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CCDR

CANADA COMMUNICABLE DISEASE REPORT

SCIENTIFIC WRITING

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Canada

CCDR
CANADA COMMUNICABLE DISEASE REPORT

The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public health professionals, and policy-makers to inform policy, program development and practice.

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T *The icon identifies articles that address the theme. CCDR will be increasingly publishing articles that are not related to the theme.*

OVERVIEW

A guide to publishing scientific research in the health sciences

P Huston[1,2], BCK Choi[2-4]*

Abstract

Effective communication of scientific research is critical to advancing science and optimizing the impact of one's professional work. This article provides a guide on preparing scientific manuscripts for publication in the health sciences. It is geared to health professionals who are starting to report their findings in peer-reviewed journals or who would like to refresh their knowledge in this area. It identifies five key steps. First, adopt best practices in scientific publications, including collaborative writing and ethical reporting. Second, strategically position your manuscript before you start to write. This is done by identifying your target audience, choosing three to five journals that reach your target audience and then learning about the journal requirements. Third, create the first draft of your manuscript by developing a logical, concise and compelling storyline based on the journal requirements and the established structure for scientific manuscripts. Fourth, refine the manuscript by coordinating the input from your co-authors and applying good composition and clear writing principles. The final version of the manuscript needs to meet editorial requirements and be approved by all authors prior to submission. Fifth, once submitted, be prepared for revision. Rejection is common; if you receive feedback, consider revising the paper before submitting it to another journal. If the journal is interested, address all the requested revisions. Scientific articles that have high impact are not only good science; they are also highly readable and the result of a collective and often synergistic effort.

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Introduction

The publication of the findings of scientific research is important for two reasons. First, the progression of science depends on the publication of research findings in the peer-reviewed literature. Second, the publication of research is important for career development. The old dictum "publish or perish" suggests the critical role publishing research has, especially for those in academia. The newer version, "publish and flourish", suggests that publishing solid scientific research is good for individual researchers and good for the scientific community. With good research, there is the potential for everyone to be better off.

The publication of scientific work is not easy. There are many books on how to write a scientific article (1-5); however, the level of detail may be overwhelming and there is a tendency to focus more on the technical aspects, such as the structure of a scientific manuscript and what to include in each section, and less on the process aspects, such as what constitutes authorship and how to choose the most appropriate journal. There is a need for a basic overview for those who would like to start publishing or refresh their knowledge in this area. The objective of this article is to provide health professionals with an overview on how to prepare manuscripts for publication.

Adopt best practices in scientific publications

Anyone who would like to author scientific publications should know about these two best practices before they begin: work collaboratively and observe ethical reporting practices.

Practice collaborative writing

Research and scientific publishing are collective enterprises that call for collaboration as a best practice. Research usually involves a research team. New research projects build on previous research done by others. It involves input from peers on both protocol development before the research is done, as well as the review of manuscripts once the research is completed. The Cochrane Collaboration is one important example of this (6). To optimize the success of your research team, cultivate strong interpersonal skills and choose your collaborators wisely. Areas to consider when you are choosing with whom to work include such things as collaborator availability, similar research interests, track record and personal suitability.

Given that a scientific publication is meant to contribute to knowledge, a good research question is essential, as is identifying the optimal scientific method to answer that question and observing ethical practices in the conduct of your research.

Once these items have been addressed, what do you need to know before you start to write?

Observe ethical reporting practices

The ethics of scientific publications can be summarized by two best practices: complete and accurate reporting and appropriate attribution of everyone's contributions (7).

Ensure complete and accurate reporting

Unethical scientific publication practices include incomplete reporting, the reporting of fraudulent data, plagiarism, duplicate publication and overlapping publications. Some people consider failure to publish the results of clinical trials as unethical (8), as it can create bias in the published record. Incomplete reporting can include selective reporting of findings or not reporting at all. It is important to report negative data, or any unexpected finding.

Falsification or fabrication of data is the most obvious breach of research ethics. One example is the fraudulent study linking autism to vaccine (9), which caused untold harm by undermining public confidence in routine childhood vaccines.

Plagiarism must be carefully avoided. Incorporating others' ideas or research results into any manuscript you write needs to be done with appropriate referencing. Journal editors routinely check manuscripts with antiplagiarism software before determining a manuscript's appropriateness for peer review. Free software programs are available for authors to check for inadvertent duplication of content such as CopyScape, DupliChecker, Plagiarisma, Plagium, Search Engine Reports, SEOTools, Site Liner and Unplag.

Duplicate publication is publishing an article that is the same or overlaps substantially with another article by the author or publisher (8). It is considered redundant, and may result in double-counting of data. This is to be distinguished from co-publication, which is when the same article is published in more than one journal at approximately the same time to increase reach to different disciplines (8). It meets specific criteria and is done with complete transparency.

Overlapping publication is a variant of duplicate publication. It typically occurs with multi-centre trials and is characterized by publications from single centres, several centres as well as all centres. This is considered unethical as it can lead to double-counting and distorts the perception of the weight of the evidence (10). It may be appropriate to have more than one publication come from a multi-centre trial, but this is usually to address secondary outcomes. Secondary publications should cite the primary analysis and all publications of trials should identify the trial registration number (8).

Give appropriate attribution

It is important to acknowledge the work of everyone who contributed to a scientific publication. Central to ethical publication is appropriate authorship. A best practice is to identify the role of each author. Authorship has been defined by the International Committee of Medical Journal Editors (ICMJE) as those who meet all of the following four criteria: substantial contributions to the conception or design of the work or to the acquisition, analysis or interpretation of data for the work; drafting the initial manuscript or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved (11).

Of note, the collection of data or the development of software for a study are not criteria for authorship, nor is securing research funding; however, these are important contributions that should be acknowledged—either in the Acknowledgements section or, if there is one, in the Contributors section. It is best practice to ensure everyone mentioned in an Acknowledgements or Contributors section is aware he/she has been identified, and is in agreement with being identified. Contractors paid to perform parts of a study (e.g., laboratory testing, software development or drafting the manuscript) are often, by definition, not authors but still merit being identified in the Acknowledgements or Contributors section.

Some unethical practices in authorship include guest authorship and ghost authorship. Guest authorship is including someone as an author who does not meet the ICMJE criteria and ghost authorship is excluding someone as an author who does meet the ICMJE criteria. Basically, ethical attribution is all about transparency.

There can be a lot of debate on the sequencing of authors. The ordering of authors differs by discipline (12). In the health sciences, the first author has the most weight; the final author also carries weight as this is often the principal or most senior investigator. In contrast, in economics, authors are usually listed alphabetically, implying equal contribution to the research work. It is useful to discuss authorship early in the manuscript planning process, and then again near the completion of the manuscript. This discussion should include an assessment of authorship against the ICMJE criteria and consideration of authorship sequence, which may change over time if there were changes in the level of input from what was originally planned.

Position your manuscript

Once your research is completed, you need to identify appropriate journals for publication. Not every manuscript can or should be published in a prestigious, high-impact journal. People can waste a lot of time and effort sending manuscripts to journals that will promptly send back a polite rejection letter, or will keep it for several months before declining it, based on the peer review. So how do you choose which journal to submit to? Discuss with your co-researchers or peers: Who is the target audience? Who will want to know about this research? What is the best journal to reach that audience? And what are those journals' specific requirements for manuscript submissions?

Identify your target audience

Before writing up results of your study, think about your potential readers. Are your research findings most appropriate for a general readership or a specialty group? This affects the choice of journal for submission, and the writing style you adopt for the manuscript.

Choose three to five journals

Based on your target readership, develop a list of three to five journals, and then order by journal impact factor. The impact factor is the average number of citations per article published in that journal, based on the performance in the previous two years (13). Submit your manuscript to one journal at a time, starting from the top of the list. If you receive a rejection letter from your "Plan A" journal, you have a ready "Plan B" journal to submit to right away. This avoids having the rejected manuscript languish on your desk.

Learn about the journal requirements

Every journal has instructions for authors that are listed online. These instructions describe the types of articles that the journal publishes and provides specific advice about format, word length, as well as what needs to be included in a cover letter at the time of submission. Consult some past issues of the targeted journals to see examples of the different types of articles that are published.

Create the first draft

Now that you have identified your target audience, what journal you are targeting first, and what its requirements are, you are ready to create the first draft. To begin you want to develop a high-level summary that establishes a logical, compelling storyline that follows the established structure for a scientific manuscript. Then, before you start to write the text, check for any reporting guides for the type of study you have done to ensure you address any specific reporting requirements.

There is a common misconception that scientific publications are simply dispassionate reports of the methods and results of research. But consider this: There are more than 30,000 biomedical journals (14). We are living in an age of information overload, so people become very selective in what they read and ask themselves "Is this important for me to read?" The objective reporting of research findings is necessary, but not sufficient. Effective authors will also provide an appropriate context and present their work in such a way that readers find it interesting and easy to understand. The sections that follow identify several ways to best present the context, data and implications of your work.

Develop a compelling storyline

The use of the term storyline here does not mean you endeavour to entertain the reader. It is how you "present your case" in the court of scientific opinion. It maps on to the basic structure of scientific articles and includes the rationale for the study, the research question, how that question was addressed, what was found and why these findings are important (3). After working for months (and sometimes years) on a research project, it is easy to get lost in the details. Establishing a clear, logical underlying structure to your scientific manuscript from the outset not only helps to avoid going off on tangents, it also vastly increases its readability. The abstract is an excellent place to set out the storyline of your manuscript. You want to respond to the questions: What is this research about? (background and objective); What did you do to answer your research question? (methods); What did you find? (results); and What are the implications and next steps? (discussion and conclusion). Then, much like establishing the theme, each section is developed in the manuscript. A well-written abstract gives readers a "road map"; after reading it they will know what you will be covering in the article.

