Understanding antimicrobial resistance using a complex adaptive systems approach

Abstract
Antimicrobial resistance (AMR) is a complex and growing public health issue with many diverse contributing factors. The main goal of this study was to create a visual model of AMR in Canada, showing the different parts of the system and reflecting the different types of individuals and factors playing a role. To ensure that the model builds on and advances current models of AMR, we engaged with people who represented diverse viewpoints not traditionally considered when discussing the issue of AMR. Over a series of four face-to-face meetings and several key informant interviews, the project objectives were to describe (a) how the actions of different people and organisations can relate to AMR, (b) factors that affect antimicrobial use (AMU), (c) key drivers of AMU and AMR, and (d) ways that diverse groups and organisations might work together for long-term reduction in AMR.

An initial model of the AMR system was developed to serve as a starting point for discussion at the first face-to-face meeting. Evolution of the model was intentionally iterative; input from participants at each meeting and set of interviews was used to revise and refine the model.

Data collected from the meetings and interviews have been used to expand the original model through the identification of new variables, connections between variables, and leverage points, or the identification of overarching concepts spanning many variables. The project is ongoing and continues until March 2017. This paper reports on data collected up until September 2016.

Keywords: antimicrobial use, antimicrobial resistance, complex adaptive system, qualitative research

Introduction
Complex adaptive systems are open systems that constantly adapt and reorganise to deal with changing environmental conditions (1,2). These systems are made up of individual agents that act independently and in ways that may not be predictable; but they are interconnected so that when one agent changes it can affect how other agents in the system behave (3).

Antimicrobial resistance (AMR) is a complex and growing public health issue that threatens the health of people and animals around the world through increased morbidity, mortality and associated negative economic impacts. A complex adaptive systems approach offers a framework to advance traditional methods of describing AMR and analysing AMR data, towards a more systemic approach that considers the dynamic relationships between the sub-systems, the environment, and all of their various components. Understanding the underlying factors that are influencing the overall AMR system will better identify actions most likely to succeed in reducing antimicrobial use (AMU) and ultimately the burden of illness posed by resistant infections.

There is growing recognition that stronger interdisciplinary collaboration is needed to develop sustainable and effective solutions to today’s complex public health challenges (4), of which AMR is one. The term ‘One Health’ has been used to describe an approach to complex health problems that recognises the important interconnections between human, animal and environmental health and the critical interdisciplinary collaborations and shared communications needed to understand the web of connections (5).

Grounded in a ‘One Health’ paradigm, and using a complex adaptive systems approach, the main goal of this study was to create a visual model of AMR in Canada, showing the different parts of the system, and reflecting the different types of individuals and factors playing a role. To ensure that the model builds on and advances current understanding of AMR, we engaged with people who represented diverse viewpoints not traditionally considered when discussing the issue of AMR. Over a series of four face-to-face meetings and (up to 20) key informant interviews, the objectives were to describe (a) how the actions of different people and organisations can relate to AMR, (b) factors that affect AMU, (c) key drivers of AMU and AMR, and (d) ways that diverse groups and organisations might work together for long-term reduction in AMR. This knowledge will enable us to recognise key gaps in our understanding of AMR and help prioritise future research and surveillance activities. Furthermore, the results of this study can help ensure that AMR research and surveillance data are interpreted in context and that the potential impacts of interventions and AMR mitigation strategies are carefully considered before they are implemented.

The project is ongoing and continues until March 2017. This paper reports on preliminary data collected up until September 2016.
Methods
Information was gathered from study participants through face-to-face meetings and key informant interviews and incorporated into a complex adaptive model for AMR. This study received ethics clearance through Health Canada and the Public Health Agency of Canada’s Research Ethics Board [REB #2015-0019] and a University of Waterloo Research Ethics Committee [ORE #21148].

Participant selection and recruitment
To ensure that the study model builds on and advances conventional models of AMR, “traditional” experts on AMR and AMU, such as veterinarians, physicians and epidemiologists employed by the Canadian federal government, were excluded from this study. A matrix of people from diverse biological, social and policy backgrounds and from different sectors and disciplines was developed from which individuals were invited to take part in the study. The matrix was populated with individuals identified through web-based search engines (e.g. Google), professional networking sites (e.g. LinkedIn), websites for professional organisations (e.g. Canadian Institute of Planners), and social media sites (e.g. Twitter). Contact information was only obtained from publicly available information sources (e.g. websites, online directories).

For each meeting, a form of purposive sampling called maximum variation sampling (6) was used to select a group of potential participants representing different sectors and disciplines, age groups, genders, and geographic locations across Canada. Prior to each meeting, the research group determined the types of perspectives they would like represented (e.g. dentistry, aquaculture, food security). Potential participants representing these different perspectives were selected from the matrix and invited to participate in the study by email. If a response was not received within one week, a reminder email was sent. If no response was received within a week of the reminder email, or if a possible participant declined the invitation, a different participant with a similar area of expertise was invited.

Development of AMR mode
An initial model of the AMR system represented as a causal loop diagram was used as a starting point. The initial model had 55 variables and 117 arrows denoting relationships. The development of the model was intended to be an iterative process; input from participants at each meeting and set of interviews was used to revise the model.

