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Facilitating primary care non-antiretroviral drug prescribing in people living with HIV: The ‘THINK ARV’ initiative

Chloe Knox1,2, Heather Leak Date1, Su S Lim1, Mark Shaw1, Brian Flynn3, Lucy Kendall4 and Jaime Vera1,2

Abstract
Objectives: Older people living with HIV (PLWH) have higher rates of multimorbidity, polypharmacy and an associated increased risk of potential drug–drug interactions (DDIs). We describe the development, implementation and evaluation of an intervention to increase community prescribers’ access to specialist prescribing advice. Methods: Phase One: a survey evaluating General Practitioners’ (GPs’) knowledge of, and confidence detecting DDIs affecting PLWH, was circulated to eight General Practices in one UK city. Phase Two: co-production was used to develop the THINK ARV intervention for prescribers in city-wide General Practices: a dedicated mobile phone and e-mail advice service staffed by HIV specialist pharmacists. Queries were audited for 6 months pre- and post-intervention. A user-satisfaction survey was emailed to enquirers. Results: Phase One: 42 GPs responded, of whom 62% requested further support identifying DDIs among PLWH. Phase Two: the number of queries received increased from 25 (6 months before ‘THINK ARV’ launch) to 63 in the following 6 months (152% increase). 94% of the queries were specifically about DDIs. Conclusions: Increasing community prescribers’ access to specialist telephone and e-mail advice resulted in increased awareness and detection of DDIs. Similar interventions could be embedded within different healthcare settings to optimise medicines and avoid potential patient harm.

Keywords
HIV, antiretroviral, prescribing, medicines-related problems, drug–drug interactions, pharmacist

Introduction
The introduction of effective antiretroviral (ARV) therapy has transformed HIV into a chronic condition, with increased multimorbidity at an earlier age than the general population.1–3 As a result, polypharmacy (≥5 drugs) is emerging as an important challenge facing older people living with HIV (PLWH).4–6

Due to the complex pharmacokinetic nature of ARVs, there is significant propensity for drug–drug interactions (DDIs) when non-ARV medications are co-prescribed. Analysis of The Pharmacokinetic and Clinical Observations in People Over 50 (POPPY) study identified that the prevalence of ≥1 potential DDI involving ARVs and non-ARVs was 57.3% in those aged over 50 years.7 Similar data reflecting increased DDIs among older PLWH has been demonstrated in the Swiss HIV Cohort Study.8

Most co-morbid conditions are managed in the community by General Practitioners (GPs) who may have limited experience of prescribing for those taking ARVs.6 Data suggests only 16% of GPs are confident regarding their knowledge of managing HIV DDIs.9

Safe community prescribing for PLWH may be further complicated by multiple prescribers and dispensing pharmacies, without regular or specialist-led reviews of all prescribed medications.6 Clinically significant DDIs may also involve ‘over the counter’ medicines, recreational substances, nutritional supplements and herbal remedies, which may not be considered.

Therefore, strategies to improve community prescribers’ knowledge and understanding of potential DDIs when...
prescribing non-ARV medications for PLWH could have significant impact on reducing potential harm.

**Methods**

**Study design and setting**

Mixed methods quality improvement initiative conducted in selected GP practices in Brighton and Hove between August 2017 and October 2018.

**Phase one: Predevelopment survey**

The city’s 35 GP practices were coded ‘high’, ‘intermediate’ or ‘low’ according to the number of PLWH among their patient cohort, estimated as the number of PLWH receiving specialist HIV care at the local clinic using its anonymised client list. A ‘low’ practice was defined as having <25 clients using the specialist HIV service registered, ‘intermediate’ as between 26–75 clients and ‘high’ as >76 individuals. A purposive sampling technique was used to fully explore the range of experience within Brighton and Hove: each practice was assigned a number and a random number generator was used to select eight (three ‘high’, two ‘intermediate’ and three ‘low’) General Practices.

Between August and November 2017, GPs were invited to complete an anonymous survey to determine their understanding of DDIs in PLWH, their confidence prescribing non-ARV medications and whether they would like support prescribing for PWLH. Paper copies of the survey were delivered to all selected practices and further copies provided electronically to Practice Managers via e-mail. The survey comprised 10 questions and took under 5 min to complete. Specific questions included how many consultations GPs had undertaken with PLWH in the last 12 months, their confidence in prescribing co-medications for those on ARVs, the degree to which they felt DDIs among PLWH was a problem, which resources they used currently to evaluate potential DDIs, whether they felt they would benefit from further prescribing support and their preferred format of this. We also included a free text box for any additional comments or concerns relating to the issue of DDIs in PLWH.