One way to strengthen the logic of your manuscript is to use the same terms and the same sequencing of information in each section. For example, if your research objective was to assess acceptability and adherence to a treatment regimen, what you do not want to do is describe the willingness to start a treatment in the Introduction, note how you measured compliance and adherence in the Methods and then describe how many people followed the treatment regime after agreeing to start it in the Results. If your research objective is to assess acceptability and adherence, define acceptability and then adherence in the Introduction, identify how you measured acceptance and then adherence in the Methods, and describe your findings for acceptance and then adherence in the Results. When you use the same terms in the same sequence in the Introduction, Methods and Results sections, it is much easier for the reader to quickly grasp what you did and what was found.

In addition, there are several writing techniques that help make your manuscript more compelling to engage the reader. The first is to have "a hook", or interesting start that draws the reader in. Titles can be a hook; for example, a recent article from the *New England Journal of Medicine* was entitled: "The Other Victims of the Opioid Epidemic" (15). It might catch your attention, as you immediately ask yourself "Who are the victims and who are the other victims?" A compelling title may pose a question that motivates people to read the article: "Can scientists and policymakers work together?" (16). Readers are also engaged by the first sentence of the abstract; for example: "The emergence and prevalence of antibiotic-resistant bacteria are an increasing cause of death worldwide, resulting in a global call to action." (17). This is a good first sentence as it gives a sense of urgency and makes the reader curious about what the call to action is. One must be careful to not sensationalize, but when there is an urgent health issue, it is important to describe why we need to be aware of it and change what we do if necessary.

Check for reporting guides

As a final step before starting to write the manuscript in full, check if there are specific reporting requirements for the type of research you have done; for example, if you have done an experimental study, you will need to mention research ethics board approval and informed consent (18). If you have done a systematic review, include a flow diagram of the included and excluded studies (19). Some journals provide author checklists to identify what is important to include in different sections for different types of studies (20,21). The Equator Network (Enhancing the Quality and Transparency of Health Research) brings together a number of reporting guidelines and is a useful resource (22).

Use the IMRAD approach

When you start to write the text, use the classic structure of a scientific article: Introduction, Methods, Results and Discussion, which is often referred to by the acronym IMRAD. But, rather than writing down everything you know that relates to your study, use each section strategically to tell the story of your research.

A good Introduction section has the structure of an inverted triangle. This means that you start with a broad topic, and then narrow down the readers' focus in logical steps until you arrive at your research question. This can be facilitated by answering the following questions:

- What is the issue?
- Why is it important?
- What do we know to date?
- What are the gaps in our knowledge?
- What is the research question that will address this gap?
- What was the objective of the research?

At this point, the reader will want to know "So what happened?" and they will keep reading. The summary of the literature is done in the present tense, as it represents generally accepted facts and principles. Define all abbreviations on first use but use only commonly-accepted ones. Too many abbreviations decrease readability. The introduction is described in the present tense (as it describes established facts).

The Methods section describes how the study was conducted. It is important to explain how the methods address the research objective. Give enough detail so that others can duplicate your study, if needed, to confirm that your results are consistent and reliable. It is useful to have subtitles. For a clinical trial, for example, this could include study population, intervention, outcome measures and analysis. Avoid the temptation to provide results in the Methods section. For example, the sampling methodology belongs to the Methods section, the response rate of the study belongs in the Results section. The Methods section is described in the past tense (as it describes what you did).

The Results section describes what was found in the study (in the same sequence of information established in the Introduction and the Methods sections). Avoid the temptation to discuss or analyze results in the Results section. For example, you can state: "there were more men than women in this study", but exploring the reason for this belongs in the Discussion section. Results are described in the past tense (as they describe what you found).

Many readers find the Discussion section to be the most interesting part of the article. The first sentence is an opportunity to summarize the most important findings of your study; for example: "Surveillance data from four Nordic countries suggested that at least 25% of gonorrhea infections were related to travel" (23). Interpret your findings in light of possible biases or sources of errors. Then it is important to consider both the strengths and weaknesses of your study; compare it to other studies with similar or different findings, consider the implications and identify the next steps. The Discussion section is an opportunity to situate your findings within the larger body of knowledge and to consider what is needed to further advance scientific understanding. The discussion is described in past, present or future tense depending on context.

Develop tables and figures to highlight key findings

There are two best practices to consider when creating tables and figures. First, to address the classic evidence-based medicine question—Are these results applicable to my patient population?—you need to describe your study population (24). The first table in a clinical study, for example, often compares the demographic characteristics of the research subjects to what is known about the study population. This helps readers assess how representative the study sample was. Second, use tables and figures to highlight your key findings. Resist the temptation to present all the data you have in tables and figures which may overwhelm the reader. You want to keep the focus on the study objective and the answer to your research question.

Tables are useful to present large quantities of data and figures are preferred to show trends over time. Titles of tables and figures should be able to "stand alone"; i.e., they are self-explanatory and complete. To be complete, include the study population, type of data presented and dates of the study. In tables, ensure each column has a heading. Make sure all data is validated and that all research subjects are accounted for (i.e., the percentages add up to 100%). Further resources on preparation of tables and figures are available (25,26). See **Table 1** for some highlights of the "Dos and Don'ts" when writing scientific manuscripts.

Table 1: Highlights of common dos and don'ts when writing scientific manuscripts

Item	Dos	Don'ts
Title	Use accurate, interesting, and catchy titles. Example: "Can scientists and policymakers work together?"	Do not use titles that are too long, such as: "A multi-sectoral mixed model study to examine the facilitators and barriers in the collaboration of scientists and policymakers in joint efforts using qualitative and quantitative methods".
Abstract	Use the abstract to attract readers and summarize your story line.	Do not include content that is not found in the article.
Introduction (Why?)		
Objectives	Carefully state your objective, as everything should follow logically from the objective.	Do not leave out the objective or just tie it in loosely to the rest of the article.
Methods (How?)		
Appropriateness	Ensure and explain how the research method addresses the research objectives. Describe the methods in sufficient detail so other people can repeat the study.	Do not use a cross-sectional study to examine causal associations because it cannot. Do not state: "our study used conventional methods" without giving a reference.

Table 1: Highlights of common dos and don'ts when writing scientific manuscripts (continued)

Item	Dos	Don'ts
Results (What?)		
Sequencing	Order the sequence of information so that the Results section addresses the objective in a logical way.	Do not present results in a random fashion or include results that are irrelevant.
Other information	Include only results of your study in the Results section.	The results of other studies belong either in the introduction (to provide context) or the discussion (to compare with your results).
Use of tables and figures	Tables and figures should highlight key study findings. Text in the Results section should complement tables and figures; for example, if a table shows "relative risk=8.5, *P*=0.02", the text might read "a strong, statistically significant association was found."	Do not simply repeat data from tables and figures in the text of the Results section; for example, "the relative risk was 8.5 and the *P*-value was 0.02" is repetitive of the information already provided in the table, and provides no additional information for the readers.
Discussion and conclusion (So What?)		
Main findings	The first sentence of the Discussion section should address your research objective and highlight the key findings of your study.	Do not simply summarize the results a second time without interpretation.
Unexpected results	If results contradict expectation, look for possible sources of bias, such as selection of subjects, methods of data collection and confounding factors.	Do not delete results simply because they contradict expectation. These may be the most important results of your study.
Contribution to knowledge	Describe the new knowledge provided by this study.	Do not just say "our study confirmed the results of previous studies".
Strengths and limitations	Discuss strengths and limitations of the study in a few paragraphs.	Do not overstate the limitations but do not hide them either.
Implications	Describe how the study may inform current practice. Suggest future research directions.	Do not just say "our study has made important contributions to science". Do not just say "this study indicates that future studies are needed".

Refine the manuscript

Most manuscripts are a team effort, so once a manuscript has been drafted, it then needs to be circulated for input by all the co-authors. Consider your own internal peer review process and then refine the manuscript for clarity before submitting it to a peer-reviewed journal. If your first language is not English, consider having the manuscript copy-edited before you submit it to a journal.

Circulate to co-authors and peers

Each research team works out their own way of writing and revising. Usually the first author develops the first draft, and then sends to other authors to provide comments (usually using the tracked changes function). The first author will then incorporate comments and produce a second draft for a second round of comments. This process continues until all authors agree on the structure and wording of the manuscript. It is also possible to have different authors draft different sections of the manuscript, once there has been consensus on the storyline and the structure. A common challenge with circulating drafts of a manuscript is version control. You may want to have only one author working on a draft at a time. If there is simultaneous feedback from multiple authors, they should all be sent to the first author by a set due date. You may also want to conduct your own internal peer review process. After being steeped in a project for months and a manuscript for weeks, it is easy to lose perspective. An unblinded internal peer review may help strengthen your manuscript before undergoing the blind external peer review that is conducted by the editorial office of scientific journals.

Apply clear writing principles

The hallmark of good scientific writing is precision and clarity (5). Based on the classic, *The Elements of Style*, here are some tips that will help bring clarity to your writing (27). Check the first sentence of each paragraph. These should signal to the reader the progression of the logic of your manuscript and introduce what the paragraph contains. When appropriate, use the active voice. To say "We developed a protocol" is more engaging than the passive voice: "A protocol was developed". Edit out needless words, such as "as noted above". When possible, use parallel construction or the repetition of a grammatical form within a sentence. For example, the phrase "Children aged 4–6 years should be given vaccine A; the administration of vaccine B is advised for those who are 13–18 years old" can be made clearer using parallel construction: "Children aged 4–6 years should be given vaccine A; adolescents aged 13–18 should be given vaccine B". Make definitive assertions; arouse interest of the reader by reporting the details that matter. In addition, you do not want to be overly complex; resources are available to help describe things in plain language (28).

