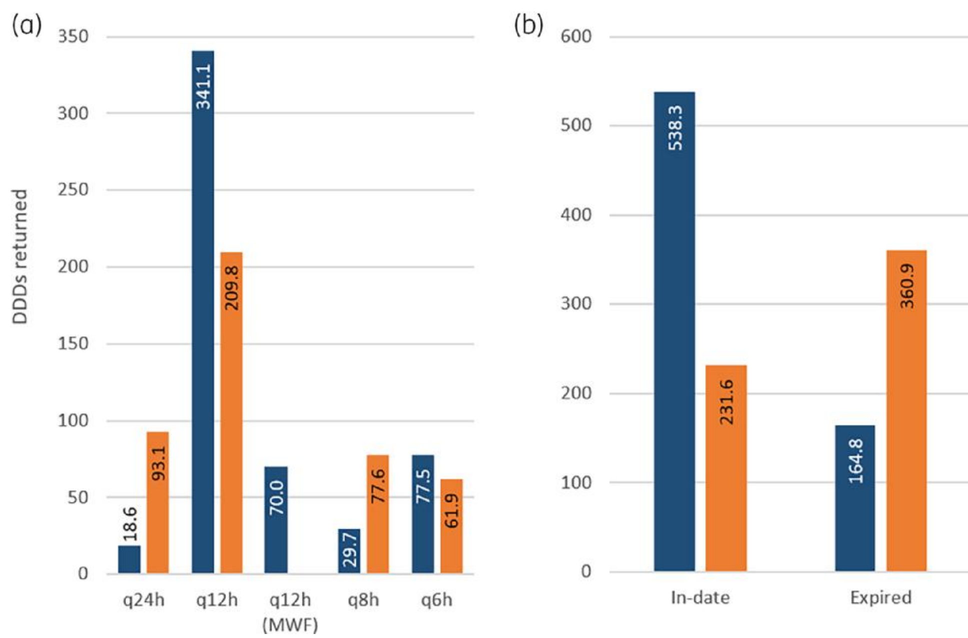

Figure 2. DDDs returned during the amnesty (dark blue bars) and post-amnesty period (orange bars) in relation to (a) dosing regimen (where MWF is Mondays, Wednesday and Fridays), or (b) in-date or expired.

dF = 118). Displaying amnesty materials (e.g. posters) in the pharmacy did not make a significant difference in the return of out-of-date products (*F* test: $F = 1.065$, $P = 0.391$, dF = 98). Formulation did not have a significant impact on whether medicines were returned expired or in-date (ANOVA: $F = 1.047$, $P = 0.353$, dF = 2).

The dispensing location was assessable for 68 returns in the amnesty period and 67 packs in the post-amnesty period. The majority (86.7%) of antibiotics returned had been originally dispensed in community pharmacies compared to secondary care settings (Figure S11). There was no difference (*t*-test, $P=0.4911$, $dF=16$) in the proportion of courses returned depending on whether they were dispensed from a community pharmacy (overall mean returned 75%±29.8%) or a hospital (overall mean returned 68.9%±29.1%) (Figure S12).

Discussion

To our knowledge, this is the first study to describe in detail the antibiotics returned during and after a regionwide antibiotic amnesty campaign. Conversations relating to returning antibiotics and the amnesty positively correlated with increasing the return of unused antibiotics, but displaying amnesty materials in the pharmacy did not have a measurable impact. We assessed 233 antibiotics that were returned to 19 selected community pharmacies in Leicestershire, identifying penicillins as the most commonly returned antibiotic class and solid oral doses as the most commonly returned formulation. We found that more antibiotic doses were returned during the amnesty period, but there was no difference in the proportion of expired antibiotics returned during each phase of the study. When considering the weight of antibiotics returned for safe disposal, the equivalent of 1.46 kg was diverted from unsafe disposal in the environment. There was a trend towards the return of more twice-daily dosing regimens compared to other dosing frequencies, but overall there was no significant difference detectable based on dosing frequency. Most antibiotics returned for disposal were dispensed from community pharmacy settings.

Our results show that antibiotics accounted for less than 4% of total returned medicines. This proportion is broadly in line with findings from other studies. Louhisalmi *et al.*[15] found that anti-infective medicines accounted for 4.4% of medicines returned to community pharmacies in a single month. A 9-month-long study of medicines returned to a single community pharmacy found that, of the 411 medicines returned, 8.8% were anti-infectives for systemic use.[16] Antibacterial medicines accounted for 13.9% of all medicines returned to four community pharmacies in Rome, Italy, over a 6-month period, of which 82% were expired.[20] A recent systematic review of medicines storage practices in urban households globally found that anti-infectives for systemic use were the most widely stored medicines.[21] Perhaps this behaviour of not disposing of antibiotics explains, to some extent, the low proportion of antibiotic returns in our data. Indeed, with retention periods of up to 17.5 years for the longest retained antibiotic in our study, this behaviour may be entrenched in some elements of the UK population. We observed fewer returns of oral liquids, which may be due to solid dosage forms being dispensed more often, yet we observed a trend towards lower proportions of the originally dispensed quantity being returned for oral liquids compared to solid dosage forms. While not statistically different, this may be a signal that patients are more likely to dispose of these at home as they often have shorter expiry dates and may require refrigeration.

