PEER REVIEW HISTORY

BMJ Paediatrics Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Large Decrease in Paediatric Hospitalisations During the COVID- 19 Outbreak in Japan
AUTHORS	Sano, Kazuaki Nakamura, Masaki Ninomiya, Hideki Kobayashi, Yasuki Miyawaki, Atsushi

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Dr. Sunil Bhopal Institution and Country: Newcastle University, Framlington Place Newcastle upon Tyne, NE1 7RU, United Kingdom of Great Britain and Northern Ireland Competing interests: not applicable
REVIEW RETURNED	04-Jan-2021
GENERAL COMMENTS	This is a wonderfully conceptualised and presented paper that very nicely captures the experience of child hospitalisation in 272 hospitals during calendar weeks 1-21 in 2020 and compares this to hospitalisation in equivalent weeks in earlier years.
	The authors are to be congratulated on the succint write-up, and high quality of presentation of figure and table.
	A few points that I hope may help improve the piece:
	1) TITLE May I suggest that the title of the letter could optimised. Perhaps to emphasise a key finding. How about: "Large decrease in hospitalisation of children seen during the Covid-19 pandemic" or similar
	2) ABSTRACT Please note number of hospitals and estimate of proportion of Japan child population covered by these (also add this to main text)
	2a) ABSTRACT Please give a hypothesis for reasons for decreased hospitalisation
	2b) ABSTRACT Please give context in first sentence so that this stands test of time - need to mention Covid-19
	3) The authors point out (page 7; line 25) that there is no evidence of reduction in appendicitis admissions. I would argue that the evidence for convincing change in admissions for inguinal hernia is also weak (from 49 to 45 admission, difference of -4, % change of -12.2%). This is, in my mind, consistent with the finding in appendicitis. Mainly for this reason I would suggest that the authors add 95% confidence intervals to all aiRRs presented in this paragraph, and point to the weaker evidence in inguinal

	hernia. This would appear to be consistent with likely explanations for these changes i.e increased social distanced reducing infectious disease, and trauma decreased perhaps due to decrease road traffic incident.
	4) Page 7: line 36 - suggest that 'significant' is not used here. Perhaps replace with 'considerable'. If the authors are referring to statistical significance (which I would strongly discourage), they will need to spell-out their significance threshold, and reason for choosing it.
	5) TABLE - I would prefer that the acronyms are spelled out - could this be made to fit?
	6) It would be worth commenting on possible changes in population size from 2017 to 2020 even if just to reference that the population of 1-17 year olds remained approximately stable
REVIEWER	Reviewer name: Dr. Emmanouil Bagkeris Institution and Country: Imperial College London, National Heart and Lung Institute / Genomic and Environmental Medicine, 1B Manresa Road, London, SW3 6LR, United Kingdom of Great Britain and Northern Ireland
	Competing interests: not applicable
REVIEW RETURNED	22-Jan-2021
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GENERAL COMMENTS	1. In the abstract please be more explicit in the first sentence and state that you refer to the COVID-19 pandemic. Furthermore, provide numbers (proportions and 95% CIs) for the estimated drop in paediatric hospitalisations.
	2. Although you report the IRR and the 95% CI for the incidence of paediatric hospitalisations, you did not provide 95% CIs for the disease-specific hospitalisations of food allergy, ALRI, KD, IDD, etc. Please be consistent throughout the manuscript.
	3. The statement "These declines may partly suggest a reduced burden of paediatric disease, possibly due to non-pharmaceutical interventions" very shortly and poorly attempts to explain the reason for the decline in hospitalisations. The reasons for this reduction are numerous, yet some possible explanations should be presented accounting for the national recommendations.

