Article details: 2017-0111	
Title	Landscape of antimicrobial stewardship programs in Ontario, Canada: a survey of hospitals
Authors	Valerie Leung BScPhm MBA, Julie Hui-Chih Wu MSc, Bradley J. Langford BScPhm PharmD, Gary Garber MD
Reviewer 1	Dr. Balthasar L. Hug
Institution	Internal Medicine, Luzerner Kantonsspital, Luzern, Switzerland
General comments (author response in bold)	General: The authors wrote a survey of antibiotic stewardship programs in Ontario hospitals and long term care facilities. The report is well written and easy to follow. The paper is timely and the topic interesting. However, there are some issues above all in the methodology section that needs to be addressed as outlined below. Above all, I am positive the authors can pull more results from their data (according to hospital setting). Specific 1. Title, suggestion: Instead of "Landscape" write "An overview of..." maybe even "A comparison of..."according to comment below. **Thank you for this suggestion. The primary goal of this study was to describe the current state of antimicrobial stewardship programs in Ontario hospitals. While we agree that a comparison adds some additional value, and have added some statistical analyses as suggested, the authors felt that "landscape" most accurately portrays the main objective of this study. This terminology is also consistent with communication to hospitals describing this initiative.** 2. Abstract, P 1, lines 28-30: "...implementation of Infectious Disease Society of America (IDSA) recommended interventions such as prospective audit and feedback appears to have increased since 2013." Why "appears"? They increased, didn't they (see Figure 1)? I would express it in an affirmative way "... increased since 2013." **We have revised the sentence to be affirmative: "The scope of ASP strategy implementation is variable however implementation of Infectious Disease Society of America/Society for Healthcare Epidemiology of America recommended interventions such as prospective audit and feedback have increased since 2013." (see line 21-23).** Methods 3. P 10, line 18: How was the questionnaire built? Did the authors use an old questionnaire or at least some questions used in previous surveys so they could benchmark the surveys against each other? Or against other published surveys of this kind? I suggest the authors write a sentence or two on this topic. **We have moved the mentioned paragraph to the "survey design" section of the methods and added further detail to be clearer with survey development, which indicated that the questionnaires were developed by the ASP team at PHO based on previous surveys of hospital ASPs and with input from stakeholders. (see line 59-72).** 4. Statistics, P 10, lines 35-37: The authors mention statistics, but 1) there are none in the paper and 2) Excel is by international convention not a statistics program and should not be mentioned as such. It is ok to set up graphics with it, but not statistics. I have two suggestions at this point: 1) do statistics in table 4 linewise with the absolute numbers (not % as outlined in the table: e.g. first line "intravenous to oral conversion" yes vs. no and the type of hospitals against each other = simple 2 by 4 table and repeat this on all the lines and 2) use an official statistics program such as SAS or SPSS or the like and Fisher's exact test or Chi-Square will be enough. Add p-values at the end of each line. With this, the authors can add some salt and pepper to their study because it offers another set of results (difference of ASP aspects according to hospital setting). Accordingly, the title of the paper and the discussion should change to e.g. title suggestion "Overview of Antimicrobial Stewardship Programs According to Hospital Setting in Ontario, Canada" or something similar. **As suggested, additional statistical analyses have been conducted using SAS and added to the methods/results section accordingly. Although the intent of this paper is to provide an overview picture of the current state of ASP in Ontario, we agree that some inferential statistics may be useful to compare hospital types with respect to key antimicrobial stewardship elements. In order to balance the interest in comparing hospitals with potential for multiple hypotheses testing, we selected key structural and strategic elements that have been previously identified as key components of hospital ASPs.** **Added to methods:** **"Statistical comparisons were performed for key structural (ASP implementation, program maturity of 3 years or greater, funding or resources and antimicrobial use as organizational priority) and strategic elements that align with IDSA/SHEA strong recommendations (therapeutic drug monitoring, intravenous to oral conversion, formulary restriction, prospective audit and feedback) using Fisher's exact test by SAS Enterprise Guide (Version 7.1)." (see line 91-96)** **Statistical analyses conducted and added to results:** **The authors selected the presence of an ASP (see line 107-108), ASP maturity (see line 109), presence of designated resources (see line 118-120), and the presence of appropriate antibiotic use on the organization's quality improvement plan (see line 115-117) were the most appropriate structural variables to conduct further analyses to better understand the ASP landscape as of 2016. Similarly, the 5 selected ASP strategies (see line 132-138) that are mostly aligned with the IDSA/SHEA strong recommendations have a section in the results already.