Submit and be ready to revise

Once all the authors sign off on the final version, submit to your journal of choice with a short cover letter noting that your manuscript has not been published previously and is not under consideration by any other journal. It is also useful to identify why your manuscript is relevant to the journal's readership. This may influence the editor's decision on whether to send your manuscript for external peer review.

Once the manuscript is submitted, brace yourself for a number of possible responses. You may receive a polite rejection letter.

Or the Editor may have comments on the manuscript that need to be addressed before it is peer-reviewed. If this is the case, it is good to address these promptly. Another possibility is that the manuscript is peer-reviewed and then declined. There are two reasons why you should carefully consider all the peer-reviewer comments, even though the journal is not interested in your manuscript. First, this is free advice, often from top-notch experts in the field, so why not use it to improve your success rate with another journal? Second, only a limited number of researchers participate in the journal peer review process. When you submit to a second journal, what you do *not* want to hear back is "I was the peer reviewer of this manuscript for another journal, and I see that none of my previous comments were considered by the authors". If you do decide to revise the manuscript to address reviewer comments, do not forget to review the instructions for authors for the new journal and reformat as necessary. Finally, after peer-review has been completed, you may receive a tentative acceptance letter from the editor, accompanied by a request for minor revisions. Or you could receive a "reject and resubmit" letter, which means that extensive revisions are needed. In either case, it indicates an interest in a revised manuscript.

Requested revisions are usually discussed jointly among the co-authors until there is consensus on how to address them. Making the revisions can either be allocated among the authors, or coordinated through one person. Usually once the revisions are underway, they do not seem as formidable as they first appeared, and the manuscript ends up being stronger and clearer as a result. Once revised, do a final check of the abstract to ensure it still reflects the revised text. Again, sign-off is needed from all the authors before submitting the revised manuscript to the journal.

Discussion

To advance science, research needs to be published. To optimize the chances of your research getting published and having an impact, it is important to demonstrate objectivity, and present your work in a way that is interesting and compelling. To do this you need clarity, logic and the use of rhetorical techniques to engage the reader in your research. This includes positioning your manuscript to reach your target audience, developing a logical, compelling storyline within the confines of the IMRAD structure, having an effective iterative approach among your co-authors to develop the manuscript and being ready to complete revisions to meet journal requirements.

Effective scientific writing rarely comes from innate talent. Writing is a skill that needs to be honed over one's professional career. Cultivate an interest in what makes good writing. As you read other peoples' work, ask yourself what makes some articles easier to read than others. Consider becoming a peer-reviewer for scientific journals to assess the manuscripts of others.

Conclusion

It is thoroughly satisfying to publish compelling research that influences people and makes a contribution to science. This is most often achieved through the synergy of collaboration with others and having a common goal of advancing the collective progression of science.

Conflict of Interest

None.

Authors' statement

Both authors worked on the conception and design together, PH developed the first draft, both contributed to multiple drafts and signed off on the final version. Dr. Patricia Huston is the Editor-in-Chief of CCDR and recused herself from taking any editorial decisions on this manuscript. Decisions were taken by the Editorial Fellow, Toju Ogunremi, with the support of the Editorial Board member, Dr. Michel Deilgat.

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Critical Appraisal Toolkit (CAT) for assessing multiple types of evidence

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Abstract

Healthcare professionals are often expected to critically appraise research evidence in order to make recommendations for practice and policy development. Here we describe the Critical Appraisal Toolkit (CAT) currently used by the Public Health Agency of Canada. The CAT consists of: algorithms to identify the type of study design, three separate tools (for appraisal of analytic studies, descriptive studies and literature reviews), additional tools to support the appraisal process, and guidance for summarizing evidence and drawing conclusions about a body of evidence. Although the toolkit was created to assist in the development of national guidelines related to infection prevention and control, clinicians, policy makers and students can use it to guide appraisal of any health-related quantitative research. Participants in a pilot test completed a total of 101 critical appraisals and found that the CAT was user-friendly and helpful in the process of critical appraisal. Feedback from participants of the pilot test of the CAT informed further revisions prior to its release. The CAT adds to the arsenal of available tools and can be especially useful when the best available evidence comes from non-clinical trials and/or studies with weak designs, where other tools may not be easily applied.

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Introduction

Healthcare professionals, researchers and policy makers are often involved in the development of public health policies or guidelines. The most valuable guidelines provide a basis for evidence-based practice with recommendations informed by current, high quality, peer-reviewed scientific evidence. To develop such guidelines, the available evidence needs to be critically appraised so that recommendations are based on the "best" evidence. The ability to critically appraise research is, therefore, an essential skill for health professionals serving on policy or guideline development working groups.

Our experience with working groups developing infection prevention and control guidelines was that the review of relevant evidence went smoothly while the critical appraisal of the evidence posed multiple challenges. Three main issues were identified. First, although working group members had strong expertise in infection prevention and control or other areas relevant to the guideline topic, they had varying levels of expertise in research methods and critical appraisal. Second, the critical appraisal tools in use at that time focused largely on analytic studies (such as clinical trials), and lacked definitions of key terms and explanations of the criteria used in the studies. As a result, the use of these tools by working group members did not result in a consistent way of appraising analytic studies nor did the tools provide a means of assessing descriptive studies and literature reviews. Third, working group members wanted guidance on how to progress from assessing individual studies to summarizing and assessing a body of evidence.

To address these issues, a review of existing critical appraisal tools was conducted. We found that the majority of existing tools were design-specific, with considerable variability in intent, criteria appraised and construction of the tools. A systematic review reported that fewer than half of existing tools had guidelines for use of the tool and interpretation of the items (1). The well-known Grading of Recommendations Assessment, Development and Evaluation (GRADE) rating-of-evidence system and the Cochrane tools for assessing risk of bias were considered for use (2,3). At that time, the guidelines for using these tools were limited, and the tools were focused primarily on randomized controlled trials (RCTs) and non-randomized controlled trials. For feasibility and ethical reasons, clinical trials are rarely available for many common infection prevention and control issues (4,5). For example, there are no intervention studies assessing which practice restrictions, if any, should be placed on healthcare workers who are infected with a blood-borne pathogen. Working group members were concerned that if they used GRADE, all evidence would be rated as very low or as low quality or certainty, and recommendations based on this evidence may be interpreted as unconvincing, even if they were based on the best or only available evidence.

The team decided to develop its own critical appraisal toolkit. So a small working group was convened, led by an epidemiologist with expertise in research, methodology and critical appraisal, with the goal of developing tools to critically appraise studies informing infection prevention and control recommendations.

This article provides an overview of the Critical Appraisal Toolkit (CAT). The full document, entitled *Infection Prevention and Control Guidelines Critical Appraisal Tool Kit* is available online (6).

Overview

Following a review of existing critical appraisal tools, studies informing infection prevention and control guidelines that were in development were reviewed to identify the types of studies that would need to be appraised using the CAT. A preliminary draft of the CAT was used by various guideline development working groups and iterative revisions were made over a two year period. A pilot test of the CAT was then conducted which led to the final version (6).

The toolkit is set up to guide reviewers through three major phases in the critical appraisal of a body of evidence: appraisal of individual studies; summarizing the results of the appraisals; and appraisal of the body of evidence.

Tools for critically appraising individual studies

The first step in the critical appraisal of an individual study is to identify the study design; this can be surprisingly problematic, since many published research studies are complex. An algorithm was developed to help identify whether a study was an analytic study, a descriptive study or a literature review (see **text box** for definitions). It is critical to establish the design of the study first, as the criteria for assessment differs depending on the type of study.

Definitions of the types of studies that can be analyzed with the Critical Appraisal Toolkit*

Analytic study: A study designed to identify or measure effects of specific exposures, interventions or risk factors. This design employs the use of an appropriate comparison group to test epidemiologic hypotheses, thus attempting to identify associations or causal relationships.

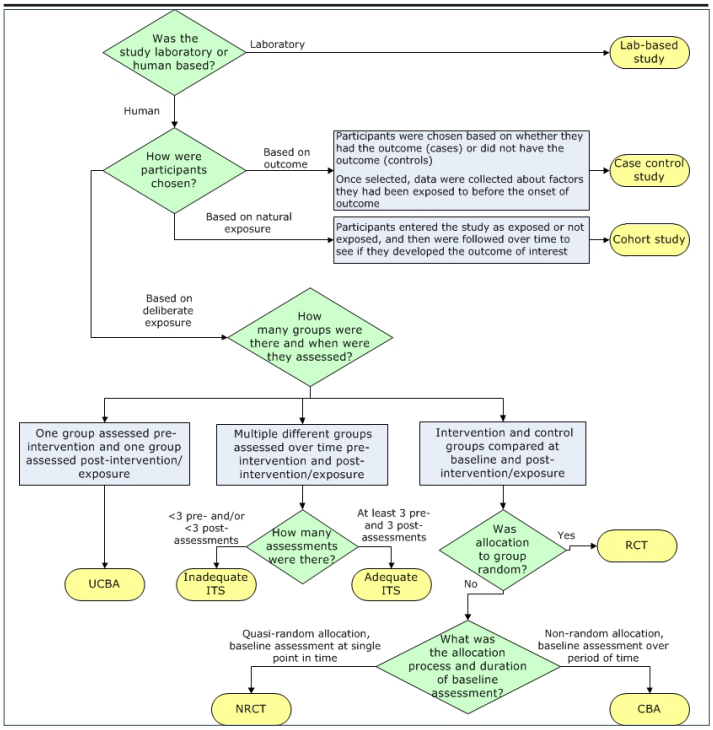
Descriptive study: A study that describes characteristics of a condition in relation to particular factors or exposure of interest. This design often provides the first important clues about possible determinants of disease and is useful for the formulation of hypotheses that can be subsequently tested using an analytic design.