REVIEWER	Reviewer name: Dr. Shu-Ling Chong Institution and Country: Department of Emergency Medicine, 100, Bukit Timah Road, Singapore, 229899, Singapore
	Competing interests: not applicable
REVIEW RETURNED	08-Jan-2021

GENERAL COMMENTS	Major concerns Given the depth of the pandemic that we are in and the amount of published literature from many sites, I am not certain how this Letter adds value to the current literature.
	Abstract "Little is known about the trends in paediatric hospitalization during the pandemic" This statement is not true because there are multiple publications now about how the pandemic (and local lockdown states) have

impacted paediatric attendances and hospitalisations throughout the world. Please revise this sentence.
Also, please ensure British spelling throughout the abstract and Letter.
"Further studies are expected to investigate the positive and negative aspects of these reduced hospitalisations"
Can the authors conclude the abstract with a stronger statement regarding the implication on health services? For example, did their study findings help to inform resource allocation for the current (or a future) pandemic?
Letter It is not clear what the authors mean by "children's environments" in the first sentence. Do they mean the utilization of paediatric health care services? Please rephrase.
"However, little is known about the overall trends in emergency and non-emergency hospitalisations during the pandemic" Again, this is not true, given the number of publications now available that describe the use of health services for children – I suggest to remove this sentence and instead to focus on how this Letter can value-add to the current literature.
Regarding the "Diagnosis Procedure Combination inpatient database", more information is required: Is this a private insurance or a public data system? Are all Japan acute-care hospitals included in this database? What does "272 continuously observed hospitals" mean?
On Page 6, the authors list the ICD 10 diagnostic codes that they aimed to trend. I suggest to remove the alphabets and just list the diagnostic codes. The current lettering extends across sentences and is confusing for the reader.
Findings – can the authors explain why inguinal hernia hospitalisations decreased? It is intuitive that appendicitis did not see a similar trend to respiratory infections and asthma exacerbations, but generally surgical conditions cannot be accounted for by lockdown states.
In the discussion, the authors did not propose reasons why there should be such a large decline in so many diagnoses – was this the effect of school cancellation and reduction in infectious disease transmission? What about mask use in the public?
The take-away from this Letter is not clear. It would be a stronger Letter if the authors can articulate why and how these trends would be useful for future resource planning.

VERSION 1 – AUTHOR RESPONSE

Subject: bmjpo-2020-001013

February 14, 2021 Dear Drs. Malcolm Brodlie and Imti Choonara, Thank you for giving us an opportunity to revise and resubmit our manuscript entitled "Large Decrease in Paediatric Hospitalisations During the COVID-19 Outbreak in Japan" (bmjpo-2020-001013). Below are the comments we received from the editors and reviewers, as well as a point-by-point response as to how we addressed them.

We hope we have adequately addressed all the points raised by the editors and reviewers. If anything remains unclear, please do not hesitate to contact us. Thank you very much for considering our manuscript for publication in BMJ Paediatrics Open.

Sincerely,

Atsushi Miyawaki, MD, PhD (Corresponding author) Assistant Professor Department of Public Health Graduate School of Medicine, the University of Tokyo Address: 7-3-1 Hongo, Bunkyo-ku, Tokyo, Japan 1130033 Email: amiyawaki-tky@umin.ac.jp Phone: +81-3-5841-3494

Associate Editor Comments to the Author: Thank you for submitting this research letter. Please respond to the points raised by reviewers fully in a revised letter. Please confirm that there was no ethical permissions required to access these data.

Ethics Board of the University of Tokyo approved this study (approval no: 2020105NI) (stated in ethic approval subsection).

This very recent publication on paediatric hospitalisations in Scotland is relevant to the discussion https://adc.bmj.com/content/early/2021/01/14/archdischild-2020-321008

Thank you for yoru suggestion. We cited this article in the Introduction section.

(Page 4: paragraph 1)

"The COVID-19 pandemic has significantly affected children's social environments and access to healthcare services worldwide. Studies have reported substantial decreases in paediatric emergency department visits and subsequent hospitalisations[1-3]."

Editor in Chief Avoid use of the word "average" in the results - use mean.

Following your suggestion, we replaced "average" with "mean" in the results.

(Page6: paragraph 1)

"The weekly mean number of paediatric hospitalisations during weeks 9–21 decreased from 2,132 in 2017–2019 to 1,314 in 2020, a reduction of 38.4% (adjusted incidence rate ratios, 0.60; 95% confidence interval, 0.53–0.69) (Figure 1 and Table 1). The weekly mean number of hospitalisations during weeks 9–21 decreased in 2020 compared with 2017–2019 for food allergy (0.61; 0.52-0.70), for ALRI (0.39; 0.26-0.58), for KD (0.77; 0.67-0.89), for IID (0.22; 0.17-0.29), for febrile convulsions (0.69; 0.57-0.84), for asthma (0.37; 0.29-0.47), for inguinal hernia (0.80; 0.67-0.95), and for trauma (0.68, 0.61-0.75)."