** Results 5. Tables 1 and 2 are nowhere referenced in the text. E.g. table 1 should get mentioned in the paragraph on hospital characteristics in the first or second sentence). Accordingly, table 2 should get mentioned when describing the characteristics of the organizations taking part in the survey. **Thank you for pointing this out, this is our oversight. Additional sentences are added to the first paragraph in the results to refer to table 1 (see line 102) and table 2 (see line 107).** 6. P 11, line 29: What exactly are "automatic stop orders"? Who stops the antibiotics? the treating physician? the ID-specialist? or automatically by the CPOE system according to antibiotic? This should be explained in the methods section. **We have added "computerized automatic stop orders" to this sentence (see line 130).** **We have also revised the methods section to be clearer with the survey questions in the methods:** **"Definitions of each strategy were included in the survey and respondents were directed to the website for further details (e.g., description, associated metrics, references)." (see line 68-69)** Tables 7. Please add all abbreviations like "CCC" as footnotes writing them out. **Thank you for pointing this out. We have added footnotes to all of the tables.**

	8. N= and (%) are not consistent on the top lines. Usually, N's are not in parenthesis (Table 1) **Thank you for pointing this out. We have corrected the table to be more consistent.** 9. Why are in Table 3 just two hospital types? Stratifying the organizations or leaving out some types of organizations because e.g. they don't have ASP resources should be explained in a footnote. **Due to the lack of reported FTE, we have excluded small community and CCC & Rehab hospitals from Table 3. We have added to the footnote to make this clear:** **"Small community and complex continuing care & rehabilitation hospitals are excluded due to lack of reported designated FTE. Small community hospitals (n=3) reported average of 0.006 pharmacist and 0 physician FTE; complex continuing care & rehabilitation hospitals (n=2) reported average of 0.55 pharmacist and 0.15 physician FTE."** Figure 10. I would add the % numbers on top of the columns **To improve brevity and meet word count requirements, figure 1 has been deleted during the revision process.** 11. Please add the N= of organizations surveyed in 2013 and 2016 in the title of the figure. **To improve brevity and meet word count requirements, figure 1 has been deleted during the revision process.**
Reviewer 2	Ms. Erin Graves
Institution	Institute for Clinical Evaluative Sciences, Toronto, Ont.
General comments (author response in bold)	This paper is very timely and an important contribution to landscape in Canada. 1. I would find it helpful to have a bit more information in the introduction on antibiotic resistance in Ontario (scope and scale) to help provide context to the ASP programming data from the survey. Otherwise, the content is clear and reported well. **Additional information has been added to the first paragraph to further describe the burden of antimicrobial resistance, particularly in Ontario.** **"Antimicrobial resistance (AMR) is an important public health issue and has been highlighted as a serious global threat to human health. Globally, 700,000 annual deaths are attributed to infections caused by antimicrobial resistant organisms, and this number is expected to grow. The burden of AMR is also evident in Canada, and the province of Ontario, with rising rates of methicillin-resistant Staphylococcus aureus, vancomycin-resistant Enterococcus bacteremia, and Enterobacteriaeceae resistant to fluoroquinolones and cephalosporins. As such, AMR has been identified as an area of significant concern for the Government of Canada, the Ministry of Health and Long-Term Care of Ontario (MOHLTC) and Public Health Ontario." (See line 33-40)**
Reviewer 3	Dr. Shannon Turvey
Institution	Faculty of Medicine & Dentistry, Department of Medicine, University of Alberta, Edmonton, Alta.
General comments (author response in bold)	Article summary The authors summarize the findings of a voluntary survey conducted in 2016 to assess the current landscape of antimicrobial stewardship in Ontario healthcare facilities. Major criticism The case is appropriate for this journal. The structure is easy to follow. The response rate was excellent for a voluntary survey. The distribution of survey responses (in terms of geography) seemed fairly representative of the distribution of hospitals across the province. However, as acknowledged by the authors, small facilities were underrepresented. Furthermore, there may be fundamental differences between the health facilities that responded to the survey and those that did not. Specifically, one might expect that health care facilities with existing stewardship programs would be more likely to respond to such a survey. 