Literature review: A study that analyzes critical points of a published body of knowledge. This is done through summary, classification and comparison of prior studies. With the exception of meta-analyses, which statistically re-analyze pooled data from several studies, these studies are secondary sources and do not report any new or experimental work.

* Public Health Agency of Canada. Infection Prevention and Control Guidelines Critical Appraisal Tool Kit (6)

Separate algorithms were developed for analytic studies, descriptive studies and literature reviews to help reviewers identify specific designs within those categories. The algorithm below, for example, helps reviewers determine which study design was used within the analytic study category (**Figure 1**). It is based on key decision points such as number of groups or allocation to group. The legends for the algorithms and supportive tools such as the glossary provide additional detail to further differentiate study designs, such as whether a cohort study was retrospective or prospective.

Figure 1: Algorithm for identifying the type of analytic study



Abbreviations: CBA, controlled before-after; ITS, interrupted time series; NRCT, non-randomized controlled trial; RCT, randomized controlled trial; UCBA, uncontrolled before-after

Separate critical appraisal tools were developed for analytic studies, for descriptive studies and for literature reviews, with relevant criteria in each tool. For example, a summary of the items covered in the analytic study critical appraisal tool is shown in **Table 1**. This tool is used to appraise trials, observational studies and laboratory-based experiments. A supportive tool for assessing statistical analysis was also provided that describes common statistical tests used in epidemiologic studies.

Table 1: Aspects appraised in analytic study critical appraisal tool

Aspect	Type of assessment
Sample and sampling methods	Representativeness of participants, control of selection bias
Internal validity	Control of biases: misclassification, information Validity and reliability of data collection instruments Adequacy of retention and follow-up
Control of confounding	Comparability of control and intervention groups Adequacy of control of major confounders
Ethics	Adequacy of ethical conduct
Analysis	Adequacy and interpretation of statistical testing Power and sample size
Screening and applicability questions	Generalizability of results Feasibility of implementation

The descriptive study critical appraisal tool assesses different aspects of sampling, data collection, statistical analysis, and

ethical conduct. It is used to appraise cross-sectional studies, outbreak investigations, case series and case reports.

The literature review critical appraisal tool assesses the methodology, results and applicability of narrative reviews, systematic reviews and meta-analyses.

After appraisal of individual items in each type of study, each critical appraisal tool also contains instructions for drawing a conclusion about the overall quality of the evidence from a study, based on the per-item appraisal. Quality is rated as high, medium or low. While a RCT is a strong study design and a survey is a weak design, it is possible to have a poor quality RCT or a high quality survey. As a result, the quality of evidence from a study is distinguished from the strength of a study design when assessing the quality of the overall body of evidence. A definition of some terms used to evaluate evidence in the CAT is shown in **Table 2.**

Table 2: Definition of terms used to evaluate evidence

Summative items assessed	Rating	Criteria
Strength of study design Note: "x > y" means x is a stronger design than y	Strong	Meta-analysis > Randomized controlled trial (RCT) > non-randomized controlled trial (NRCT) = lab experiment > controlled before-after (CBA)*
	Moderate	Cohort > case-control > interrupted time series with adequate data collection points > cohort with non-equivalent comparison group
	Weak	Uncontrolled before-after (UCBA) > interrupted time series with inadequate data collection points > descriptive (cross-sectional > epidemiologic link > ecologic or correlational)
Quality of the study	High	No major threats to internal validity (bias, chance and confounding have been adequately controlled and ruled out as an alternate explanation for the results)
	Medium	Minor threats to internal validity that do not seriously interfere with ability to draw a conclusion about the estimate of effect
	Low	Major threat(s) to internal validity that interfere(s) with ability to draw a conclusion about the estimate of effect
Number of studies	Multiple	Four or more studies
	Few	Three or fewer studies
Consistency of results	Consistent	Studies found similar results
Consistency of results (continued)	Inconsistent	Some variation in results but overall trend related to the effect is clear
	Contradictory	Varying results with no clear overall trend related to the effect
Directness of evidence	Direct evidence	Comes from studies that specifically researched the association of interest
	Extrapolation	Inference drawn from studies that researched a different but related key question or researched the same key question but under artificial conditions (e.g., some lab studies)

* Considered strong design if there are at least two control groups and two intervention groups. Considered moderate design if there is only one control and one intervention group

Tools for summarizing the evidence

The second phase in the critical appraisal process involves summarizing the results of the critical appraisal of individual studies. Reviewers are instructed to complete a template evidence summary table, with key details about each study and its ratings. Studies are listed in descending order of strength in the table. The table simplifies looking across all studies that make up the body of evidence informing a recommendation and allows for easy comparison of participants, sample size, methods, interventions, magnitude and consistency of results, outcome measures and individual study quality as determined by the critical appraisal. These evidence summary tables are reviewed by the working group to determine the rating for the quality of the overall body of evidence and to facilitate development of recommendations based on evidence.

Rating the quality of the overall body of evidence

The third phase in the critical appraisal process is rating the quality of the overall body of evidence. The overall rating depends on the five items summarized in Table 2: strength of study designs, quality of studies, number of studies, consistency of results and directness of the evidence. The various combinations of these factors lead to an overall rating of the strength of the body of evidence as strong, moderate or weak as summarized in **Table 3**.

A unique aspect of this toolkit is that recommendations are not graded but are formulated based on the graded body of evidence. Actions are either recommended or not recommended; it is the strength of the available evidence that varies, not the strength of the recommendation. The toolkit does highlight, however, the need to re-evaluate new evidence as it becomes available especially when recommendations are based on weak evidence.

Table 3: Criteria for rating evidence on which recommendations are based

Strength of Evidence	Grades	Criteria
Strong	AI	Direct evidence from meta-analysis or multiple strong design studies of high quality, with consistency of results
	AII	Direct evidence from multiple strong design studies of medium quality with consistency of results OR At least one strong design study with support from multiple moderate design studies of high quality, with consistency of results OR At least one strong design study of medium quality with support from extrapolation from multiple strong design studies of high quality, with consistency of results
Moderate	BI	Direct evidence from multiple moderate design studies of high quality with consistency of results OR Extrapolation from multiple strong design studies of high quality, with consistency of results
	BII	Direct evidence from any combination of strong or moderate design studies of high/medium quality, with a clear trend but some inconsistency of results OR Extrapolation from multiple strong design studies of medium quality or moderate design studies of high/medium quality, with consistency of results OR One strong design study with support from multiple weak design studies of high/medium quality with consistency of results
Weak	CI	Direct evidence from multiple weak design studies of high/medium quality, with consistency of results OR Extrapolation from any combination of strong/moderate design studies of high/medium quality, with inconsistency of results
	CII	Studies of low quality regardless of study design OR Contradictory results regardless of study design OR Case series/case reports OR Expert opinion

Pilot test of the CAT

Of 34 individuals who indicated an interest in completing the pilot test, 17 completed it. Multiple peer-reviewed studies were selected representing analytic studies, descriptive studies and literature reviews. The same studies were assigned to participants with similar content expertise. Each participant was asked to appraise three analytic studies, two descriptive studies and one literature review, using the appropriate critical appraisal tool as identified by the participant. For each study appraised, one critical appraisal tool and the associated tool-specific feedback form were completed. Each participant also completed a single general feedback form. A total of 101 of 102 critical appraisals were conducted and returned, with 81 tool-specific feedback forms and 14 general feedback forms returned.

The majority of participants (>85%) found the flow of each tool was logical and the length acceptable but noted they still had difficulty identifying the study designs (**Table 4**).

Table 4: Pilot test feedback on user friendliness

Items	Analytic Critical Appraisal Tool (%) n=39 of 51*	Descriptive Critical Appraisal Tool (%) n=28 of 34*	Literature review Critical Appraisal Tool (%) n=14 of 17*
Logical flow	89.7	96.4	100
Acceptable length	97.4	100	100
Clear phrasing and explanations	72.2	88.5	76.9
Tool was helpful for critical appraisal process	92.3	85.7	92.9

* Number of tool-specific forms returned for total number of critical appraisals conducted

The vast majority of the feedback forms (86–93%) indicated that the different tools facilitated the critical appraisal process. In the assessment of consistency, however, only four of ten analytic studies appraised (40%), had complete agreement on the rating of overall study quality by participants, the other six studies had differences noted as mismatches. Four of the six studies with mismatches were observational studies. The differences were minor. None of the mismatches included a study that was rated as both high and low quality by different participants. Based on the comments provided by participants, most mismatches could likely have been resolved through discussion with peers. Mismatched ratings were not an issue for the descriptive studies and literature reviews. In summary, the pilot test provided useful feedback on different aspects of the toolkit. Revision were made to address the issues identified from the pilot test and thus strengthen the CAT.

Discussion

The *Infection Prevention and Control Guidelines Critical Appraisal Tool Kit* was developed in response to the needs of infection control professionals reviewing literature that generally did not include clinical trial evidence. The toolkit was designed to meet the identified needs for training in critical appraisal with extensive instructions and dictionaries, and tools applicable to all three types of studies (analytic studies, descriptive studies and literature reviews). The toolkit provided a method to progress from assessing individual studies to summarizing and assessing the strength of a body of evidence and assigning a grade. Recommendations are then developed based on the graded

body of evidence. This grading system has been used by the Public Health Agency of Canada in the development of recent infection prevention and control guidelines (5,7). The toolkit has also been used for conducting critical appraisal for other purposes, such as addressing a practice problem and serving as an educational tool (8,9).

The CAT has a number of strengths. It is applicable to a wide variety of study designs. The criteria that are assessed allow for a comprehensive appraisal of individual studies and facilitates critical appraisal of a body of evidence. The dictionaries provide reviewers with a common language and criteria for discussion and decision making.