Table 1 list conditions in full, ie avoid abbreviations. List numerically, ie most frequent first and Total at bottom

We spelled out the abbreviations and changed the order as you suggested.

Reviewer: 1

This is a wonderfully conceptualised and presented paper that very nicely captures the experience of child hospitalisation in 272 hospitals during calendar weeks 1-21 in 2020 and compares this to hospitalisation in equivalent weeks in earlier years.

The authors are to be congratulated on the succint write-up, and high quality of presentation of figure and table.

A few points that I hope may help improve the piece:

1) TITLE May I suggest that the title of the letter could optimised. Perhaps to emphasise a key finding. How about: "Large decrease in hospitalisation of children seen during the Covid-19 pandemic" or similar

Following your suggestion, we changed the title to "Large Decrease in Paediatric Hospitalisations During the COVID-19 Outbreak in Japan."

2) ABSTRACT Please note number of hospitals and estimate of proportion of Japan child population covered by these (also add this to main text)

We noted the number of hospitals in the abstract. Unfortunately, we could not obtain the information on all paediatric hospitalisations in Japan. Thus, we added the proportion of hospitalisations covered by our dataset to the abstract and the main text.

(Page 3: paragraph 1)

"Using inpatient data from 272 acute-care hospitals covering 12.4% of all admissions in Japan, we analyzed the number of hospitalisations of children aged 1–17 years for weeks 9–21 of 2020 (during the outbreak) vs. 2017-2019."

(Page 4: paragraph 2)

"The database included 272 Japanese acute-care hospitals that consented to data utilisation (covering 12.4% of all admissions into acute-care hospitals in Japan in January 2019)."

2a) ABSTRACT Please give a hypothesis for reasons for decreased hospitalization

There are some possible explanations for the decreased hospitalisations, including reduced infectious disease incidence and accidents due to non-pharmaceutical interventions and deferred/cancelled treatment and examinations. Though we could not fully include the reasons because of the maximum word count of 100 words, we referred to the importance of non-pharmaceutical interventions as the most possible reason for decreased hospitalizations especially for communicable diseases and trauma.

(page 3: paragraph 1)

"There were reductions in communicable diseases and trauma, possibly through non-pharmaceutical interventions, but not in appendicitis."

2b) ABSTRACT Please give context in first sentence so that this stands test of time - need to mention Covid-19

Following your suggestion, we mentioned COVID-19 in the first sentence.

(Page 3: paragraph 1)

"We evaluated the nationwide overall trends in paediatric hospitalisations including non-emergency hospitalisations during the COVID-19 pandemic."

3) The authors point out (page 7; line 25) that there is no evidence of reduction in appendicitis admissions. I would argue that the evidence for convincing change in admissions for inguinal hernia is

also weak (from 49 to 45 admission, difference of -4, % change of -12.2%). This is, in my mind, consistent with the finding in appendicitis. Mainly for this reason I would suggest that the authors add 95% confidence intervals to all aiRRs presented in this paragraph, and point to the weaker evidence in inguinal hernia. This would appear to be consistent with likely explanations for these changes i.e increased social distanced reducing infectious disease, and trauma decreased perhaps due to decrease road traffic incident.

We added 95% confidence intervals to all aIRRs in main text. Concerning inguinal hernia, the degree of the decrease might be modest but we think that a noticeable decrease in week 13 was due to the deferred elective surgeries because this week corresponds to the spring break in Japan and more surgeries seem to have been performed in this week in usual years. Thus, we stated this hypothesis in the discussion.

(Page 6: paragraph 1)

"The weekly mean number of paediatric hospitalisations during weeks 9–21 decreased from 2,132 in 2017–2019 to 1,314 in 2020, a reduction of 38.4% (adjusted incidence rate ratios, 0.60; 95% confidence interval, 0.53–0.69) (Figure 1 and Table 1). The weekly mean number of hospitalisations during weeks 9–21 decreased in 2020 compared with 2017–2019 for food allergy (0.61; 0.52-0.70), for ALRI (0.39; 0.26-0.58), for KD (0.77; 0.67-0.89), for IID (0.22; 0.17-0.29), for febrile convulsions (0.69; 0.57-0.84), for asthma (0.37; 0.29-0.47), for inguinal hernia (0.80; 0.67-0.95), and for trauma (0.68, 0.61-0.75). We found no evidence that the number of hospitalisations for appendicitis decreased (0.96; 0.82-1.12)."

