Author’s response to reviews

Title: Observational study of a new strategy and management policy for measles prevention in medical personnel in a hospital setting

Authors:

Chang-Pan Liu (joeliu5929@hotmail.com.tw)
Hsi-Peng Lu (lu@mail.ntust.edu.tw)
Tainyi Luor (dr.luor@gmail.com)

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Author’s response to reviews:

No.: INFD-D-18-01774R 1

Title: A new strategy and management policy for measles prevention in medical personnel

Dear editors,

Thank you for reviewing the manuscript entitled “A new strategy and management policy for measles prevention in medical personnel” and your kindness in allowing revision and resubmission. We have included the study design and setting to the title. The title of the revised manuscript is “Observational study of a new strategy and management policy for measles prevention in medical personnel in a hospital setting”.

The comments by the editor and reviewers have been of great help in addressing deficiencies in the paper and are highly appreciated. The manuscript had been reorganized and many sentences have been rephrased in accordance to recommendations from the reviewers. We have also carefully made point by point corrections for each of the reviewer’s comments and the relevant parts of the revised text of the manuscript have been underlined when necessary. We hope that the clear manuscript meets the requirements for publication in your esteemed Journal.

Yours sincerely,

Hsi-Peng Lu, Ph.D.

Corresponding author,
Reviewers' comments:

We found the referee’s comments most helpful and have revised the manuscript as referee’s recommendation.

Reviewer #1: (Dr Vicky Sheppeard)

1. This paper contains a large range of information about a local response to imported measles. While I am sure that much of this information is very useful for local evaluation I recommend that a published manuscript focus on the aspects which are novel and may provide guidance to other institutions facing similar challenges.

ANS: The comments by Dr Vicky Sheppeard have been of great help in addressing deficiencies in the paper and are highly appreciated. We have studied your recommendations carefully. The manuscript had been reorganized and many sentences have been rephrased in accordance to recommendations from the reviewer. We have also carefully made point by point corrections for your comments and the relevant parts of the revised text of the manuscript have been underlined when necessary.

Hence there was an urgent need to implement a new strategy to interrupt measles transmission for epidemic prevention. In the new strategy, first-line medical personnel would be screened free of charge for measles antibody, and measles vaccination promoted for those who were seronegative, thus increasing vaccination coverage. The goal was to achieve zero tolerance for intra-hospital transmission. (In Background section, Page 6, Paragraph 3, Line 1-5)

In the knowledge stage; prior conditions included unknown status of seropositivity in our medical personnel and occurrence of outbreak, while the innovative characteristic was testing for measles antibody which was rapid, convenient and free of charge. (In Method section, Page 7, Paragraph 4, Line 1 to Page 8, Line 1-3)

The frequency for laboratory testing of measles antibody was increased from thrice a week to daily from Monday to Saturday. If the measles antibody test was performed in the morning, results were available by afternoon; so that those who were seronegative could visit the outpatient clinic on the same day and receive measles vaccination within 24 hours of antibody testing, reducing complexity. (In Method section, Page 8, Paragraph 2, Line 4-8)
2. Hence I recommend that the paper focus on the interesting finding of differing seropositivity by age amongst health care workers, and the increased uptake of vaccine amongst those shown to be seronegative.

ANS: We are pleased to note the favorable comments of the reviewer. Your useful comments are greatly appreciated. The main endpoints of the study focused on the finding of differing seropositivity by age amongst medical personnel and increased uptake of vaccination coverage amongst the seronegative personnel, as recommended.

The overall measles seropositivity was 85.8% (617/719) at baseline. By age group, the seropositivity of measles antibody was 70.7% for those aged 20-30 years, 80.5% (169/210) for those aged 30-40 years, 94.4% (185/196) for those aged 40-50 years, 99.2% (126/127) for those aged 50-60 years, and 100% (19/19) for those aged 60-70 years [Fig. 2]. The seropositivity of measles antibody was 76.1% (287/377) in the vaccinated generation, and 96.5% (330/342) in the unvaccinated generation (\(p < 0.001\)). (In Results section, Page 12, Paragraph 1, Line 4-10)

Finally, in the confirmation stage (collection of data on vaccination coverage and policy compliance), vaccination coverage reached 86.3% (88/102) in the first month under the new strategy. Reasons for refusal of vaccination were: too busy/no time (64.3%, 9/14), preparing for pregnancy or pregnant (28.6%, 4/14), and illness (7.1%, 1/14). At the end of the second month, only 4 medical personnel who had contraindications for vaccination had not yet been vaccinated, while the remaining seronegative medical personnel received vaccination. Vaccination coverage under the new strategy was 96.1% (98/102) at the end of the second month. (In Results section, Page 12, Paragraph 2, Line 1-8)

3. I suggest that the measles outbreak be reported briefly in the introduction (give context that there is no endemic measles in Taiwan, however occasional imported cases; in the setting of an importation with several generations of spread that several health care workers were exposed) and also briefly outline the vaccination policy of the institution, and the measured level of adherence.