The CAT also has a number of limitations. The tools do not address all study designs (e.g., modelling studies) and the toolkit provides limited information on types of bias. Like the majority of critical appraisal tools (10,11), these tools have not been tested for validity and reliability. Nonetheless, the criteria assessed are those indicated as important in textbooks and in the literature (12,13). The grading scale used in this toolkit does not allow for comparison of evidence grading across organizations or internationally, but most reviewers do not need such comparability. It is more important that strong evidence be rated higher than weak evidence, and that reviewers provide rationales for their conclusions; the toolkit enables them to do so.

Overall, the pilot test reinforced that the CAT can help with critical appraisal training and can increase comfort levels for those with limited experience. Further evaluation of the toolkit could assess the effectiveness of revisions made and test its validity and reliability.

A frequent question regarding this toolkit is how it differs from GRADE as both distinguish stronger evidence from weaker evidence and use similar concepts and terminology. The main differences between GRADE and the CAT are presented in **Table 5**. Key differences include the focus of the CAT on rating the quality of individual studies, and the detailed instructions and supporting tools that assist those with limited experience in critical appraisal. When clinical trials and well controlled intervention studies are or become available, GRADE and related tools from Cochrane would be more appropriate (2,3). When descriptive studies are all that is available, the CAT is very useful.

Table 5: Features of the Critical Appraisal Toolkit (CAT) and GRADE

Feature	CAT	GRADE
Study designs addressed	Can be used for all types of studies (randomized and non-randomized controlled trials, other analytic studies including observational studies, descriptive studies and systematic reviews). Tools are provided for identifying study designs.	Focuses on the strongest types of evidence (randomized and non-randomized controlled trials; observational studies).
Type of reviewers	Individuals with less experience with research.	Individuals with more experience with research.
Assessment of individual studies	Tools are provided for the critical appraisal of individual studies and a quality rating given per study.	Each study is individually assessed, but no quality rating is provided per study.
Assessment of body of evidence	Overall body of evidence is graded based on criteria provided.	Overall body of evidence is graded on criteria provided.
Scoring and criteria	A qualitative assessment is made based on strength of study designs, the quality of studies, number of studies, consistency of results, and directness of the evidence. A grade is assigned based on the assessment.	A numeric score is calculated based on whether the evidence is randomized or non-randomized, risk of bias, inconsistency, indirectness, imprecision and publication bias. The score is translated to a grade.
Grade of evidence	Evidence is graded as strong, moderate or weak quality.	Evidence is graded as high, moderate, low or very low certainty.
Grade of recommendations	Recommendations are not graded, actions are either recommended or not.	Recommendations are graded as strong or weak/conditional.
Guidance for reviewers	Detailed criteria and explanations for use are provided in a single toolkit.	Detailed criteria and instructions provided in multiple documents and training available.

Abbreviation: GRADE, Grading of Recommendations Assessment, Development and Evaluation

Conclusion

The *Infection Prevention and Control Guidelines Critical Appraisal Tool Kit* was developed in response to needs for training in critical appraisal, assessing evidence from a wide variety of research designs, and a method for going from assessing individual studies to characterizing the strength of a body of evidence. Clinician researchers, policy makers and students can use these tools for critical appraisal of studies whether they are trying to develop policies, find a potential solution to a practice problem or critique an article for a journal club. The toolkit adds to the arsenal of critical appraisal tools currently available and is especially useful in assessing evidence from a wide variety of research designs.

Author's Statement

DM – Conceptualization, methodology, investigation, data collection and curation and writing – original draft, review and editing

TO – Conceptualization, methodology, investigation, data collection and curation and writing – original draft, review and editing

KD – Conceptualization, review and editing, supervision and project administration

Conflict of interest

None.

Contributor

Jennifer Kruse, Public Health Agency of Canada – Conceptualization and Project administration

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A reporting guide for Rapid Communications

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A Rapid Communication is a timely notification of a change in the nature or spread of an infectious disease. It is a "heads up" that something new is on the horizon that may have immediate implications. For example, in December 2013, the first local transmission of the mosquito-borne chikungunya virus was confirmed in several Caribbean islands. A month later, clinicians in Canada were advised to consider this possibility in patients presenting with fever and arthralgia who had a positive travel history from one of the affected islands (1). A year later, chikungunya virus had spread throughout the Caribbean and around the world and there was a documented spike in the number of travel-related cases of chikungunya virus in Canada (2). Soon after, a similar pattern of expansion occurred with Zika virus (3).

A Rapid Communication can be a preliminary outbreak report or an alert of a change in disease severity, risk factor(s), transmission patterns, reservoir, geographic spread or susceptibility to available therapies. It is a summary of what is currently known, the epidemiology (who is affected), how it is detected, what investigations are needed to establish the diagnosis and what clinical and public health measures are indicated to address it. The difference between a Rapid Communication and an Outbreak Report is that Outbreak Reports are generally written after an outbreak is over. Rapid Communications are written soon after an outbreak begins or a change in disease activity is identified. Reports of this nature can sometimes be published as a Brief Communication if the implications are not of an urgent nature.

The strength of a Rapid Communication—its advisory nature of alerting people to something new—is also its potential weakness, as some information may be lacking. If a new agent has been detected, information on incubation period, level of infectivity or even route of transmission may not be known. Early cases may not be representative of cases once the disease has spread. Therefore, in the assessment section of a Rapid Communication, what is known and what is not yet known needs to be well-summarized.

The *Canada Communicable Disease Report* (CCDR) has developed a 16-item checklist for reporting on Rapid Communications based on best practices in scientific communications (**Table 1**). Such reports are generally 1,000 to 1,500 words in length. As with all submissions, check CCDR's Information for Authors for general manuscript preparation and submission requirements (4).

Table 1: Checklist for reporting on Rapid Communications

Reporting item	Item #	Description
Title/Summary		
Title	1	Compose a title that includes the disease, population and/or place and time.
Summary	2	Develop a 150-word summary as an unstructured abstract.
Introduction		
Issue identification	3	Identify the issue: What has happened (context, events)? What makes this important to report on now?
Current situation		
Overview	4	Identify what is known to date: the setting, the date of onset and how and when it was identified.
Description of cases	5	Describe who has been affected, including presenting symptoms, demographic data (e.g., age, sex and where they were from) and any epidemiologic links among the cases—in a way that respects patient confidentiality.
Epidemiologic curve	6	Provide an epidemiologic curve (if indicated).
Extent of the disease	7	Describe the extent and severity of the disease and outcomes to date (e.g., number of hospitalizations and deaths).
Investigations	8	Identify how the outbreak was investigated, including the laboratory tests that were conducted to identify the causative agent and the sample site(s).
Causative agent	9	Describe and summarize what is known to date on this agent.
Interventions	10	Describe the clinical measures that were put in place to treat and manage affected patients (e.g., infection prevention and control procedures and treatments).
	11	Describe the public health measures that were put in place to control the outbreak (e.g., case definition, contact tracing, risk management, communications, etc.).

Table 1: Checklist for reporting on Rapid Communications (continued)

Reporting item	Item #	Description
Conclusion		
Assessment	12	Summarize what is known and identify what is not yet known (e.g., route of transmission, disease reservoir, estimated incubation period, risk factors and effectiveness of treatment).
	13	Consider any relevant reference to previous or similar events.
Implications	14	Consider the implications of the outbreak for clinical practice, including any recommendations for case identification and management, infection control and reporting. Identify any sex or gender implications.
	15	Consider the implications for public health practice, including any recommendations for surveillance, prevention, risk management and communications.
Conclusion	16	Provide a wrap-up summary of what is known to date and the direction of future efforts to understand and control the disease.

Abbreviation: #, number

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A reporting guide for Surveys

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Surveys are useful to describe "what is". They are used in health and public health research to learn about current opinions, knowledge and practice, to estimate the prevalence of a condition, to assess self-reported health status, to document risk-seeking and health-seeking behaviours and to gather preliminary information for future studies (1). Survey methods have changed from being paper-based to being largely electronic-mediated. Most surveys are now self-administered and completed online, by email, with apps or a combination of these (such as an email invitation with a link to an online questionnaire). A Cochrane review found that survey results from apps may have data equivalence to those obtained by more traditional methods when the setting, frequency and clinical application, in which the survey instrument was validated, remain the same (2).

Survey research is used for exploratory or descriptive research as it is relatively inexpensive, can cover a broad geographical area, includes thousands of people and allows for greater honesty when anonymity is assured. Surveys are not useful for causal research due to the risk of confounding bias (where an observed association between two variables is due to an association of both variables with an unmeasured third variable).

Usually surveys do not require a formal ethics review. Informed consent is still indicated, however, and can be met by identifying who is conducting the survey, the purpose, how long it will take to complete, any incentives and how personal information will be protected. For web-based surveys it is a best practice to calculate participation rate by measuring the number of unique visitors who filled out the first page of the survey, divided by the number of unique site visitors (3).

When reporting on survey research it is important to describe the objective, study population, development of the survey instrument and how the study was conducted, including the sampling strategy. The results need to include the response rate and the discussion needs to consider if and how the response rate, selection bias, positive response bias and threats to the reliability and validity of the survey questions may have influenced the results.

The *Canada Communicable Disease Report* (CCDR) has developed a 22-item checklist for reporting on surveys in the area of infectious diseases, which is based on the Checklist for Reporting Results of Internet E-Surveys (CHERRIES) (3), a previous checklist (4) as well as best practices in scientific communications (**Table 1**). A survey report is generally 1,500 to 2,000 words in length. As with all submissions, check CCDR's *Information for Authors* for general manuscript preparation and submission requirements (5).