**Phase two: Intervention design and implementation**

Intervention design was informed by the predevelopment survey and aimed to increase community prescribers’ awareness of, and rapid access to, HIV Specialist Pharmacist advice. It was co-produced by a team comprising an HIV specialist physician, HIV specialist pharmacists and a GP, with project management support from Merck Sharp & Dohme (MSD). This shared expertise informed all elements of intervention design and implementation, including creating:

1. a dedicated HIV pharmacist mobile phone service for community prescribers to ring during normal working hours for urgent queries about prescribing for a PLWH
2. a specialist e-mail contact service for non-urgent queries (response within three working days)
3. the ‘THINK ARV’ name and logo
4. a bespoke ‘THINK ARV’ sticker incorporating the new service details and highlighting the risk of DDIs with ARVs; this was designed to be attached to a computer monitor, to be visible to GPs at the point of prescribing.

These additional services were implemented in addition to the pre-existing routes used by primary care practitioner for all queries, including medication-related: a non-dedicated landline phone within the HIV secondary care service, a non-dedicated e-mail address and by letter to the client’s named Consultant.

The initiative was launched at a city-wide primary care educational event in April 2018, followed by the distribution of an information pack about the service (including THINK ARV stickers) to all 35 GP practices. Over the next few months, information about the service and the importance of being alert to DDIs when prescribing for PLWH was also included in two editions of the regular medicines management newsletter which was emailed to all GPs.

**‘THINK ARV’ evaluation**

Monitoring and evaluation were conducted for 6 months before and 6 months after the service launch (October 2017 to April 2018 and April to October 2018). For each community prescriber query logged during this period, the following data were recorded: ARV regimen, non-ARV drugs, nature of query, recommended action and communication method. The University of Liverpool HIV Drug Interactions website rating system was then applied to each query to categorise potential DDI severity.10 This resource provides evidence-based information regarding DDIs between ARVs and co-medications, categorised as either:

1. Red – these drugs should not be co-administered.
2. Amber – Potential interaction may require close monitoring, alteration of drug dosing or timing of administration.
3. Yellow – Potential interaction likely to be of weak intensity. Additional action/monitoring or dosage adjustment is unlikely to be required.
4. Green – No clinically significant interaction expected.

A user-satisfaction survey was e-mailed to all community prescribers who logged an enquiry during the study period and provided contact details.
Increased life-expectancy of PLWH is associated with increased prevalence of multi-morbidity, resulting in increased co-prescription of non-ARV medications. Cohort studies of older PLWH have found higher rates of polypharmacy among older PLWH compared to both younger PLWH and HIV-negative controls, which is associated with an increased risk of potential DDIs.\textsuperscript{7,8} Chronic co-morbidities are typically managed by GPs (community prescribers), who may have varying levels of awareness and expertise in identifying DDIs between medicines they prescribe and ARVs.

Phase one (predevelopment survey) demonstrated that despite varying levels of confidence among community prescribers regarding awareness of DDIs among PLWH, the majority of those surveyed felt they would benefit from additional support and education. This is consistent with similar surveys of GP, suggesting this may be reflective of wider community practice.\textsuperscript{11}

Drug–drug interactions among PLWH are associated with increased morbidity and healthcare costs.\textsuperscript{12} A cross-sectional study of a nationwide healthcare database in France estimated that avoidance of DDIs among an older PLWH could result in a decrease in the annual healthcare cost for an individual by 13.6%\textsuperscript{12}.

There is therefore a need for strategies to improve community prescribers’ knowledge and understanding of potential DDIs when prescribing non-ARV medications for PLWH in order to prevent potential patient harm and enhance management. A Cochrane systematic review found that PLWH receiving outpatient care by clinicians with increased training or expertise in HIV resulted in improved medical and social outcomes.\textsuperscript{13} Enhanced collaboration between general practice and secondary care HIV services has also been highlighted as a priority by BHIVA’s 2017 Shared Care Report.\textsuperscript{14}

The THINK ARV intervention has demonstrated that simple interventions focused on increasing community prescriber awareness of the potential for DDIs when co-prescribing non-ARV medications among PLWH can have a significant impact. Our post-development data represents both increased total numbers of queries, increased number of queries specifically related to DDIs among this population and increased detection of potential DDIs. This suggests that the intervention has resulted in increased community prescriber understanding of the issue of DDIs among PLWH, increased awareness of the resources available to support them with prescribing advice and the reduction in potential patient harm.

