

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A cross-sectional population survey of public knowledge, attitudes and practices related to antibiotic use and resistance in Singapore
AUTHORS	Lim, Jane; Duong, Minh Cam; Cook, Alex R; Hsu, Li Yang; Tam, Clarence C

VERSION 1 – REVIEW

REVIEWER	McNulty, Cliodna Public Health England, Primary Care Unit
REVIEW RETURNED	26-Jan-2021

GENERAL COMMENTS	<p>This is an interesting paper and adds to the research around public surveys. It would be useful to refer to more survey publications in the discussion and compare results with other public surveys and campaigns outside Singapore. The multivariable analysis and the grouping of knowledge/attitude scores is very useful</p> <p>below are my comments</p> <ol style="list-style-type: none">1. in the appendix A it would be very useful to state which statements are true or false. if all the statements and results are in the results table this appendix is not needed2. Appendix B - I noticed in the scoring system that most of the attitude statements were false, these often lead to poorer responses. you may need to say this is a limitation of the study -3. Page 7 lines 33 and 40 : it would have been useful to analyse those respondents with RTI who didn't go to see their doctor - as these may have had the best attitude to antibiotics. is it possible to do this?4. Page 7 line 40: also is it possible to look at severity of RTI and whether they visited a GP, and whether they requested an antibiotic?5. page 9 line 7: please state how many of the 706 had an RTI first - it does not say in the methods that this was an inclusion criteria. the percentages here - are they all of the 706? or a fraction of those with RTI? it appears from line 11 that all 706 had an RTI.6. page 15 table 1: - it would be useful to include p values or other statistics to show the deviation the participants demographics from the general population,7. table 2 and appendix and discussion: the questions "Antibiotic resistance occurs when antibiotics become less powerful so they don't work as well"; Antibiotic resistance occurs when your body becomes resistant to the antibiotics and they no longer work as well; Antibiotic resistance occurs when bacteria become resistant to the antibiotics so they are more difficult to kill" are quite complex and you can understand misinterpretation - it may be worth saying something in limitations about this.8. figure - it would be useful to have percentages on this.
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	<p>9. It would be useful to have more of the actual numerical results in the abstract, shortening the background and conclusion.</p> <p>10. strengths and limitations.</p> <p>a. First bullet – important to say somewhere in the manuscript that if this is to form a baseline – the same methods and exactly the same question wording will be needed in future surveys to allow comparison – this is often forgotten.</p> <p>b. the second bullet is not a limitation or strength. you should maybe cover here any limitations with the questions as the resistance ones are quite nuanced and require a lot of understanding about antibiotic resistance to answer correctly.</p> <p>c. Strength maybe numbers gained.</p> <p>d. In bullet 3 say exactly how it is not representative of the population –</p> <p>e. Limitation: none under 21 years – many other surveys have found this under 21 years group to have less favourable behaviours</p> <p>f. Limitation on-line means that questions cannot be explained as in face to face or misunderstood – e.g. when antibiotics become less powerful (48.5% yes) is a difficult concept</p> <p>11. In the introduction it would be useful to say</p> <p>a. Population of Singapore</p> <p>b. where most of antibiotics are sourced.</p> <p>12. Methods line 40: - need to say a bit more about how they are selected for the panel</p> <p>13. Methods line 48 – was this completed on PCs or also handheld device accessible</p> <p>14. Page 8 results cold/flu practices line 7 Of the 706 respondents, 50.6% chose to see a doctor – and nearly half were given an antibiotic discuss in relation to publications outside the Singapore later in the paper as this is higher than UK and other northern EU countries – a strategy to reduce antibiotic use could be to reduce these consultations.</p> <p>a. Discuss Why doctors prescribe in 50% How do doctors get paid ? do they get paid for antibiotics prescribed – is this a cause of overuse? What reward do they get – maybe mention a cognitive theory (theory of planned behaviour, or theoretical domains framework, or COM-B, as a way to look at behaviours of patients and prescribers. What rewards (real or perceived) do they both get?</p> <p>15. Discussion page 10 line 3 – agree that greater deprivation and lower education associated with lower knowledge – find other references to support these statements</p> <p>16. Please check the positioning of references – as for example reference 25 is not about antibiotic guidelines.</p> <p>17. Also many of the statements in the discussion do not have references to support them – please add.</p> <p>18. Although the discussion covers all the salient areas it does not cover many other surveys and compare to them allowing for some lessons learnt from other campaigns.</p>
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REVIEWER	Gualano, Maria University of Turin, Department of Public Health
REVIEW RETURNED	04-Mar-2021

GENERAL COMMENTS	<p>The manuscript is good and represents an important contribution to the knowledge of this topic in Singapore, nevertheless I have some concerns that Authors should address:</p> <ul style="list-style-type: none"> - In the abstract, please be more informative: include some percentages and numbers
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	<p>- Please specify in a more detailed way the criteria to be included in the Panel, in which way the 1000 participants were chosen?</p> <p>- in the discussion, results should be discussed more in detail, by adding more findings from similar studies published in scientific literature</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer Reports:

Reviewer: 1

Dr. Clodna McNulty, Health Protection Agency

Comments to the Author:

This is an interesting paper and adds to the research around public surveys. It would be useful to refer to more survey publications in the discussion and compare results with other public surveys and campaigns outside Singapore. The multivariable analysis and the grouping of knowledge/attitude scores is very useful

Below are my comments

1. in the appendix A it would be very useful to state which statements are true or false. if all the statements and results are in the results table this appendix is not needed

Appendix A includes the full questionnaire that was used for the study as reference. We have included the questions used for participants' knowledge and attitude scores in Appendix B with scoring indications of incorrect or non-favourable responses.