Table 1: Checklist for reporting on surveys

Reporting item	Item #	Description
Title/Abstract		
Title	1	Compose a title that identifies the topic of the survey and the population studied.
Abstract	2	Provide a 250-word structured abstract that includes the objective, methodology (including study setting, population and questionnaire development and administration), results (including the response rate and key findings) and conclusion.
Introduction		
Issue identification	3	Identify the topic of the study and why it is important.
Rationale for study	4	Cite the relevant literature and identify how this survey will add to what is already known.
Objective and rationale	5	Clearly articulate the objective of the study and explain why the survey was the appropriate method to address it.
Methods		
Population, time and place	6	Describe the setting and study population for the survey, including the dates it was undertaken. Note if it was a convenience sample.
Correlation with the research objective	7	Demonstrate how the research questions addressed the research objective by identifying the different topics covered in the questionnaire.
Development of the survey instrument	8	Describe how the survey questionnaire was developed, including reliability and validity testing, pre-testing and pilot testing.
Sampling technique	9	Unless the entire study population was surveyed, identify how the sampling was done, including any inclusion or exclusion criteria (to establish the representativeness of your sample) and how the survey was sent (via email, internet, etc.).
Informed consent	10	Describe how potential participants were informed about who was conducting the survey, its purpose or objective, how long it would take to complete, any incentives and how personal information would be protected.

Table 1: Checklist for reporting on surveys (continued)

Reporting item	Item #	Description
Methods (continued)		
Optimization of response rate	11	Note what procedures were done to optimize the response rate (e.g., if an explanatory letter was sent beforehand, or if reminders were sent to non-responders).
Measurement	12	Describe all the measurements used in the study, including characterization of the study population, outcome measures and the potential confounding factors.
Analysis	13	Describe how the sample size was calculated and any statistical analysis that was undertaken.
Results		
Response rate and representativeness of sample	14	Present the number of responses, the response rate and, if possible, compare the characteristics of your sample with what you know about the study population (e.g., a physician survey might include age, sex, years in practice and location).
Presentation of results	15	Present the findings from the different topic areas in the same sequence that the topics were described in the Methods.
Tables and figures	16	Have tables and figures that present the key findings and ensure all participants are accounted for.
Discussion		
Summary of key findings	17	Summarize the main findings and indicate how these address the objective of the study. Highlight any statistically significant results of clinical or social relevance.
Comparative analysis	18	Explore how these findings were consistent with or different from other studies on a similar topic in the literature.
Strengths and limitations	19	Identify the strengths and limitations of your study. If the respondents were not representative of the total sample, or the sample was not representative of the population of interest, consider the implications of this. Consider if and how potential bias has been avoided or remains.
Implications	20	Consider the "so what?" of your findings in terms of how it adds to scientific knowledge, policy or practice.
Next steps	21	Propose next steps or further areas for inquiry without extrapolating too far from your findings.
Conclusion	22	Ensure the conclusion integrates the key findings and addresses the objective of the survey.

Abbreviation: #, number

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Salmonella Thompson outbreak associated with consumption of chicken shawarma and the usefulness of genome sequencing in the investigation

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Abstract

Background: A sudden increase in *Salmonella* Thompson (*S.* Thompson) cases distributed throughout three border regions in the province of Quebec in November 2016 triggered a provincial investigation to identify a common source of contamination and to put the appropriate control measures into place.

Objective: To report on the outbreak and to describe the use of genomic sequencing to identify the salmonella serotype responsible.

Methods: A descriptive survey of all reported cases of *Salmonella* serogroup C1 that had occurred between October 1, 2016 and February 15, 2017 was conducted. A case definition was developed. Pulsed field gel electrophoresis supplemented by analyses of genome sequences using the single nucleotide variant phylogenomics method were used to demarcate and manage the outbreak.

Results: Eighteen cases of *S.* Thompson were identified through whole genome sequencing. The onset dates of symptoms for the 16 cases that presented enteric symptoms were November 21—December 2, 2016. Two cases that presented with atypical symptoms were not reported until February 2017. Among the 18 cases, 16 had eaten or probably eaten chicken shawarma at the same restaurant chain and nine of these cases ate it at the same restaurant. In total, five restaurants from this chain, spread throughout three border regions of Quebec, were identified.

Conclusion: Outbreaks associated with chicken shawarma have been identified in the past. Efforts must be made to ensure that the owners of this type of restaurant know the contamination risk associated with this type of cooking and take the necessary steps to reduce this risk. The use of the genome sequencing method was very useful in defining the outbreak.

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Introduction

Salmonella Thompson (*S.* Thompson) is a salmonella serotype belonging to serogroup C1, which occurs sporadically year-round. Since 2012, an average of 60 to 70 cases are reported annually in the province of Quebec, corresponding to between three and six cases a month, according to data from the mandatory reportable disease system (Maladies à Déclaration Obligatoire, MADO); however, in November 2016 alone, 12 cases of *S.* Thompson were reported to the Quebec public health agencies (Direction de la Santé Publique, DSPublique).

Details of outbreaks associated with *S.* Thompson have been published previously (1-4). One outbreak which occurred in 2012 involved 1,149 confirmed cases in the Netherlands, which was attributed to the consumption of smoked salmon (1). Other studies have identified various vehicles: bread, possibly contaminated by a food handler (2); fresh cilantro (3); and rucola grown in Italy (4). In Canada, two national outbreaks have been investigated. The first outbreak occurred in 2012 with 105 cases, 29 of which were in Quebec, and the source was not identified. The second outbreak occurred in 2014 with 59 confirmed cases,

16 of which were in Quebec, and the most likely source of contamination was chicken (*unpublished data*).

On December 2, 2016, DSPublique of Montréal notified the Bureau de surveillance et de vigie (BSV) of the Ministère de la Santé et des Services sociaux (MSSS) of a time-place cluster of five cases of *Salmonella* serogroup C1 detected in a group of persons aged 13 to 19 years. The suspected source of contamination was a fast food restaurant chain serving chicken shawarma (*shish taouk*). The serotyping of the initial cases enabled detection of the Thompson serotype. On December 15, 2016, after cases appeared in other regions of Quebec surrounding Montréal, the BSV launched and coordinated a provincial investigation. The objective of the investigation was to identify the source of the outbreak and adopt the appropriate control measures.

Methods

Case reporting

In Quebec, salmonellosis is a mandatory reportable disease (MADO). Infections detected by hospital laboratories are reported to regional DSPublique agencies. Isolates are then sent to the Laboratoire de santé publique du Québec (LSPQ) for detailed characterization. Outbreaks and clusters are surveyed by regional DSPublique agencies.

Outbreak detection

The Montréal DSPublique conducts a daily watch of MADOs in its territory. SaTScanTM (version 9.4.2) statistical analysis software is used to detect time and time-place clusters. Clusters of enteric diseases are surveyed based on certain criteria, including the number of cases, the density of the cluster, demographic factors with an unusual distribution and the specificity of the pathogen.

A time-place cluster (spatio-temporal permutation method) of eight cases of salmonellosis was detected on December 2, 2016. Among these cases, five were serogroup C1, one was serogroup D and two are pending identification of the serogroup. Excluding the serogroup D case, the seven remaining salmonellosis cases were considered part of a potential cluster, which included four youths aged 13 to 19 years, who were prioritized for surveying as a common event was suspected. After identifying a restaurant chain as a probable common source for the outbreak, the survey was expanded to other age groups. Subsequent surveys reinforced the suspicion of a common source and the presence of an outbreak.

Epidemiological surveys

The regional survey forms were used prior to launching the provincial survey. The BSV, which coordinates the investigation of provincial outbreaks, asked the DSPublique to survey all cases of *Salmonella* serogroup C1 using a hypothesis-generating food survey form, prior to obtaining the serotype in order to reduce survey time.

The information gathered on the survey forms was demographic, clinical and dietary food (consumption in the home or at restaurants in the three days prior to the onset of symptoms, etc.). Once completed, the questionnaires were numbered and sent to the BSV and the Ministère de l'Agriculture, des Pêcheries et de l'Alimentation du Québec (MAPAQ). Data analysis was descriptive in nature. Data were compiled and analyzed using the EXCEL (Microsoft Office 2010) program. The surveys were conducted between December 15, 2016 and February 15, 2017.

Laboratory analyses

Salmonella serogroup C1 strains from the regional laboratories were serotyped at LSPQ. Pulsed field gel electrophoresis (PFGE) was performed at the LSPQ on several *S.* Thompson isolates received in November and December 2016.

In addition, as *S.* Thompson behaves in a very clonal manner, whole genome sequencing was used at the LSPQ on *S.* Thompson isolates with sampling dates between September 22, 2016 and February 3, 2017. A phylogenetic tree, constructed using the maximum likelihood method with the single nucleotide variant phylogenomics (SNVPhyl) pipeline, served to determine the level of proximity of isolates, based on position and the number of robust single nucleotide polymorphisms (SNP) of genomes, allowing identification of the strains that caused the outbreak.

A case definition was developed: a case was confirmed for a resident of, or a visitor to, Quebec who had a *S.* Thompson infection, whose onset of symptoms or sampling date was on or after October 1, 2016 and whose whole genome sequence was identical or similar (one nucleotide variation). This was designated ST7.

Food safety investigation

The MAPAQ proceeded to conduct a food safety investigation at the targeted establishments in collaboration with its representatives the City of Montréal's food inspection division (Division de l'inspection des aliments, DIA) and the Canadian Food Inspection Agency.

Follow up interviews conducted with regard to cases and interventions (in-person and by telephone) took place at the restaurants where the cases had been exposed, from the Montréal, Lanaudière and Montérégie regions, as well as at the central kitchen that supplies these restaurants. At the central kitchen, the Canadian Food Inspection Agency acted as an intermediary of the MAPAQ for the survey.