(Page 7: paragraph 1)

"Second, deferred/cancelled treatments or examinations may explain the modest decrease in inguinal hernia hospitalisations, especially in week 13 (corresponding to the spring break) of 2020 compared with previous years."

4) Page 7: line 36 - suggest that 'significant' is not used here. Perhaps replace with 'considerable'. If the authors are referring to statistical significance (which I would strongly discourage), they will need to spell-out their significance threshold, and reason for choosing it.

Following your suggestion, we replace 'significant' with 'considerable'.

(Page 6: paragraph 2)

"There were considerable decreases in paediatric hospitalisations across Japanese acute-care hospitals during the COVID-19 outbreak, especially concerning conditions related to communicable diseases and trauma, but not for appendicitis."

5) TABLE - I would prefer that the acronyms are spelled out - could this be made to fit?

Following your suggestion, we spelled out the acronyms.

6) It would be worth commenting on possible changes in population size from 2017 to 2020 even if just to reference that the population of 1-17 year olds remained approximately stable

Thank you for your insightful comments. As the reviewer pointed out, it is true that Japan's child population has been declining recently (3.7% decrease in the population of children [<15 years] from 2017 to 2020). However, we believe that it was unlikely that the number of children declined more drastically during the pandemic than during the same period in the previous three years (most Japanese residents are originated from Japan, so border control during the pandemic was unlikely to reduce the child population). The current study compared the change in the number of hospitalizations before and after the pandemic to the changes during the same period in the previous three years (this study was not a simple pre-post study). Thus, we believe that changes in the child population size have not affected our results.

Reviewer: 2 Major concerns 1) Given the depth of the pandemic that we are in and the amount of published literature from many sites, I am not certain how this Letter adds value to the current literature.

As we state in the reponse to the next comment, we believe that this study is valuable in that we evaluated the nationwide trends in paediatric hospitalizations including non-emergency hospitalisations.

2) Abstract

"Little is known about the trends in paediatric hospitalization during the pandemic" This statement is not true because there are multiple publications now about how the pandemic (and local lockdown states) have impacted paediatric attendances and hospitalisations throughout the world. Please revise this sentence.

We apologise that we did not clearly state the importance of our study. As the reviewer pointed out, studys have reported decreases in paediatric emergency department visits and subsequent hospitalisations[a, b]. In addition, some studies have shown changes in hospitalisations including non-emergency ones[c-f]. However, most of these studies seem to be limited to a single hospital. Thus, we believe that our study is important in that it evaluates nationwide trends in paediatric hospitalisation not lmited to emergency ones across Japan (trends in a single/ a few medical institutions may not represent underlying patterns nationwide). Here, we removed "Little is known about ..." due to word limit and simply stated as follows:

(Page 3: paragraph 1)

"We evaluated the nationwide overall trends in paediatric hospitalisations including non-emergency hospitalisations during the COVID-19 pandemic."

[a] Pines JM, Zocchi MS, Black BS, et al. Characterizing pediatric emergency department visits during the COVID-19 pandemic. Am J Emerg Med Published Online First: 23 November 2020. doi:10.1016/j.ajem.2020.11.037

[b] Williams TC, MacRae C, Swann O V, et al. Indirect effects of the COVID-19 pandemic on paediatric healthcare use and severe disease: a retrospective national cohort study. Arch Dis Child Published Online First: 15 January 2021. doi:10.1136/archdischild-2020-321008

[c] Chong SL, Soo JSL, Allen JC, et al. Impact of COVID-19 on pediatric emergencies and hospitalizations in Singapore. BMC Pediatr 2020;20:1–9. doi:10.1186/s12887-020-02469-z
[d] Wilder JL, Parsons CR, Growdon AS, et al. Pediatric Hospitalizations During the COVID-19 Pandemic. Pediatrics 2020;146:e2020005983. doi:10.1542/peds.2020-005983

[e] Chelo D, Mekone Nkwelle I, Nguefack F, et al. Decrease in Hospitalizations and Increase in Deaths during the Covid-19 Epidemic in a Pediatric Hospital, Yaounde-Cameroon and Prediction for the Coming Months. Fetal Pediatr Pathol 2020;0:1–14. doi:10.1080/15513815.2020.1831664

[f] Akcaboy M, Terin H, Senel S. Changes in hospitalization in children during COVID-19 pandemic quarantine in a single center in Turkey. J Pediatr Published Online First: 14 December 2020. doi:10.1016/j.jpeds.2020.12.014

Also, please ensure British spelling throughout the abstract and Letter.