Data collection
A total of four face-to-face meetings were held in Guelph, Ontario, in March, June, September, and November of 2016. The research plan was that the first three meetings would include 6-8 participants, and the fourth meeting would include 10-14 participants. Each meeting was: led by a facilitator, guided by a pre-tested semi-structured interview guide, 4-4.5 hours in duration, and audio-recorded. Each face-to-face meeting was supplemented with up to five key informant

interviews to capture detail that might not be available in a group setting or to fill knowledge gaps identified by the group. The interviews were: guided by a semi-structured interview guide, up to one hour in length, conducted by phone or in person, and audio-recorded.

Each meeting and interview began with a brief presentation to provide participants with background information about AMU, AMR, the objectives of the project, and the current draft of the AMR system model. Participants were asked to provide their thoughts and perspective on the model. Specifically they were asked about: potential variables to add/remove, missing connections, key leverage points, and relevant stakeholders at each variable.

Following each meeting and set of interviews, revisions were made to the model based on participants’ comments. Audio recordings from the meetings and interviews were transcribed and transcripts were analysed for recurrent themes. Verbatim quotes were used to support themes emerging from the analysis and changes to the model.

Results
To date, two of four planned face-to-face meetings and sets of key informants have been conducted. Table 1 outlines the backgrounds of the participants to date.

<table>
<thead>
<tr>
<th>Event</th>
<th>Participants</th>
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<tbody>
<tr>
<td>Face-to-face meeting 1 (March 2016)</td>
<td>1) owner/operator of a family farm, 2) agricultural economist, 3) food security practitioner, 4) food retail representative, 5) public health diettian, 6) health research specialist at a public health unit</td>
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<tr>
<td>Key informant interviews 1</td>
<td>1) professor of food security, 2) owner of a pharmaceutical company, 3) crop producer, 4) representative of the agriculture industry</td>
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<tr>
<td>Face-to-face meeting 2 (June 2016)</td>
<td>1) swine producer, 2) beef producer, 3) executive from a quick-service retail chain, 4) professor of agricultural economics and trade, 5) professor of consumer sciences, 6) representative from an organisation that aims to build public trust and confidence in food and farming, 7) representative from a farm animal welfare organisation, 8) health research specialist at a public health unit</td>
</tr>
<tr>
<td>Key informant interviews 2</td>
<td>1) labour professor, 2) social science nutrition professor, 3) dentist, 4) land use planner</td>
</tr>
<tr>
<td>Face-to-face meeting 3 (September 2016)</td>
<td>1) swine producer, 2) dairy producer, 3) dentist, 4) professor of pharmacy, 5) land use planner, 6) veterinarian from a drug company, 7) aquaculture company representative, 8) poultry feed specialist</td>
</tr>
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</table>

For the first meeting, 27 email invitations were sent and six individuals attended. For the second meeting, 38 invitations were sent and eight individuals attended. For the upcoming third meeting, 32 invitations were sent and eight individuals accepted the invitation.

Despite participants having a diverse range of backgrounds and areas of expertise, the discussions were flowing, interactive and congenial. Participants appeared to be
genuinely interested in hearing the perspectives of others in the group and several exchanged contact information.

When asked if they saw themselves in the model, all participants reported seeing themselves in multiple places (e.g. in variables related to their own areas of work or experience, and in variables related to consumers and the general public). Suggestions for new variables have been made in many different areas of the systems model. A number of variable name changes have been suggested for clarity, greater inclusivity, and better representation.

Participants have commented on the complexity of the map (“Where do you start?”) and how the current two-dimensional model does not account for different levels of power and influence, different scales, or related variables. Suggestions have included grouping related variables into clusters, using different colours and font sizes, and using “lenses” or “acetates” to visually highlight different aspects of the model.

For the third meeting in September 2016, participants will be asked to comment on the fourth iteration of the AMR system model. This draft of the model includes 105 variables and 235 arrows. Final results for this study will be available in April 2017.

Discussion
The aim of the study was to build a full visual model of the AMR system in Canada showing the complexity of the system, all the relevant stakeholders involved, and the interconnected relationships. By visually communicating the complex nature of the AMR system, the systems model can show how a change in one variable has the potential to impact many other parts of the system either directly or indirectly and consequently may have both intended and unintended consequences. The presentation of a comprehensive AMR model is intended to provide a framework that will support and provide context for interpretation of research and surveillance findings as well as policy development and assessment. Derivative maps will be developed from the full system map to highlight particular variables and pathways, and to help make the overall model more approachable and less daunting.

The qualitative model is not intended to be mathematical, nor will it demonstrate measurable change in AMR. Furthermore, no attempts will be made to explain the behaviour of the system with a causal theory. However, the completed model will be useful for informing the development of future quantitative models, risk assessment, expansion or change to surveillance programmes, or even implementation of interventions to ensure key variables are included or considered.

Assessment of this conceptual model will enable the identification of critical leverage points, which are those aspects of the system that need to shift or change so that the whole system can adapt. This new model, together with ongoing surveillance activities and parallel qualitative and quantitative research projects are all needed to support long-term, sustainable interventions for AMR. It is envisioned that at the end of this project, the individuals, agencies and organisations described in this conceptual model will recognise their shared responsibility both in maintaining the current AMR system and in shifting or enabling the model to adapt to a new reality.

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References
5. Gibbs EPJ. Vet Record 174, 85-91, 2014