ANS: Thanks for your suggestions. According to the two reviewers’ suggestions, we have reported on the measles outbreak briefly in the introduction. We focused on the fact that there is no endemic measles in Taiwan. However, there are occasional imported cases, and the hospital was an important site of spread since several health care workers were exposed. Hence, we have rewritten the paragraph in the introduction as recommended. We also have briefly outlined the vaccination policy of the institution, and the measured level of adherence.

Although measles is not endemic in Taiwan, there are occasional import-linked cases, with 14 cases of measles reported in 2016, and 6 cases in 2017. However, from January 2018 to May
2018, 26 cases of measles were reported [10]. (In Background section, Page 5, Paragraph 3, Line 1-3)

In Taiwan, routine two-dose attenuated measles-mumps-rubella (M-M-R) vaccination for children was implemented since 1978; with a vaccination rate of > 97%. Seropositivity in the vaccinated generation decreases with time. As a result, the vaccinated generation (those born after 1978) have the opportunity to be infected with measles [10, 11]. M-M-R vaccine is safe and well-tolerated [12]. However, some medical personnel at our hospital still refused vaccination for personal reasons. (In Background section, Page 4, Paragraph 3, Line 1-6)

Measles vaccination is not mandatory in Taiwan for medical personnel, but highly recommended for those working in high risk divisions [10]. (In Background section, Page 4, Paragraph 4, Line 5-7)

Prior to implementation of the new policy, the prevailing policy for infection control at our hospital was encouragement of vaccination for physicians and nurses working in high risk divisions (Divisions of Emergency Medicine, Infectious Diseases, Gynecology and Pediatrics) without prior antibody testing. (In Background section, Page 6, Paragraph 2, Line 4-8)

4. I would not bother with describing models of care, nor dwelling on measles vaccine supply or who paid, although it is informative to include relative serology and vaccine costs. Just simply describe the vaccination history of the health care workers, how this related to seropositivity and age, and the vaccination response. Remove figures 1, 2, 3, and 5, and amend figure 4 to remove reference to the model.

ANS (for Q4-1): We are pleased to note the favorable comments of reviewer. Your useful comments are highly appreciated. Firstly, following the suggestion of the referee, we have rephrased the related paragraph to describe the vaccination history of medical personnel and the vaccination response. Please see page 4, paragraph 4, line 1-7 and page 5, paragraph 2, line 1-6 in the background section.

In 1987 the United States was the first country to establish a measles vaccine policy for health care personnel [13]. Later, Australia, Canada, and some Caribbean and European countries implemented policies for measles vaccination in health care personnel. Measles vaccination was mandatory for medical personnel in Finland [14, 15], while in China vaccination was recommended, but not mandatory [15]. Measles vaccination is not mandatory in Taiwan for medical personnel, but highly recommended for those working in high risk divisions [10]. (In Background section, Page 4, Paragraph 4, Line 1-7)

In the past decade, the number of measles cases in Europe has been increasing [1, 17]. From 1989 to 2013, 53 worldwide published studies reported measles transmission from patients to
medical personnel [14]. Among a staff of 890, 19 health care workers were infected with measles due to hospital-based transmission in Xinjiang Autonomous Region, China in 2016 [15]. Susceptible medical personnel are at higher risk of acquiring measles (estimated to be 2 to 19 times) and transmitting measles than the general population [14]. (In Background section, Page 5, Paragraph 2, Line 1-6)

ANS (for Q4-2): We are pleased to note the favorable comments of reviewer. We have also deleted figures 1,2,3,5 and all the detail parts in the paragraph concerning “The health continuum of measles care model” in the Methods section. We have amended figure 4 to remove reference to the model and rearranged the numbering of the figures. Please see “Fig. 1 The flow chart of the research framework in the study (Ab, antibody)”. 

5. The paper also requires a discussion of primary and secondary measles vaccine failure, and how these may be contributing to the serostatus of the health care workers, and what risks may persist, even after revaccination.

