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Background: Antibiotic overuse is the major driver of rising antimicrobial resistance rates. Unnecessary antibiotic use is associated with adverse medication side effects and rising rates of resistance. In Ontario, which has over 30,000 physicians, there are approximately 3500 primary care physicians (~10% of all physicians) that prescribe more than 50% of all antibiotics (3.9 million prescriptions annually). Peer-comparison antibiotic feedback is a potentially effective tool to improve antibiotic prescribing. We need innovative trials that examine how to reliably implement audit and feedback (A&F) to scale that are effective and sustainable. Mailing letters to high antibiotic prescribers in other countries have shown variable effects on reducing antibiotic prescribing.¹⁻³

Objective: To evaluate the impact of a letter to the 25% of primary care physicians who prescribe the most antibiotics in Ontario on total antibiotic prescribing.

Secondary objectives: To test the impact of different formats of a notification letter on antibiotic prescribing. Our primary hypothesis is that notifying physicians that antibiotic use is being monitored will decrease total antibiotics. We further hypothesize that targeted change ideas on antibiotic initiation or duration will have differential impacts on total antibiotic prescribing and prolonged duration prescribing, respectively.

Methods: The effect of letter mail outs to the top 25% prescribing primary care physicians will be evaluated using a randomized controlled trial (RCT) design. We will allocate physicians to intervention versus control arms in a 6:1 ratio to maximize the number of physicians exposed to the intervention. We will use the IQVIA Xponent database from March 2017 to February 2018 to identify the top 25% of primary care physician antibiotic prescribers in Ontario (family physicians or general practitioners) defined by total numbers of antibiotic prescriptions. They will be mailed a letter to indicate that they prescribe more antibiotics than 75% of Ontario primary care physicians, based on total numbers of antibiotic prescriptions per year. The letter will encourage them to sign up for HQO My Practice primary care reports which in the future may include antibiotic indicators.

The letter was designed using proven theoretical frameworks of behaviour change to improve antibiotic prescribing by physicians. Most physicians are aware of the global public health threat of antimicrobial resistance, however many underestimate its importance locally. Furthermore, unnecessary antibiotic prescribing is frequently attributed to external factors out of their control, such as patient expectations and patient adherence to medication.⁴ For this intervention we focused on two behaviour change theories previously demonstrated to be associated with prescribing behaviour; Theory of Planned

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Behaviour (TBP) and Operant Learning Theory (OLT).⁵ The letter will provide some social normative comparison by indicating to these physicians that they prescribe more antibiotics than their peers (TPB). By providing change ideas and information on the consequences of unnecessary antibiotic use, we are attempting to change the physicians' *risk perception* (TPB) and *anticipated consequences* (OLT) of prescribing antibiotics for acute respiratory tract infections. This letter represents a form of *persuasive communication* behaviour change technique (BCT). This form of BCT has shown to be effective in modifying OLT driven behaviours.^{6,7}

To test different change ideas, we will simultaneously evaluate two types of letters to be randomly distributed to the physicians in the top 25% of prescribers allocated in 3:3:1 ratios; a) Providing change ideas from Choosing Wisely Canada on appropriate initiation of antibiotics for acute respiratory conditions; b) Providing change ideas on appropriate duration of antibiotics.

Designs of the letters went through user testing and were iteratively refined by a sample of Ontario primary care physicians. The letters will be co-branded with OMA Section of General and Family Practice and Choosing Wisely Ontario. The letters were also reviewed by the Ontario College of Family Physicians, HQO and members of the study team to provide input and edits to the language and content. Based on the trial results we will send the most effective letter to all 3500 physicians the following year (12 months later).

Primary outcome: Total number of antibiotic prescriptions over 12 months post-intervention.

Secondary outcomes: The number of antibiotic prescriptions that were prolonged (defined as >7 days duration) and antibiotic drug costs.

Sample Size: As the sample size was fixed by all available physicians in the top quartile of Ontario, we calculated the detectable difference given the available sample size. Using ANCOVA, sample sizes of 1,500 in each of the two intervention arms versus 500 in the control arm achieves 84% power to detect a mean difference of 70 prescriptions in at least one of the two intervention arms versus control using an F test at a two-sided significance level of 2.5%, corrected for two comparisons. We assumed a standard deviation of 700 prescriptions (obtained from baseline data) and a correlation with the baseline mean prescriptions of 0.8.

Multiplicity-adjusted pairwise comparisons will also be made between each of the intervention arms versus the control and between the different versions of the letters. We will evaluate predictor variables of new enrollment including baseline physician prescribing (>90th %ile vs 75-90th %ile), years in medical practice (<10y, 11-24y, vs 25y), physician gender (M vs F), rural vs urban practice, and patient age/sex groupings (<18yM, <18yF, 18-64yM, 18-64yF, 65+M, and 65+F) using modified robust Poisson regression analysis.

We will evaluate quarterly antibiotic prescribing outcomes with IQVIA data, over a one year interval post-intervention accounting for the baseline measure of each outcome in the year before randomization, using ANCOVA analysis. We will evaluate subgroups including baseline physician

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prescribing (>90th %ile vs 75-90th %ile), years in medical practice (<10y, 11-24y, vs 25y), physician gender (M vs F), rural vs urban practice, and patient age/sex groupings (<18yM, <18yF, 18-64yM, 18-64yF, 65+M, and 65+F) using IQVIA data.

Limitations: We can only monitor total antibiotics prescribed with this dataset, instead of per patient volume. This measure appears to be a reasonable antibiotic use measure within a physician as it is stable over time in high prescribing physicians.

Ethical considerations: Antimicrobial stewardship and combating antimicrobial resistance is a provincial and national priority. The Xponent database with prescribing data at an individual prescriber level is already held by PHO and is kept in a secure location. The agreement with IQVIA allows PHO to provide direct feedback to physicians. The letters will be addressed to the physician and marked confidential. The only data within them will be that they have been identified as a high antibiotic prescriber. We will not provide specific prescription counts or any patient-level data.

We have designed this study to maximize potential impact through a 6:1 allocation. Furthermore, we will send a debrief and follow-up letter to all physicians the following year so that all high prescribing physicians will have the opportunity to receive this information and sign up for HQO reports. Physicians will be given an email address to contact PHO with any questions or concerns regarding the letter. All results will be aggregated and reports will not divulge any prescriber details.

We believe a waiver of consent for this quality improvement initiative is reasonable and meets TCPS-2 criteria. Specifically, this intervention involves minimal risk and burden to participants (letters are sent to physicians from government agencies routinely; these letters do not require an immediate response). There is no anticipated impact on the welfare of physicians by receiving this letter. The intervention would be impractical if consent were required. A consent process even if feasible, would likely create selection bias and make it impossible to answer the research question posed. In addition, the consent process would include a greater burden to physicians than this single letter intervention itself. This quality improvement initiative has the potential to benefit physicians by providing helpful recommendations on optimal antibiotic prescribing practices. A PHO contact email will be provided on the letter to provide physicians the opportunity to contact PHO and opt-out of future letters.

References

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