**Recommendations for implementation**

The ‘THINK ARV’ intervention has been adopted across the city as the recommended standard of care, raising awareness of the importance of DDIs among PLWH and enabling increased access to specialist prescribing advice.
for community prescribers. This intervention is ongoing, with a plan to review later in 2021 to assess the impact of the ongoing COVID-19 pandemic on the service.

The ‘THINK ARV’ intervention has significant potential to be established in other settings to improve management of PLWH and prevent potential patient harm. We propose three key recommendations for establishing an effective service.

**Co-production at the core of intervention development.** Individual services should seek to establish the needs of community prescribers in their region, which may differ to those described here. Multi-stakeholder engagement through co-production between HIV specialists in secondary care, HIV specialist pharmacists and GPs is vital to ensure the developing services meet the requirements of those utilising them.

**Multiple targeted approaches to increase awareness and provide support.** To implement widespread change in practice among community prescribers, it is important to utilise a variety of methods to increase awareness of new resources, as well as regularly remind practitioners of their availability.

**Proactive and sustained promotion of service.** Generating awareness of the issue of DDIs among PLWH and sharing resources for further prescribing support is a core component of our intervention strategy. Committing to promote the intervention for a sustained period is recommended to establish the intervention within the routine practice of community prescribers.

### Challenges to implementation

Phase two of this quality improvement intervention required an additional 0.3 whole time equivalent HIV specialist pharmacist for 1 year (funded by MSD). The additional workload (responding to queries) has been absorbed by existing staff.

In addition, there was a challenge to adequately publicise the new service among community prescribers. This was overcome through multiple approaches including advertising the service at a local educational event for primary care practitioners, the development of the bespoke computer monitor prompt sticker, as well as providing literature to all general practices across the city. Sustained efforts to promote the service will be needed to maintain community prescriber awareness of the resources of further support available.

Initially, engagement with the programme involves additional work on behalf of GPs to raise queries by e-mail and telephone, await prescribing advice and then implement the prescribing recommendations made in the community. However, wherever possible, responses to mobile phone queries are made in real time, minimising the impact on GP workload. It is also anticipated that the service may contribute to GP education, minimising repeat queries as GPs

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**Figure 1.** Method of contact used pre- and post-intervention (n).

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**Figure 2.** Nature of query pre- and post-intervention (n).
develop experience in managing common comorbidities among PLWH.

Limitations

The main limitations of this study are the small sample size and relatively short period of data collection pre- and post-intervention. Sampling of selected GP practices in the pre-development survey was non-random, reducing the generalisability of the results. However, the purposive sampling strategy used allowed us to understand the nuances of individual understanding and confidence of GPs by their relative experience to providing care for PLWH.

A potential limiting factor in the direct application of this intervention to other regions is related to the specific organisation of services. HIV care for the majority of PLWH who live in the city is managed from a single secondary care centre, which contributed to efficient implementation of this intervention. In geographical areas where HIV care is facilitated through multiple centres, implementation within a similar time frame may be less feasible.

Conclusion

We describe a pilot intervention to increase collaboration between community prescribers, specialist pharmacists and local HIV secondary care services. The ‘THINK ARV’ intervention has demonstrated that increasing community prescribers’ access to specialist advice through mobile phone and e-mail resulted in increased awareness and detection of DDIs. Following local pilot success, similar interventions could be co-produced and embedded within different healthcare services to increase other prescribers’ and pharmacists’ knowledge and confidence, and thus reduce potential morbidity, mortality, and healthcare costs, associated with DDIs among PLWH.

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Authors’ contributions

CK contributed to the pre-development survey concept and design, interpretation of data and drafting of article. HLD contributed to THINK ARV study concept and design, analysis and interpretation of data and critical revision of article. SSL contributed to the THINK ARV concept and design, and led Phase Two (implementation, data collection and preliminary analysis). MS and BF contributed to THINK ARV study concept and design. LK contributed to project management. JV contributed to concept, design and analysis of both Phase One (predevelopment survey) and Phase Two (THINK ARV intervention) and critical revision of article. All authors contributed to the acquisition of data and revision of article. All authors read and approved the final article.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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