2. Appendix B - I noticed in the scoring system that most of the attitude statements were false, these often lead to poorer responses. you may need to say this is a limitation of the study –

We thank the reviewer for their comment. Participants did score slightly better on 'positive' attitude statements (mean % of respondents who answered favourably = 86.1% across 2 questions) compared to 'negative' attitude statements (mean % of respondents who answered favourably = 62.7% across 9 questions). However, this should not influence the interpretation of our study's findings as all participants were scored on the same scale for both knowledge and attitude scores; our regression results thus estimate the relative effect on the dependent variable of scoring higher on the scale.

3. Page 7 lines 33 and 40 : it would have been useful to analyse those respondents with RTI who didn't go to see their doctor - as these may have had the best attitude to antibiotics. is it possible to do this?

We explored this in our initial regression models, but respondents with RTIs who did not see their doctor did not have significantly different knowledge or attitude scores.

4. Page 7 line 40: also is it possible to look at severity of RTI and whether they visited a GP, and whether they requested an antibiotic?

Unfortunately we did not ask participants about the severity of their RTI.

5. page 9 line 7: please state how many of the 706 had an RTI first - it does not say in the methods that this was an inclusion criteria. the percentages here - are they all of the 706? or a fraction of those with RTI? it appears from line 11 that all 706 had an RTI.

In the survey (Appendix A, Section 3), we asked all 706 respondents about their health behaviours the last time they had symptoms of the common cold or flu. We have re-phrased the

relevant text as follows for clarity: "We asked all 706 respondents what they did the last time they had symptoms of the common cold or flu (Figure 1). More than half (50.6%) chose to see a doctor"

6. page 15 table 1: - it would be useful to include p values or other statistics to show the deviation the participants demographics from the general population

Thank you for the comment. However, while non-significant p-values could be because the sampling did not reflect the census distribution, it could also be because the sample size was too small to detect differences in specific demographic strata. Further, as this survey was designed to provide baseline information against which to measure the progress of future AMR interventions, and not to test for deviations from the census distribution, we do not think that p-values will add to the information provided in Table 1.

7. table 2 and appendix and discussion: the questions "Antibiotic resistance occurs when antibiotics become less powerful so they don't work as well"; Antibiotic resistance occurs when your body becomes resistant to the antibiotics and they no longer work as well; Antibiotic resistance occurs when bacteria become resistant to the antibiotics so they are more difficult to kill" are quite complex and you can understand misinterpretation - it may be worth saying something in limitations about this. We thank the reviewer for their constructive comment. We used these questions in our survey for comparability with WHO's multi-country antibiotic resistance public awareness survey, which included these questions. However, we recognise that respondents may have misinterpreted questions relating to the mechanisms of antibiotic resistance, especially in an online survey where the research team is unable to clarify or answer questions in-person. We have added this to the limitations of the study in the main text on page 9, line 18 – 22.

8. figure - it would be useful to have percentages on this.

Thanks for the suggestion – we have added percentages to Figure 1 (updated version attached to submission).

9. It would be useful to have more of the actual numerical results in the abstract, shortening the background and conclusion.

Thanks for the suggestion – we have included actual numerical results in the abstract to be more informative.

10. strengths and limitations.

a. First bullet – important to say somewhere in the manuscript that if this is to form a baseline – the same methods and exactly the same question wording will be needed in future surveys to allow comparison – this is often forgotten.

Thanks for the suggestion. We have clarified this in the manuscript (page 9, line 8 – 10).

b. the second bullet is not a limitation or strength. you should maybe cover here any limitations with the questions as the resistance ones are quite nuanced and require a lot of understanding about antibiotic resistance to answer correctly.

We have also clarified this in the manuscript (page 3, line 11 – 13).

c. Strength maybe numbers gained.