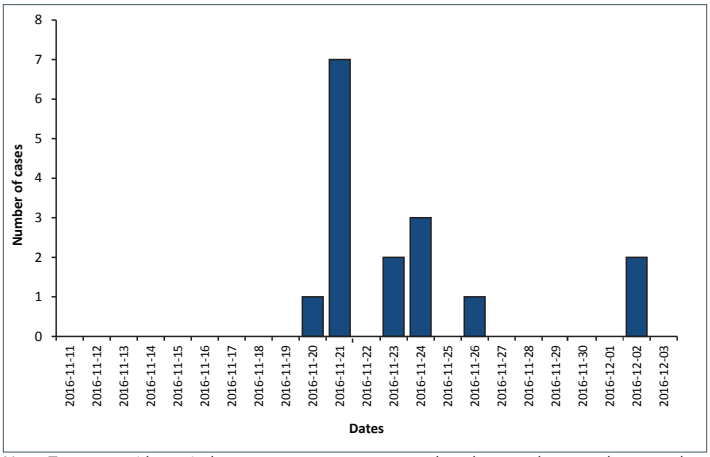
During interventions at each of the restaurants, an evaluation of critical control points was conducted to determine, among other things, whether the cooking method used for the preparation of chicken shawarma allowed a safe cooking temperature to be reached and to check cross contamination risks, storage temperature and the source of the food. During interventions at the central kitchen, a check was made of, among other things, the source of the targeted foods and the method of preparation of marinated chicken, and the restaurants that had received the batches of the chicken in question were identified. Food samples were taken at some of the chain's restaurants and at the central kitchen. These samples came from different batches than those consumed by the cases, as the batches distributed during the outbreak period were no longer available.

Results

Descriptive epidemiology

In total, 18 cases were associated with the outbreak, all corresponding to the confirmed case definition. The cases resided in the regions of Montréal (thirteen, all in the same area), Montérégie (three) and Lanaudière (two). Sixteen cases had enteric symptoms (**Figure 1**). The symptom onset dates were between November 21 and December 2, 2016. Two cases, not reported until February 2017, were found to be associated with the outbreak following laboratory results confirming the presence of the outbreak strain in a hemoculture following osteomyelitis and sampling from an anal abscess.

Figure 1: Epidemic curve according to the date of onset of enteric symptoms, for the outbreak of *Salmonella* Thompson pulsovar 1 in the Province of Quebec, November-December 2016



Note: Two cases with atypical symptoms are not represented on the curve because the onset date of symptoms could not be clearly established (n=16). The *S.* Thompson pulsovar 1 was designated ST7 by whole genome sequencing method

Demographic data were available for all cases. The median age of cases was 25 years and the average was 27.8 years (range: less than one year to 69 years). The male-female ratio was 2:1. Six cases were hospitalized. No deaths were associated with the outbreak.

Food exposure

In the survey, 13 out of the 16 cases that presented with enteric symptoms reported having eaten chicken shawarma type food at restaurants associated with the same fast food chain during their exposure period, all within the last two weeks of November 2016. Nine cases ate at the same restaurant. A fourteenth case (out of the 16 cases) reported having consumed chicken shawarma regularly at one of the restaurants of this chain within that period, but was not able to specify the date.

The two cases reported in February 2017 did not present enteric symptoms. It was, therefore, difficult to determine an exact date of the onset of symptoms and establish an exposure period. These two cases reported that they probably consumed shawarma around the end of November at one of the restaurants identified in the outbreak because they ate there regularly.

Sixteen out of 18 cases reported either having eaten shawarma at the same restaurant chain in the three days prior to the onset of their illness or probably having eaten it at the restaurant chain because they ate there regularly. Three restaurants of the chain visited are located in Montréal and two restaurants are in neighbouring regions.

Of the two cases that did not frequent these restaurants, one had eaten chicken at an Asian restaurant and the other had purchased bagged raw turkey at a supermarket.

Laboratory analyses

The *S.* Thompson isolates analyzed by PFGE that were sampled in November or December 2016 were all pulsovar 1 (Quebec name) and STHXAI.0002/STHBNI.0015 (Canadian name). This pulsovar is common for *S.* Thompson in Quebec. Indeed, out of 440 strains of *S.* Thompson typed by EGCP at the LSPQ since 2002, 383 strains were pulsovar 1 (87%).

Genome sequencing was used to better distinguish between strains and to define the outbreak. Among the 25 isolates of *S.* Thompson sampled between September 22, 2016 and February 4, 2017, that were analyzed at the LSPQ using the SNVPhyl method, 18 had an identical genome sequence (designated ST7), which was the outbreak strain. The sampling dates for the 16 cases with enteric symptoms were between November 22 and December 15, 2016. The two cases with the less common clinical manifestations (osteomyelitis and anal abscess) were sampled on January 29 and February 3, 2017.

The 18 strains of the sequence type designated ST7 had either no nucleotide variation or only one nucleotide variation between them, which constitutes a strong genomic similarity (based on the SNVPhyl method). This cluster of strains is distinct from other strains of *S.* Thompson sequenced during the same period, with between three and 771 SNP variations. The strain with 771 SNP is a strain of *S.* Thompson acquired on a trip, according to data from the public health branch in the region where the case originated.

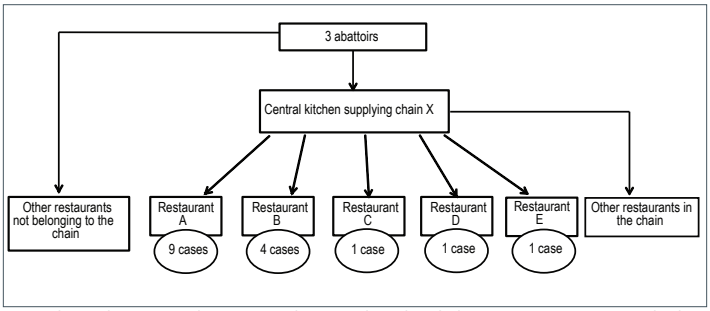
Food safety investigation

During inspections by Montréal's DIA and the MAPAQ, shortcomings were observed in the target establishments, including storage temperatures, cleaning and sanitation, and risks of cross contamination.

The restaurant chain in question is supplied by a central kitchen that distributes, among other things, raw marinated chicken to its affiliated restaurants. The central kitchen is supplied by three Quebec abattoirs. The batches of chicken targeted by this survey were slaughtered at these three abattoirs on November 7 and 8, 2016. They would have been marinated on November 10 and 14 at the central kitchen and sent out to the various restaurants in the chain between November 17 and 21, 2016. Several restaurants associated with Chain X, other than those targeted by the surveys and located in the Montréal, Montérégie, Laval and Lanaudière regions, would also have received the batches of chicken involved in the outbreak. According to the food safety surveys, approximately forty restaurants, including Chain X, received the batches of the chicken in question.

DIA inspection of an Asian restaurant, where food was consumed by a person who later exhibited symptoms of infection by *S.* Thompson belonging to the same strain identified in the outbreak, determined that the chicken supply for the restaurant came from two of the three abattoirs involved (**Figure 2**).

Figure 2: Distribution of *Salmonella* Thompson ST7 cases, according to the place of consumption, Quebec 2016



Note: The S. Thompson pulsovar 1 was designated ST7 by whole genome sequencing method

A total of 33 food samples were taken at the restaurants identified and at the central kitchen. No strains of *S.* Thompson were isolated. One of the samples from the Asian restaurant was found to be positive for *S. enteritidis*. A summary of the samples taken and the results of microbiological analysis are presented in **Table 1**.

Table 1: Sampling sites and foods sampled and analysed for *Salmonella* Thompson outbreak, Province of Quebec, 2016*

Sampling site	Foods sampled (# samples)	# Samples	Results of analyses for *Salmonella* Thompson
Central kitchen (supplier of marinated chicken to affiliated restaurants)	Raw chicken from Abattoir "1" (2x) Raw chicken from Abattoir "2" (2x) Raw marinated chicken (2x)	6	Absent
Restaurant 1	Salad RTE mashed potato Cooked rice Cooked chicken Garlic sauce with mayonnaise Hummus	6	Absent
Restaurant 2	Salad RTE mashed potato Cooked rice Cooked chicken Garlic sauce with mayonnaise House vinaigrette	6	Absent
Restaurant 3	RTE lettuce (3x) RTE tomato Tahini Garlic sauce Hummus RTE turnip Cooked chicken (2x) Raw marinated chicken	11	Absent
Supplier (Asian restaurant)	Raw chicken	4	3 Absent 1 sample positive for *Salmonella enteritidis*

Abbreviations: RET, ready-to-eat; #, number
* The *S.* Thompson pulsovar 1 was designated ST7 by whole genome sequencing method

Discussion

In November 2016, the sudden increase in the number of reports of *S.* Thompson and their location in the same area of the Montréal region suggested a common source of contamination. The outbreak was delimited in time and space, all of the cases having occurred in three neighbouring regions. Chicken cooked in the shawarma style (*shish taouk*) was the common food eaten or probably eaten in the majority of these cases. Chicken shawarma is a specialty food that originates in the Middle East and is prepared by placing marinated meat (chicken, beef or lamb) on a spit to form a cone shape that is roasted in front of a grill. The meat around it is sliced off as needed and served in pita bread or with rice and condiments. This cooking method can lead to insufficient cooking, especially with chicken (5).

The restaurant chain identified in the survey was supplied by a central kitchen, which is itself supplied by three abattoirs in Quebec. It is therefore possible that one batch of chicken from one or more of these three abattoirs could have been contaminated by *S.* Thompson and distributed over the course of this period throughout this restaurant chain. According to the food safety surveys, about 40 restaurants received the batches of chicken in question; however, only five restaurants were implicated. Shortcomings were observed in the targeted restaurants during the food inspection.