Thank you. We have checked spelling throughout the manuscript again.

3) "Further studies are expected to investigate the positive and negative aspects of these reduced hospitalisations"

Can the authors conclude the abstract with a stronger statement regarding the implication on health services? For example, did their study findings help to inform resource allocation for the current (or a future) pandemic?

We replaced the sentnece with a stronger sentence referring to resource reallocation.

(Page 3: paragraph 1)

"This study highlights the importance of reallocating paediatric care resources under the pandemic."

4) Letter

It is not clear what the authors mean by "children's environments" in the first sentence. Do they mean the utilization of paediatric health care services? Please rephrase.

We made this phrase clearer.

(Page 4: paragraph 1) "The COVID-19 pandemic has significantly affected children's social environments and access to healthcare services worldwide."

5) "However, little is known about the overall trends in emergency and non-emergency hospitalisations during the pandemic"

Again, this is not true, given the number of publications now available that describe the use of health services for children – I suggest to remove this sentence and instead to focus on how this Letter can value-add to the current literature.

As we stated above in the response to Point 2, we revised this sentence.

(Page 4: paragraph 1)

"However, little is known about the nationwide overall trends including non-emergency hospitalisations during the pandemic."

Regarding the "Diagnosis Procedure Combination inpatient database", more information is required: Is this a private insurance or a public data system? Are all Japan acute-care hospitals included in this database?

What does "272 continuously observed hospitals" mean?

We used a de-identified inpatient claims database for Diagnosis Procedure Combination/Per-Diem Payment System. In Japan, many acute-care hospitals are reimbursed for inpatient services through Diagnosis Procedure Combination/Per-Diem Payment System (this is similar to the Diagnosis Related Group [DRG] payment system in the US). This payment system is applied for all the beneficiaries of the public health insurance systems (public health insurance systems cover more than 99.9% of the Japanese residents). Therefore, this inpatient database included all the hospitalisation (reimbursed by public health insurance system) for each hospital during the study period. In the current study, we used a database constructed by Medical Data Vision Co, Ltd., which directly collected these claims data from acute-care hospitals that consented to the data utilization (part of acute-care hospitals in Japan).

We made the explanation clearer and added a reference for the payment system. In addition, we added the proportion of hospitalisations covered by our dataset. The phrase "272 continuously observed hospitals" means that these hospitals were continuously observed during the study period. To avoid readers' confusion, we deleted "continuously observed".

(Page 4: paragraph 2)

"We used a de-identified inpatient claims database collected under Diagnosis Procedure Combination/Per-Diem Payment System, built by Medical Data Vision Co, Ltd (Tokyo, Japan)[4]. Briefly, this payment system is part of public health insurance reimbursement system in Japan[5], and therefore, the database consists of demographic/clinical information of all the hospitalisations for each hospital. The database included 272 Japanese acute-care hospitals that consented to data utilisation (covering 12.4% of all admissions into acute-care hospitals in Japan in January 2019)."

On Page 6, the authors list the ICD 10 diagnostic codes that they aimed to trend. I suggest to remove the alphabets and just list the diagnostic codes. The current lettering extends across sentences and is confusing for the reader.

Following your suggestion, we deleted the alphabets. ICD10 code were stated in the legend of the Table (due to word limit).