ANS: Thank you very much for your review. Your useful comments are greatly appreciated. We have added new paragraph to discuss primary and secondary measles vaccine failure and how they may contribute to the serostatus of medical personnel. We have also described the risks after revaccination, as suggested. We think that the paper is strongly improved by this additional information.

However, the potential risk for measles infection remains because of the possibility of the primary and secondary measles failure. Failure to develop protective antibody levels in those immunized with two doses of measles vaccine (primary failure), and waning immunity over time (secondary failure) may result in measles infection [14, 27]. Thus, measles vaccination does not guarantee lifelong immunity. (In Discussion section, Page 17, Paragraph 2, Line 1-5)

Taiwan has maintained a vaccination coverage of greater than 95%-97% with two-dose of M-M-R vaccine in the preschool stage [22, 23], but 3 clusters of measles still occurred in 2018. Hence, continuous vigilance and surveillance is required for the early detection of measles cases. Infection control measures are crucial in preventing the spread of measles. Following detection of a measles case, there should be immediate investigation of all the medical personnel who had contact with the case, and all high risk groups should be immediately tested for measles IgG as soon as possible. Seronegative personnel should receive measles vaccine or intramuscular immunoglobulin (IMIG) [28] as post-exposure prophylaxis. (In Discussion section, Page 17, Paragraph 3, Line 1-9)

I greatly appreciate your help and the recommendations made by the reviewers concerning improvements to this paper. I hope that the revised manuscript is now suitable for publication.
Best Regards,

Corresponding author: Hsi-Peng Lu, Ph.D.

E-mail address: lu@mail.ntust.edu.tw / hsipeng@cs.ntust.edu.tw

Mar 14, 2019

Reviewers’ comments:

We found the referee’s comments most helpful and have revised the manuscript as referee’s recommendation.

Reviewer #2:

REVIEWER COMMENTS

Overall, this is a really interesting in-depth look at how a hospital can respond to a measles outbreak. My impression of the study is that it offers good information about what hospitals can do in a measles outbreak situation.

The authors have done well to provide a lot of quantitative information about vaccination compliance, and to situate this into the continuum of care model.

Although most of the pieces of this manuscript are there, I’ve provided comments on how to restructure introduction and discussion to provide a better flow of information in the manuscript.

ANS: The comments by the reviewer have been of great help in addressing deficiencies in the paper and are highly appreciated. We have studied your recommendations carefully. The manuscript had been reorganized and many sentences have been rephrased in accordance to recommendations from the reviewer. We have also carefully made point by point corrections for each of the reviewer’s comments and the relevant parts of the revised text of the manuscript have been underlined when necessary.
REQUESTED REVISIONS:

Main suggestions

Overall your paper is very logically oriented and is an interesting case study of how to improve measles vaccination coverage. Although I understand why you structured your paper the way you did, I think the background is a bit bulky. Your aim, as I see it and as you wrote it, is to “explore the effectiveness of a new strategy for preventing spread of measles in medical personnel”.

1. Therefore, I think the information about the number of personnel vaccinated at baseline actually would belong in results. I would change sections of the introduction as follows:

Page 5 line 10-30: I would move this to results where you can directly do before-after comparison.

ANS: We are pleased to note the favorable comments of reviewer. Your useful comments are greatly appreciated. We have moved Page 5 line 10-30 in the previous version to Results in the revised version. We have retained compliance for new strategy and vaccination coverage for comparison. We have also rephrased these sentences for the before-after comparison of vaccination coverage and policy compliance in medical personnel, as recommended.

Under the former policy, among the 462 physicians and nurses working in high risk divisions in our hospital with unknown antibody status, 68 refused vaccination, including 5 (one physician and four nurses) who worked in the high-risk Emergency Room. (In Results section, Page 11, Paragraph 4, Line 1-4)

Finally, in the confirmation stage (collection of data on vaccination coverage and policy compliance), vaccination coverage reached 86.3% (88/102) in the first month under the new strategy. Reasons for refusal of vaccination were: too busy/no time (64.3%, 9/14), preparing for pregnancy or pregnant (28.6%, 4/14), and illness (7.1%, 1/14). At the end of the second month, only 4 medical personnel who had contraindications for vaccination had not yet been vaccinated, while the remaining seronegative medical personnel received vaccination. Vaccination coverage under the new strategy was 96.1% (98/102) at the end of the second month. (In Results section, Page 12, Paragraph 2, Line 1-8)