The proportion of expired antibiotics returned for disposal during the amnesty period matched an Australian audit by Bettington *et al.*[17] of medicines returned to community pharmacies as part of a national scheme to promote safe disposal. Their study found that three antibiotics (cefalexin, amoxicillin and co-amoxiclav) were amongst the top 20 most commonly returned medicines. Their study also found that 36% of all medicines returned were expired, matching our finding of 36% expired medicines returned for disposal in the amnesty period. Although not significantly different, the increase in expired antibiotics in the post-amnesty period (53.4%) is unexplained but could be confounded by the outbreak of Group A streptococcus in the UK during December 2022 to January 2023.[22] This outbreak led to increases in antibiotic prescribing due to a lowering of the threshold to prescribe antibiotics in national guidance for the management of acute sore throat, coupled with acute shortages of commonly used antibiotics, particularly oral liquid formulations utilized for paediatric patients. It is possible that the increased prescribing, particularly liquids, and public concerns about the availability of antibiotics led to hoarding and subsequent expiry of these drugs that was detected in our post-amnesty period data, particularly for amoxicillin, phenoxymethylpenicillin and clarithromycin.

Although limited, our data suggest that patients hold on to antibiotics for significant periods of time. This highlights the importance of messaging around the safe disposal of antibiotics and adds weight to the findings of the study by McNulty *et al.*[9] Their study suggested that, in addition to sharing with others or disposing of them unsafely, patients hoard antibiotics for future use. In our study, displaying amnesty promotional materials did not have an impact on the number of antibiotics returned, suggesting that amnesty conversations may be the most important part of an amnesty campaign. However, only one-third of pharmacies were displaying posters, which could have limited their impact. That said, this may be a phenomenon where an active intervention (conversations) was more powerful at driving a behaviour change (returning antibiotics) compared to passive interventions (displaying materials such as posters). This aligns with our results whereby antibiotic conversations correlated with an increased number of antibiotics returned. This is supported by several studies that highlight conversations and advice from pharmacists increase patients' adherence to antibiotics[23–25] and written information can further augment this and even reduce wastage.[26]

We explored whether the frequency of drug administration would impact the likelihood of an antibiotic being returned, as multiple-daily dosing regimens are associated with poorer compliance than single-daily dosing regimens.[27] Our data showed the opposite, with once-daily and twice-daily dosing regimens being more frequently returned than four-times daily regimens. Most once-daily regimens were for co-trimoxazole, which may have been prescribed as long-term medical prophylaxis, and there is evidence to show that adherence is poor with long-term regimens.[27]

Our study does have some limitations. We were not able to get data on the total number of antibiotics and formulations dispensed by each of the participating community pharmacies during both data collection periods. Medicines returned were batched and assessed by pharmacy students on defined visits to the pharmacies. Due to operational pressures on pharmacies, we did not mandate the contemporaneous recording of the date of return of each antibiotic, meaning that our assessment of whether the medicine was returned in date or expired, and the time lag between dispensing and return for disposal, was a pragmatic estimation based on the date of the audit. A significant volume of medicines was returned without their outer packaging, limiting some granular data collection. There may be several reasons for this, from patients not wanting their name to be known as this is present on the dispensing label to pharmacies asking patients to just return primary packaging to save space (anecdotal from authors working in community pharmacy).

No difference was found in the return rates for community pharmacies displaying amnesty posters, which may be explained by the relatively small number of participating pharmacies delivering the campaign in whatever way suited their pharmacy best. This uncontrolled study design may have limited the ability to detect the impact of displaying amnesty materials. Therefore, future research should study the impact of the amnesty campaign in a more controlled design. More research is also needed to better understand the motivation and behaviours of patients regarding hoarding and disposal of antibiotics, their views on antibiotic amnesty campaigns to better design future campaigns, and to more closely measured any sustained impact in the post-amnesty period.

This work was carried out in Leicestershire, and the findings may not be generalizable to other counties in England or other countries. However, Leicestershire has a mixture of densely populated urban centres and rural areas. The community pharmacies in our study were located in Lower Super Output Areas with population densities ranging from 170 to 16 901 people per square kilometre and had an Index of Multiple Deprivation ranging from 3.66 to 47.5.[28]

To date, there has been limited assessment of the impact of antibiotic amnesty campaigns. Previous work done in the Midlands demonstrated that these campaigns do result in the return of full and part packs of antibiotics,[14] but that research was unable to describe the nature of the returns. Our study has addressed that gap, but more research is needed to understand the behaviour of patients around antibiotic hoarding and their views on public health campaigns such as antibiotic amnesties.

In conclusion, our Midlands antibiotic amnesty did increase the amount of antibiotics returned to community pharmacies for safe disposal compared to a post-amnesty period, but there was no evident impact on the return of in-date versus expired medicines. We were unable to assess which elements of the campaign had the greatest impact on antibiotic returns, and more research on this important topic is needed, given the public health impact of AMR.

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Transparency declarations

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Supplementary data

Figures S1–S12 and Tables S1 and S2 are available as Supplementary data at *JAC-AMR* Online.

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