1. I would like to see some clarification of whether the survey was distributed to all health care facilities in the province or not. This remains unclear to me at this point. The authors state "To target those responsible for antimicrobial stewardship, a distribution list was created based on a hospital organization list from the MOHLTC Health Analytics branch..." It is clear that significant efforts were made to capture an appropriate sample and that multiple resources were utilized. However, it is not clear to me whether a representative at all hospital organizations, including community and rehabilitation hospitals, received a copy of the survey and an invitation to participate. It is also not clear to me what is meant by "131 eligible hospital organizations" in the Results section. What would have made an organization ineligible to participate? Are there only 131 hospital organizations in Ontario? **All of the hospital organizations except those primarily providing mental health or ambulatory services were eligible for the survey and invitation to participate were sent to all; this included acute teaching, large community, small community, and complex continuing care and rehabilitation hospitals (classified by the Ontario Hospital Association) totalling to 131 at the time of survey distribution. A list provided by the MOHLTC was used to ensure all eligible organizations were contacted. We have made the methods clearer to address this comment:** **"All hospital organizations in Ontario were eligible for inclusion except for those that were categorized by the Ontario Hospital Association as primarily providing mental health or ambulatory services since ASPs are not required by Accreditation Canada for this type of organization." (see line 77-79)** **"This survey was distributed to all hospitals addressed to the individual that is most responsible for antimicrobial stewardship in their organization (e.g., ASP pharmacist or physician) with the instruction that those individuals should complete the survey and that there should be only one response per organization unless there are multiple sites and submission of site-specific responses was desired." (see line 82-86)** 2. A major strength of the article is that it reports data on current formal allocation of resources to Ontario ASP programs, and the discrepancy between larger sites and smaller sites. It would be nice to see some discussion about the way this may have impacted the breadth of ASP strategies that have been implemented on the ground at sites of varying sizes (recognizing that this study format is not intended to capture causality). **This is an interesting point. This survey was able to capture the number of ASP elements implemented but not the extent or fidelity of implementation. Hence, it presents a challenge to draw an association between funding and ASP strategy implementation. This is both a limitation of this survey and an opportunity for future work. A statement has been added to the discussion to address this:** **"Given the discrepancy in resource allocation among hospital types and the need to further describe both the scope and breadth of ASP implementation, future research should address the impact of resources on the extent or fidelity of ASP implementation and evaluate outcomes at both patient and population levels." (see line 219-222)**

	3. Trends in implementation of particular antimicrobial stewardship strategies are reported in Results, but not unpacked in the Discussion. For instance, from 2013 to 2016, there was almost no increase in the percentage of organizations implementing formulary restriction as an ASP strategy. It is unclear how many organizations reported full or partial information on timing of program component implementation. The Figure 1 caption states simply that organizations that responded "not known" to implementation year were excluded from analysis. **Based on this suggestion we have added further detail to the discussion to address trends between the 2013 and 2016 ASP surveys:** **"It is encouraging that implementation of impactful strategies such as prospective audit and feedback has increased over time and is now in place in the majority of responding organizations.13 The proportion of responding organizations that have implemented prospective audit and feedback (65%) in this survey is comparable to that reported in the CDC survey (63%).14 Conversely, formulary restriction is less commonly implemented in Ontario hospitals (54% and 29% without and with preauthorization, respectively). IDSA/SHEA guidelines recommend preauthorization and/or prospective audit and feedback as core strategies in a hospital ASP. It is likely that many organizations prefer prospective audit and feedback as this approach is more collegial and provides an opportunity for prescriber engagement and education, aspects that are lacking with a restrictive strategy." (see line 182-191). To improve brevity and meet word count requirements, figure 1 has been deleted during the revision process.** 4. It would also have been nice to see a greater focus on how sites are prospectively monitoring program impact. Importantly, the authors highlight current heterogeneity in strategies for monitoring antimicrobial utilization across facilities within the province. The authors make an important point about the potential benefits of standardizing antimicrobial use data in the province. **The authors agree with this point. The intent of the survey was to understand the overview landscape of ASP in hospitals as such data is currently lacking. Due to the lengthiness of the survey, it was decided that we would conduct a separate survey as a follow up to gather more detailed information.** Overall, this article is an important contribution to our current understanding of the ASP landscape in Canada, and identifies some key barriers to more effective ASP implementation. Minor criticism The manuscript contains some grammatical errors and typos. For example: 1. Page 12, third paragraph "released evidenced-based guidelines" should read: "released evidence-based guidelines". 2. Page 13, fourth paragraph. "Consistent the CDC survey". Should read: "consistent WITH the CDC survey" **Thank you for pointing this out. Typos have been revised accordingly.**
Reviewer 4	Dr. Noémie Savard
Institution	Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Que.