Compliance for the former policy and the new strategy were determined in the confirmation stage. At the end of first month after implementation of the new strategy, 98.1% (705/719) of the medical personnel were seropositive or revaccinated (88 were seronegative and received measles vaccination and 617 were seropositive), and reached 99.4% (715/719) in the second month. (In Results section, Page 12, Paragraph 3, Line 1-2 and Page 13, Line 1-3)

In before-after comparison, compliance for the new strategy was higher than for the former policy (705/719 =98.1% vs. 394/462=85.3%, p <0.001). Furthermore, vaccination coverage
under new strategy was also higher than that of former policy (98/102=96.1% vs. 394/462=85.3%). It is notable that of the five emergency medical personnel who had previously refused vaccination under the former policy, two who were seronegative received measles vaccination immediately. (In Results section, Page 13, Paragraph 2, Line 1-6)

2. Page 5 line 33-52: this could be heavily abbreviated – better info would be how many cases worldwide are due to hospital-based transmission, or examples from other locales.

ANS: Thank you for useful comments. This part (previous version Page 5 line 33-52) has been rewritten. Following the referee’s comments, we have added related information on the number of cases due to hospital-based transmission into the paper.

In the past decade, the number of measles cases in Europe has been increasing [1, 17]. From 1989 to 2013, 53 worldwide published studies reported measles transmission from patients to medical personnel [14]. Among a staff of 890, 19 health care workers were infected with measles due to hospital-based transmission in Xinjiang Autonomous Region, China in 2016 [15]. Susceptible medical personnel are at higher risk of acquiring measles (estimated to be 2 to 19 times) and transmitting measles than the general population [14]. (In Background section, Page 5, Paragraph 2, Line 1-7)

3. On page 6 line 1 and line 26 you mention “three clusters of measles cases” – are these the same 3? overall – this paragraph could be simplified to focus on the outbreak you are studying.

ANS: Thanks for your suggestions. Taiwan’s CDC announced that three clusters were found in the same period. For simplification, we have rephrased the paragraph in the introduction as recommended.

In the measles cluster linked to Tigerair Taiwan, the index case was a male Taiwanese in his 30s who got measles infection in Thailand and travelled back to Taiwan. He then flew to Okinawa, Japan causing infection clusters in Taiwan and Japan [10]. The cluster of measles detected in Chang Gung Memorial Hospital, located near an airport in northern Taiwan in April 2018 included a male nurse in his 20s. Continuous monitoring was required for 491 people who had contact with him during the communicability period, including 13 nurses from the MacKay Memorial Hospital who studied with him in the same classroom. (In Background section, Page 5, Paragraph 4, Line 1-4 to Page 6, Line 1-4)
4. Missing from the introduction is a bit of basic information on the worldwide standards associated with measles vaccination in health care workers – is it mandated in certain locations? / what specific policies are there?

ANS: Thanks a lot. Your useful comments are greatly appreciated. We have added some basic information on measles vaccination policies in medical personnel worldwide, as you suggested. We think that the paper is strongly improved by this additional information.

In 1987 the United States was first country to establish a measles vaccine policy for health care personnel [13]. Later, Australia, Canada, and some Caribbean and European countries implemented policies for measles vaccination in health care personnel. Measles vaccination was mandatory for medical personnel in Finland [14, 15], while in China vaccination was recommended, but not mandatory [15]. Measles vaccination is not mandatory in Taiwan for medical personnel, but highly recommended for those working in high risk divisions [10]. (In Background section, Page 4, Paragraph 4, Line 1-7)

In order to assist countries to develop national policies for the vaccination of health care workers, the WHO recently updated and recommended worldwide standards and policies for measles vaccination. Accordingly, all medical personnel must be immune against measles and proof or documentation of immunization is required as a condition for employment [16]. (In Background section, Page 4, Paragraph 5, Line 1 to Page 5, Line 1-4)

Overall

5. There is some inconsistency in how many decimal points you report. I recommend only one – which would seem to be enough precision, but if you want two, just use two for every reported statistic.

ANS: Thank you very much for your suggestion. Your useful comments are highly appreciated. In order to achieve consistency in decimal points in our report, we have changed two decimal points to one decimal point for every reported statistic in the entire manuscript as recommended.