We have added this key strength to bullet 2 (page 3, line 5 – 6).

d. In bullet 3 say exactly how it is not representative of the population –

Thanks for the comment. We have added this to bullet 3 (page 3, line 7 – 10).

e. Limitation: none under 21 years – many other surveys have found this under 21 years group to have less favourable behaviours

We specifically conducted our survey among adults. In Singapore, the legal age of consent for participation in research is 21 years, which meant that those under 21 years of age were excluded from participation.

f. Limitation on-line means that questions cannot be explained as in face to face or misunderstood – e.g. when antibiotics become less powerful (48.5% yes) is a difficult concept
We used these questions, such as the one above referring to antibiotics becoming less 'powerful', because previous qualitative research has indicated that these are different ways in which people understand the concept of antibiotic resistance (Antibiotic Resistance Poorly Communicated and Widely Misunderstood by UK Public). We recognise, however, that in an online survey we have less control over how the questions themselves are understood. We have added this to the limitations of the study in the main text on page 9, line 18 – 22.

Antibiotic resistance poorly communicated and widely misunderstood by UK public. Wellcome. Retrieved April 7, 2021, from <https://wellcome.org/press-release/antibiotic-resistance-poorly-communicated-and-widely-misunderstood-uk-public>

11. In the introduction it would be useful to say

a. Population of Singapore

We have clarified that the study population refers to the population of Singapore in the introduction section (highlighted in main text).

b. where most of antibiotics are sourced.

Thanks for the comment. Unfortunately, there is no publicly available information about where antibiotics are sourced and imported from. Currently, all antimicrobials for human use in Singapore are prescription-only and are regulated by the Health Sciences Authority (HSA) – the national authority that enforced health product regulation and registration. We have also added this to the introduction in the manuscript (page 4, line 14-16).

12. Methods line 40: - need to say a bit more about how they are selected for the panel
Participants in the panel are recruited using two main strategies. The first strategy is a door-to-door approach conducted to recruit eligible community-dwelling Singaporeans and/or permanent residents. The second strategy involves mailing invitations to de-identified household addresses available from the Singapore Department of Statistics. The following information has been added to the manuscript (page 4, line 37 – 41).

13. Methods line 48 – was this completed on PCs or also handheld device accessible

Participants could complete the surveys on any of their personal digital devices, including but not limited to PCs, laptops, tablets or mobile phones.

14. Page 8 results cold/flu practices line 7 Of the 706 respondents, 50.6% chose to see a doctor – and nearly half were given an antibiotic discuss in relation to publications outside the Singapore later in the paper as this is higher than UK and other northern EU countries – a strategy to reduce antibiotic use could be to reduce these consultations.

We thank the reviewer for the suggestion. In the main text, we discuss decreasing the frequency of medical consultations pertaining to respiratory illnesses as a possible effective strategy in reducing ambulatory antibiotic prescriptions (page 8, line 44 – 46).

a. Discuss Why doctors prescribe in 50% How do doctors get paid ? do they get paid for antibiotics prescribed – is this a cause of overuse? What reward do they get – maybe mention a cognitive theory

(theory of planned behaviour, or theoretical domains framework, or COM-B, as a way to look at behaviours of patients and prescribers. What rewards (real or perceived) do they both get? Prior research in Singapore has suggested that drivers of inappropriate prescribing in the medical community are multi-pronged, including 1) profit-making from antibiotic prescription, especially in the private primary care sector where doctors also dispense antibiotics, 2) pressure and expectations from patients, 3) lack of clinical treatment guidelines for antibiotics and 4) the lack of accessibility of diagnostic tools before prescribing antibiotics. We have added this to the discussion section on page 8, line 48 to page 9, line 4.

15. Discussion page 10 line 3 – agree that greater deprivation and lower education associated with lower knowledge – find other references to support these statements
Thanks for the suggestion. We have found other references to support these statements.

16. Please check the positioning of references – as for example reference 25 is not about antibiotic guidelines.
Thanks for the comment. We have checked and corrected positioning of the references in the main text.

17. Also many of the statements in the discussion do not have references to support them – please add.
We have added relevant references to the discussion section in the main text.

18. Although the discussion covers all the salient areas it does not cover many other surveys and compare to them allowing for some lessons learnt from other campaigns.
Thanks for the suggestion. We have added more information and lessons learnt from previous surveys and campaigns conducted in similar contexts and highlighted the changes in the main text.

Reviewer: 2
Prof. Maria Gualano, University of Turin

Comments to the Author:

The manuscript is good and represents an important contribution to the knowledge of this topic in Singapore, nevertheless I have some concerns that Authors should address:

- In the abstract, please be more informative: include some percentages and numbers
Thanks for the suggestion – we have included percentages and numbers in the abstract to be more informative.

- Please specify in a more detailed way the criteria to be included in the Panel, in which way the 1000 participants were chosen?

Thanks for the clarification. Participants in the panel were recruited using two main strategies. The first strategy was a door-to-door approach conducted to recruit eligible community-dwelling Singaporeans and/or permanent residents. The second strategy involved mailing invitations to de-identified household addresses available from the Singapore Department of Statistics. The following information has been added to the manuscript (page 4, line 37 – 41).

- in the discussion, results should be discussed more in detail, by adding more findings from similar studies published in scientific literature

Thanks for the suggestion. We have added more information and lessons learnt from previous surveys and campaigns conducted in similar contexts and highlighted the changes in the main text.