(Page5: paragraph 2)

"We used nine common conditions (determined based on International Classification of Diseases 10 code), including food allergy, acute lower respiratory infections (ALRI) except COVID-19, Kawasaki disease (KD), intestinal infectious diseases (IID), febrile convulsions, asthma, appendicitis, inguinal hernia and trauma. "

Findings – can the authors explain why inguinal hernia hospitalisations decreased? It is intuitive that appendicitis did not see a similar trend to respiratory infections and asthma exacerbations, but generally surgical conditions cannot be accounted for by lockdown states

The decrease in inguinal hernia hospitalisations may be attributed to the deferred elective surgeries in week 13 because this week corresponds to the spring break in Japan and more surgeries seem to have been performed in this week in usual years. Thus, we stated this hypothesis in the discussion.

(Page7: paragraph 1)

"Second, deferred/cancelled treatment or examinations may explain the modest decrease in inguinal hernia hospitalisations, especially in week 13 (corresponding to the spring break) of 2020 compared with previous years."

In the discussion, the authors did not propose reasons why there should be such a large decline in so many diagnoses – was this the effect of school cancellation and reduction in infectious disease transmission? What about mask use in the public?

We think physical distancing measures including school closures and individual hygiene measures such as mask use in public lead to the reductions in infectious diseases. School closures and stay-at-home requests seem to have led to decreased trauma. We added these reasons.

(Page 6: paragraph 2)

"First, non-pharmaceutical interventions (physical distancing and individual hygiene measures) probably reduced infections. School closures and stay-at-home requests presumably decreased accidents."

The take-away from this Letter is not clear. It would be a stronger Letter if the authors can articulate why and how these trends would be useful for future resource planning.

Thank you for your suggestion. We agree to the reviewer that the reduced paediatric hospitalization during the early stage of the pandemic may allow policymakers/society to reallocare paediatric hospital resources to other areas (care for COVID-19, work in public health center). We added this suggestion in the manuscript.

(Page 6: paragraph 2)

"Our findings may encourage policymakers to reallocate paediatric care resources under the pandemic. There are several possible explanations for these reductions."

Reviewer: 3

1. In the abstract please be more explicit in the first sentence and state that you refer to the COVID-19 pandemic. Furthermore, provide numbers (proportions and 95% CIs) for the estimated drop in paediatric hospitalisations.

In the first sentence, we made the purpose of this study more explicit and referred to the COVID-19 pandemic. In addition, we added the percentage of the drop and the adjusted incidence rate ratio with 95% CI.

(Page 3: paragraph 1)

"We evaluated the nationwide overall trends in paediatric hospitalisations including non-emergency hospitalisations during the COVID-19 pandemic."

(Page 3: paragraph 1)

"Hospitalisation decreased during the COVID-19 outbreak by 38.4% (adjusted incidence rate ratio, 0.60;

95% confidence interval, 0.53-0.69)."

2.Although you report the IRR and the 95% CI for the incidence of paediatric hospitalisations, you did not provide 95% CIs for the disease-specific hospitalisations of food allergy, ALRI, KD, IDD, etc. Please be consistent throughout the manuscript.

We added 95% Cis for desease-specific hospitalisations.

(Page 6: paragraph 1)

"The weekly mean number of hospitalisations during weeks 9-21 decreased in 2020 compared with 2017–2019 for food allergy (0.61; 0.52-0.70), for ALRI (0.39; 0.26-0.58), for KD (0.77; 0.67-0.89), for IID (0.22; 0.17-0.29), for febrile convulsions (0.69; 0.57-0.84), for asthma (0.37; 0.29-0.47), for inguinal hernia (0.80; 0.67-0.95), and for trauma (0.68, 0.61-0.75). We found no evidence that the number of hospitalisations for appendicitis decreased (0.96; 0.82-1.12)."

3.The statement "These declines may partly suggest a reduced burden of paediatric disease, possibly due to non-pharmaceutical interventions" very shortly and poorly attempts to explain the reason for the decline in hospitalisations. The reasons for this reduction are numerous, yet some possible explanations should be presented accounting for the national recommendations.

We made "non-pharmacutical interventions" more specific and added the second reason, which account for the redcuction in inguinal hernia.

(Page 6: paragraph 2)

"There are several possible explanations for these reductions. First, non-pharmaceutical interventions (physical distancing and individual hygiene measures) probably reduced infections. School closures and stay-at-home requests presumably decreased accidents. Second, deferred/cancelled treatments or examinations may explain the modest decrease in inguinal hernia hospitalisations, especially in week 13 (corresponding to the spring break) of 2020 compared with previous years."