The overall measles seropositivity was 85.8% (617/719) at baseline. By age group, the seropositivity of measles antibody was 70.7% for those aged 20-30 years, 80.5% (169/210) for those aged 30-40 years, 94.4% (185/196) for those aged 40-50 years, 99.2% (126/127) for those aged 50-60 years, and 100% (19/19) for those aged 60-70 years [Fig. 2]. The seropositivity of measles antibody was 76.1% (287/377) in the vaccinated generation, and 96.5% (330/342) in the unvaccinated generation (p <0.001). (In Results section, Page 12, Paragraph 1, Line 4-10)

Finally, in the confirmation stage (collection of data on vaccination coverage and policy compliance), vaccination coverage reached 86.3% (88/102) in the first month under the new strategy. Reasons for refusal of vaccination were: too busy/no time (64.3%, 9/14), preparing for
pregnancy or pregnant (28.6%, 4/14), and illness (7.1%, 1/14). At the end of the second month, only 4 medical personnel who had contraindications for vaccination had not yet been vaccinated, while the remaining seronegative medical personnel received vaccination. Vaccination coverage under the new strategy was 96.1% (98/102) at the end of the second month. (In Results section, Page 12, Paragraph 2, Line 1-8)

6. You sometimes report the “compliance rate” and also the “non-compliance rate” – I think it should be the same for the sake of simplicity. (I also might just rephrase this as “vaccination compliance” because compliance rate could be a bit vague)

ANS: Your useful comments are highly appreciated. We have removed the terms “compliance rate” and also the “non-compliance rate”, and then replaced them with “vaccination coverage” and compliance of new strategy or formed policy. In order to avoid confusion and misunderstanding, we have reworded “the compliance rate for measles vaccination” in Abstract (Background) to “vaccination coverage”. Please see page 1, line 6, in Abstract (Background) section.

Abstract

Background: At the end of March 2018, a clustered outbreak of measles associated with health care workers occurred in northern Taiwan. Prior to this study, the policy for measles vaccination for physicians and nurses in MacKay Memorial Hospital, Taiwan was encouragement of vaccination in medical personnel working in the emergency room or other high risk divisions without prior testing for measles antibody, and vaccination coverage was only 85.3%.

Compliance for the former policy and the new strategy were determined in the confirmation stage. At the end of first month after implementation of the new strategy, 98.1% (705/719) of the medical personnel were seropositive or revaccinated (88 were seronegative and received measles vaccination and 617 were seropositive), and reached 99.4% (715/719) in the second month. (In Results section, Page 12, Paragraph 3, Line 1-2 and Page 13, Line1-3)

In before-after comparison, compliance for the new strategy was higher than for the former policy (705/719 =98.1% vs. 394/462=85.3%, p <0.001). Furthermore, vaccination coverage under new strategy was also higher than that of former policy (98/102=96.1% vs. 394/462=85.3%). It is notable that of the five emergency medical personnel who had previously refused vaccination under the former policy, two who were seronegative received measles vaccination immediately. (In Results section, Page 13, Paragraph 2, Line 1-6)
7. **Background:** what do you mean by compliance rate? maybe “vaccination uptake among health care workers”?

ANS: Thank you for your useful comments. We have removed the term compliance rate and replaced it with the terms: compliance for the former policy and compliance for the new strategy, and these have been explained in the revised version. Please see page 7, paragraph 3, line 1-6 in Methods section. We have rephrased these sentences and the research flow is shown in Fig. 1.

Compliance for the former policy describes the percentage of medical personnel that adhere to the former policy (vaccination for all first-line physicians and nurses at high risk of measles infection without prior antibody testing). Compliance for the new strategy describes the percentage of medical personnel that follow the new policy (implementation of measles IgG testing for first-line medical personnel and vaccination of seronegative personnel). (In Method section, Page 7, Paragraph 3, Line 1-6)

Please see “Fig. 1 The flow chart of the research framework in the study (Ab, antibody)”.

8. **Conclusions:** you mention immunization coverage increased from 85.81% to 98.05% - but is that 85.81% related to the 85.3% in the background?

ANS: We are pleased to note the favorable comments of reviewer. The “85.81%” in conclusion is not related to the “85.3%” in the background.

The “85.3%” in the background (Abstract, previous version) is the vaccination coverage under former policy (394/462, 85.3%). The “85.81%” in the Abstract is the overall seropositivity in baseline (617/719, 85.8%). To avoid confusion and misunderstanding, we have clarified and rephrased the sentences, as recommended.

Abstract

Background: At the end of March 2018, a clustered outbreak of measles associated with health care workers occurred in northern Taiwan. Prior to this study, the policy for measles vaccination for physicians and nurses in MacKay Memorial Hospital, Taiwan was encouragement of vaccination in medical personnel working in the emergency room or other high risk divisions without prior testing for measles antibody, and vaccination coverage was only 85.3%.