General comments (author response in bold)	This is a well written manuscript on an important topic. Work such as this one, done by public health organizations, should be published more often so that knowledge gained can be shared across jurisdictions. Here are a few suggestions, although overall I think the manuscript is well structured, clearly written, and that the essential information is present. 1) The IDSA recommendations (and how some of the PHO ASP strategies align with them) are introduced in the Results section, and the fact that they are "strong recommendations with moderate quality evidence" is mentioned in the Discussion. I think it would be useful to have them introduced earlier, so that we know from the Introduction that some of the PHO ASP strategies asked about in the survey are evidence-based. Additionally, it could be mentioned in the Methods section that you analysed these specific evidence-based strategies with respect to the year of implementation. **Thank you for the suggestion. We have added to the introduction where we introduced the 32 PHO ASP strategies with the following sentence: "A subset of these strategies also correspond to an evidence-based framework to implement ASP released by the Infectious Diseases Society of America/Society for Healthcare Epidemiology of America (IDSA/SHEA) in 2016 with a number of strong recommendations." (see line 51-53)** **Appendix 1 included adaptive question structure with: "Respondents who reported having a formal ASP were presented questions about program structure. All respondents were asked if their organization had implemented each of the 32 ASP strategies, as defined by Public Health Ontario ASP, since these activities can be implemented in the absence of a formal ASP. Year of implementation was then collected."** 2) The results for "Structural Elements" and for "Measuring ASP Impact" are well discussed. In comparison, relatively little is said about the "Implementation of Stewardship Strategies", especially considering the amount of information presented in Table 4. A few things could help the reader (who is not necessarily familiar with PHO ASP strategies) to make sense of this large amount of information. Maybe indicate in the Results, in addition to the most frequently implemented strategies, which ones are least frequently implemented, and then maybe discuss the reasons and/or impact (e.g. Are some of those least implanted strategies part of the evidence-based subset of strategies? What is their priority level?). Other ways of guiding the reader could work as well. **As suggested, a list of the least commonly implemented strategies has been added to the results:** **"Least commonly implemented strategies include clinical decision support systems/computerized physician order entry (12%), checklists (14%) and improved antimicrobial documentation (23%)." (see line 130-132)** **Since there are 32 strategies, our discussion tends to focus on the subset strongly recommended by IDSA/SHEA. As such we have added further information to the discussion to address discrepancies in implementation of some of these core strategies:** **"It is encouraging that implementation of impactful strategies such as prospective audit and feedback has increased over time and is now in place in the majority of responding organizations.13 The proportion of responding organizations that have implemented prospective audit and feedback (65%) in this survey is comparable to that reported in the CDC survey (63%).14 Conversely, formulary restriction is less commonly implemented in Ontario hospitals (54% and 29% without and with preauthorization, respectively). IDSA/SHEA guidelines recommend preauthorization and/or prospective audit and feedback as core strategies in a hospital ASP. It is likely that many organizations prefer prospective audit and feedback as this approach is more collegial and provides an opportunity for prescriber engagement and education, aspects that are lacking with a restrictive strategy." (see line 182-191)**

	3) Page 13, line 32 says: "Another important limitation is that while organizations had the option to submit site-specific responses, most were at the organizational level". It would be important to mention in the Results how many organizations responded at the site level, and explain how it was dealt with in terms of denominators. E.g. there were 97 responses out of 131 organizations. Are some of those 97 responses for the same organization but for different sites? Or is it that 97 organisations responded, but some gave different answers for different sites? **Most organizations do not have multiple sites (59/97). Eight multisite organizations submitted site-specific responses with no overlap with the other site(s). This is reflected on line 101-103.** 4) The "PHO ASP" is first mentioned in the Methods. Although we can have a good idea of what the "PHO ASP" is, it is not explicitly stated. I think it would be helpful to mention (and maybe describe briefly) what PHO ASP refers to in the Introduction. Alternatively, it could just be said in the Methods that the Ontario ASP Landscape survey was, "developed by PHO based on …" **We have revised it to "The Ontario ASP Landscape survey was developed by the ASP team at Public Health Ontario based on previous hospital ASP surveys, an environmental scan of ASP elements in acute care settings, and input from stakeholders …" (see line 60-62)** 5) I am assuming that the survey questions about strategic ASP elements refer directly to the 32 PHO strategies mentioned in the Introduction. This could be made more explicit in the Methods section. **To improve brevity and meet word count requirements, details about the survey have added to the appendix to be more explicit with:** **"Respondents who reported having a formal ASP were presented questions about program structure. All respondents were asked if their organization had implemented each of the 32 ASP strategies, as defined by Public Health Ontario ASP, since these activities can be implemented in the absence of a formal ASP. Year of implementation was then collected."** 6) The survey questions should be annexed, to allow proper understanding of the different strategies. Ideally, PHO ASP strategies should also be annexed if possible. **The survey question is now attached as Appendix 1. Due to the detailed information on each of the strategies so respondents can fully understand them, a definition of each of the 32 strategy strategies was included in the survey and respondents were directed to the PHO website for further details. For the manuscript, we have provided a link to the publically available website that contains all of the information in the introduction.** 7) Table 4: I think that having the absolute numbers would be helpful. **Absolute numbers have been added to the Table 4.** Typo/corrections: 1. Table 2: "Presence formal …" should probably read "Presence of formal …" 2. Table 2: % are missing in the last column. 3. Page 13, lines 56-57: "to explore the relationship between specific structural and strategic elements on drug utilization" should probably read "to explore the relationship between specific structural and strategic elements and drug utilization" **Thank you for pointing these out, typos has been revised.** **The next step is to determine the potential impact of ASP elements (structure/strategy) on drug utilization. We have revised this sentence to be clearer: "Work is underway to explore the relationship between specific structural and strategic elements and drug utilization in a subset of Ontario hospitals. " (see line 223-225)**