Animals destined for food, including bird species, naturally carry pathogens in their intestinal tract that can contaminate raw meat products during slaughter and processing (6). In Canada, a recent study conducted from December 2012 to December 2013 demonstrated that the national prevalence of salmonella in batches of broiler chickens sampled at the abattoir was as high as 25.6%. Batches from chickens raised in the eastern provinces were more frequently tainted by salmonella. In processed products, which are whole chicken carcasses and parts of carcasses processed in establishments authorized by the federal government, the prevalence of salmonella reached 16.9% (whole

chickens) and 29.6% (parts) (6). Similarly, samples of raw chicken products were taken from supermarket chains, butcher shops and independent grocers in 33 large cities in Canada. The prevalence of salmonella was found to be 21% (whole chickens) and 31.6% (parts) (6).

In the United States, limits of acceptability with regard to the percentage of chicken contaminated by salmonella were established by the food inspection agencies in 1996 (7). The percentage of broiler chicken contaminated by salmonella at the abattoir can reach a maximum of 20%. The performance standard is recognized under the Hazard Analysis and Critical Control Points (HACCP) system (8). Between 10 and 19% of abattoirs in the United States have been found to exceed this limit and this percentage is higher for small abattoirs (9-12).

Several salmonella serotypes can be found in chicken and *S.* Thompson is part of the group of 12 salmonella serotypes most often found in raw chicken (13,14).

Although meat-producing chicken is expected to be contaminated by salmonella, adequate cooking should render it inactive. This investigation suggests that the cooking method for making shawarma may represent a risk. Several outbreaks have been associated with this method of preparation (15-18). With this method of cooking, the raw meat may be in contact with the cooked meat. When a restaurant is busy, it is possible that cooking times may not be adhered to and the meat served may contain parts that are undercooked. To prevent cross contamination or undercooking, restaurants of this type sometimes cook the meat a second time before serving it to customers. Cross contamination may also have occurred in the handling of the raw chicken.

Although the foods sampled did not demonstrate the presence of *S.* Thompson, the survey strongly suggests a link between the illness occurring and the consumption of chicken shawarma at these restaurants. The time between the onset of symptoms and the reporting of cases to public health authorities is around 10 to 14 days; thus, the chicken sampled at the central kitchen and in the restaurants did not come from the batch delivered and consumed during the cases' exposure period. This delay is inherent to food outbreak investigations and may explain the negative results.

The isolates were sent to the LSPQ for PFGE to assess their degree of similarity; however, this bacterium shows little diversity and the PFGE pattern 1 is often identified in *S.* Thompson. Whole genome sequencing was needed to establish the genetic similarity between isolates and allow the outbreak to be delimited. Strains implicated in the outbreak were identical or had only a single nucleotide variation. The other strains of *S.* Thompson analyzed had three or more nucleotide variations and the epidemiological information available regarding the cases with these exposures was different. Genome sequencing has proven to be effective in several outbreaks (19-23). The use of the whole genome sequencing technique provides additional powers of discrimination, beyond serotyping and PFGE, to delimit and investigate an outbreak (20-25). The results of genome sequencing must be interpreted based on available epidemiological information. This report represents one of the first Canadian outbreaks of salmonella to use whole genome sequencing in the case definition.

A survey reports only laboratory-confirmed cases, and it is likely that other people were affected but did not consult a physician or fecal cultures were not obtained. In the mandatory reportable disease system, only a fraction of actual cases are reported, which could explain why only five restaurants in the chain were identified even though the chicken from the same batch was distributed to more than 40 restaurants. Chicken was identified as the probable source of contamination as it is the food that is most likely to have been contaminated with *S.* Thompson.

In conclusion, we have documented an outbreak of salmonella associated with the consumption of shawarma meals in a series of restaurants. Other outbreaks associated with this type of product have been identified in the past and Health Canada has issued recommendations to prevent future outbreaks of enteric illnesses associated with the preparation of shawarma (5). Additional efforts may assist owners of this type of restaurant to become more aware of the contamination risk associated with this method of cooking and take the necessary steps to reduce the risk. If an outbreak does occur, genome sequencing has proven to be an important tool for defining the outbreak.

Authors' statement

All of the authors (CG, MF, CD, DR, NS, AU, PAP, VU, SB) participate in enteric disease monitoring. CG, DR and SB prepared the first draft and all of the other authors contributed to the final version by adding comments and suggestions.

Conflicts of interest

None.

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Concurrent infection increases mortality from other illnesses

1. Source: Marrie TJ, Tyrrell GJ, Majumdar SR, Eurich DT. **Concurrent Infection with Hepatitis C Virus and *Streptococcus pneumoniae***. Emerg Infect Dis. 2017 Jul;23(7):1118-1123. http://dx.doi.org/10.3201/eid2307.161858.

Little is known about concurrent infection with hepatitis C virus (HCV) and *Streptococcus pneumoniae*, which causes invasive pneumococcal disease (IPD). We hypothesized that co-infection with HCV and *S. pneumoniae* would increase risk for death and complications. We captured sociodemographic and serologic data for adults with IPD in a population-based cohort study in northern Alberta, Canada, during 2000-2014. IPD patients infected with HCV were compared with IPD patients not infected with HCV for risk of in-hospital deaths and complications by using multivariable logistic regression. A total of 355 of 3,251 patients with IPD were co-infected with HCV. The inhospital mortality rate was higher for IPD patients infected with HCV. Prevalence of most IPD-related complications (e.g., cellulitis, acute kidney injury, mechanical ventilation) was also higher in HCV-infected patients. Infection with HCV is common in patients with IPD, and HCV is independently associated with an increased risk for serious illness and death.

2. Source: Delgado A, Reveles IA, Cabello FT, Reveles KR. **Poorer outcomes among cancer patients diagnosed with *Clostridium difficile* infections in United States community hospitals**. BMC Infect Dis. 2017 Jun 23;17(1):448. http://dx.doi.org/10.1186/s12879-017-2553-z.

BACKGROUND: Cancer predisposes patients to *Clostridium difficile* infection (CDI) due to health care exposures and medications that disrupt the gut microbiota or reduce immune response. Despite this association, the national rate of CDI among cancer patients is unknown. Furthermore, it is unclear how CDI affects clinical outcomes in cancer. The objective of this study was to describe CDI incidence and health outcomes nationally among cancer patients in the United States (U.S.).

METHODS: Data for this study were obtained from the U.S. National Hospital Discharge Surveys from 2001 to 2010. Eligible patients included those at least 18 years old with a discharge diagnosis of cancer (ICD-9-CM codes 140-165.X, 170-176.X, 179-189.X, 190-209.XX). CDI was identified using ICD-9-CM code 008.45. Data weights were applied to sampled patients to provide national estimates. CDI incidence was calculated as CDI discharges per 1000 total cancer discharges. The in-hospital mortality rate and hospital length of stay (LOS) were compared between cancer patients with and without CDI using bivariable analyses.

RESULTS: A total of 30,244,426 cancer discharges were included for analysis. The overall incidence of CDI was 8.6 per 1000 cancer discharges. CDI incidence increased over the study period, peaking in 2008 (17.2 per 1000 cancer discharges). Compared to patients without CDI, patients with CDI had significantly higher mortality (9.4% vs. 7.5%, $p < 0.0001$) and longer median LOS (9 days vs. 4 days, $p < 0.0001$).

CONCLUSIONS: CDI incidence is increasing nationally among cancer patients admitted to U.S. community hospitals. CDI was associated with significantly increased mortality and hospital LOS.

Breast milk and microbes

Source: Pannaraj PS, Li F, Cerini C, Bender JM, Yang S, Rollie A, Adisetiyo H, Zabih S, Lincez PJ, Bittinger K, Bailey A, Bushman FD, Sleasman JW, Aldrovandi GM. **Association Between Breast Milk Bacterial Communities and Establishment and Development of the Infant Gut Microbiome**. JAMA Pediatr. 2017 May 8. http://dx.doi.org/10.1001/jamapediatrics.2017.0378. [Epub ahead of print]

IMPORTANCE: Establishment of the infant microbiome has lifelong implications on health and immunity. Gut microbiota of breastfed compared with nonbreastfed individuals differ during infancy as well as into adulthood. Breast milk contains a diverse population of bacteria, but little is known about the vertical transfer of bacteria from mother to infant by breastfeeding.

OBJECTIVE: To determine the association between the maternal breast milk and areolar skin and infant gut bacterial communities.

DESIGN, SETTING, AND PARTICIPANTS: In a prospective, longitudinal study, bacterial composition was identified with sequencing of the 16S ribosomal RNA gene in breast milk, areolar skin, and infant stool samples of 107 healthy mother-infant pairs. The study was conducted in Los Angeles, California, and St Petersburg, Florida, between January 1, 2010, and February 28, 2015.

EXPOSURES: Amount and duration of daily breastfeeding and timing of solid food introduction.

MAIN OUTCOMES AND MEASURES: Bacterial composition in maternal breast milk, areolar skin, and infant stool by sequencing of the 16S ribosomal RNA gene.

RESULTS: In the 107 healthy mother and infant pairs (median age at the time of specimen collection, 40 days; range, 1-331 days), 52 (43.0%) of the infants were male. Bacterial communities were distinct in milk, areolar skin, and stool, differing in both composition and diversity. The infant gut microbial communities were more closely related to an infant's mother's milk and skin compared with a random mother (mean difference in Bray-Curtis distances, 0.012 and 0.014, respectively; $P < .001$ for both). Source tracking analysis was used to estimate the contribution of the breast milk and areolar skin microbiomes to the infant gut microbiome. During the first 30 days of life, infants who breastfed to obtain 75% or more of their daily milk intake received a mean (SD) of 27.7% (15.2%) of the bacteria from breast milk and 10.3% (6.0%) from areolar skin. Bacterial diversity (Faith phylogenetic diversity, $P = .003$) and composition changes were associated with the proportion of daily breast milk intake in a dose-dependent manner, even after the introduction of solid foods.

CONCLUSIONS AND RELEVANCE: The results of this study indicate that bacteria in mother's breast milk seed the infant gut, underscoring the importance of breastfeeding in the development of the infant gut microbiome.

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