Abstract

Results: A total of 719 first-line medical personnel were enrolled for the general survey. Measles seropositivity was 76.1% (287/377) in the generation born after 1978 (vaccinated), and 96.5% (330/342) in the generation born before 1978 (p <0.001), while the overall seropositivity was 85.8% (617/719). Vaccination coverage of susceptible personnel under the new strategy reached 86.3% in the first month (88/102) following the survey. At the end of the first month after
Implementation of the new strategy, 98.1% of the medical personnel were seropositive or revaccinated, and reached to 99.4% at the end of the second month.

9. Also your conclusions in abstract seem more results-oriented. The first sentence works well as a conclusion, the second one not so much – maybe switch to something that extends what you are referring to in first sentence.

ANS: Thank you very much for your review. Your useful comments are greatly appreciated. We have rephrased these sentences, as recommended.

Abstract

Conclusions: In this study, rapid, free antibody screening during a measles outbreak and subsequent vaccination of those susceptible resulted in most of the first-line medical personnel being seropositive or revaccinated. The new strategy was effective, time saving, used little manpower, and of low cost. In medical personnel caring for the confirmed cases or in those who had been in contact with measles patients, an outbreak of infection could be avoided by prompt vaccination of seronegative medical personnel and implementation of infection control measures.

Introduction

10. Page 5 line 55 – I appreciate you discussing case counts in Taiwan. Has Taiwan officially eliminated measles? as in, are all cases import-linked?

ANS: Thanks for your comments. Measles is officially eliminated in Taiwan, but there are occasional import-linked cases. We have added this information in Background section.

Although measles is not endemic in Taiwan, there are occasional import-linked cases, with 14 cases of measles reported in 2016, and 6 cases in 2017. However, from January 2018 to May 2018, 26 cases of measles were reported [10]. (In Background section, Page 5, Paragraph 3, Line 1-3)

11. I get what you are saying when you write “40’s-year-old woman” but in English we would probably reword as “woman in her 40s” (similar for “20’s-year-old male nurse” etc)

ANS: Thank you very much for your review. Your useful comments are greatly appreciated. We have reworded “40’s-year-old woman” to “woman in her 40s”, and similar changes have been made in the entire manuscript.
In the measles cluster linked to Tigerair Taiwan, the index case was a male Taiwanese in his 30s who got measles infection in Thailand and travelled back to Taiwan. He then flew to Okinawa, Japan causing infection clusters in Taiwan and Japan [10]. The cluster of measles detected in Chang Gung Memorial Hospital, located near an airport in northern Taiwan in April 2018 included a male nurse in his 20s. Continuous monitoring was required for 491 people who had contact with him during the communicability period, including 13 nurses from the MacKay Memorial Hospital who studied with him in the same classroom. (In Background Section, Page 5, Paragraph 4, Line 1-4 to Page 6, Line 1-4)

On April 11, 2018, a woman in her 40s in northern Taiwan who had travelled to Hong Kong visited the emergency room and was admitted to a negative pressure isolation room in MacKay Memorial Hospital, and measles infection was confirmed [10]. (In Background section, Page 6, Paragraph 2, Line 1-4)

Discussion:

12. Page 16 line 21 to page 17 line 42 are mostly just a reprinting of results. I would heavily simplify them within 1 paragraph

ANS: Thank you for useful comments. For the sake of simplicity, we have rewritten the related information into 1 paragraph as recommended.

During this period, our hospital had a surplus of vaccines, and self-paid vaccines were available to the public who visited the outpatient clinics of MacKay Memorial Hospital seeking urgent vaccination. Thus beneficial health care service was provided during the period of vaccine shortage. In the event of a measles outbreak, it is not essential to provide compulsory free vaccination to all the medical personnel; only the seronegative, susceptible personnel require vaccination, reducing complexity and difficulty. (In Discussion section, Page 15, Paragraph 1, Line 1-7)

13. Page 20 line 32-39: would delete – sort of seems coming out of nowhere – or more clearly link to next paragraph.

ANS: Thank you very much for your review. Your useful comments are greatly appreciated. We have deleted page 20 line 32-39, as recommended.

I greatly appreciate your help and the recommendations made by the reviewers concerning improvements to this paper. I hope that the revised manuscript is now suitable for publication.
Best Regards,

Corresponding author: Hsi-Peng Lu, Ph.D.

E-mail address: lu@mail.ntust.edu.tw / hsipeng@cs.ntust.edu.tw

Mar 14, 2019