PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Acute paediatric asthma treatment in the pre-hospital setting: a retrospective observational study
AUTHORS	Craig, Simon; Delardes, Belinda; Nehme, Ziad; Wilson, Catherine; Dalziel, Stuart; Nixon, Gillian; Powell, Colin; Graudins, Andis; Babl, Franz

VERSION 1 – REVIEW

REVIEWER	Giudice, Michele Miraglia Del University of Campania Luigi Vanvitelli
REVIEW RETURNED	25-Mar-2023

GENERAL COMMENTS	Craig and coworkers' study shows that most children with asthmatic exacerbation do not require escalated therapy (in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators) during their pre-hospital treatment from ambulance paramedics. The work itself is interesting. I have some comments and revisions to improve the manuscript. 1) Were the patients included in the study already treated for asthma? Provide information on the therapeutic background of the patients. 2) Most patients who were assisted in pre-hospital settings were school-age children. There were some risk factors (allergy, obesity, coexisting respiratory diseases, etc...) in this group of patients that made them more likely to develop an acute asthma attack than others? 3) Line 33-35 page 11 'For those receiving bronchodilators, a median (IQR) of 1 (1-2) doses was administered'. What do the authors mean by dose? Does this sentence mean that they were administered a median of 1-2 puffs? According to the GINA guidelines for the management of asthmatic exacerbations should be administered SABA 4-10 Puffs by pMDI + spacer, repeated every 20 minutes for 1 hour. https///ginasthma.org/wp-content/uploads/2020/04//Main-pocket-guide_2020_04_03-final-wms.pdf. Please explain. 4) How many times has the administration of bronchodilators been repeated? Please specify.

	5) Specify in the text the administered dose of inhaled and nebulised salbutamol, inhaled and nebulised ipratropium and systemic corticosteroids depending on the mild, moderate, and severe clinical condition.

REVIEWER	Fainardi, Valentina University of Parma
REVIEW RETURNED	29-Mar-2023

GENERAL COMMENTS	Interesting data. Only a minor comment. Surprisingly, most cases looked like mild but still required ambulance intervention. Might be useful adding a comment on this. Were children not on daily therapy despite a diagnosis of asthma (not sure if you have data on that)? no asthma plan to follow? need of more education about asthma?

REVIEWER	Fingleton, James Te Whatu Ora Health New Zealand Capital Coast and Hutt Valley
REVIEW RETURNED	10-Apr-2023

GENERAL COMMENTS	The authors present the findings or a retrospective observational study looking at pre-hospital asthma care in Victoria, Australia. The main focus of the manuscript is the proportion of children requiring "escalated care", defined as need for respiratory support of parenteral adrenaline. The topic is of interest and the manuscript is well written. The study is clearly reported and in line with the STROBE guidelines. The analysis is descriptive and appropriate to the data available- the small number of patients receiving escalated care precludes a more detailed analysis. Limitations are appropriately acknowledged. Comments: The authors don't comment on whether there was any form of ethics review. If one occurred details should be provided and if they believe it was not required a statement to that effect would be reasonable. The authors do not specify if the protocol/analysis plan was finalised and shared publicly prior to analysis but as this is an exploratory/descriptive analysis this is not a major issue. The inclusion of all, or virtually all, ambulance call outs for the state is a strength of the dataset on which the paper is based. However there is relatively limited data presented about the details of care and outcomes. For example there is no information given on the range of medication doses administered and no information on final observations, e.g. respiratory rate and heart rate. It may be that this is a limitation of the dataset but if they are available the authors could consider including this data as it would strengthen the paper. The STROBE checklist contains a statement "Funding disclosures provided". I am unable to identify a funding statement in the manuscript and one should be provided, even if it simply states that this was an unfunded study. The checklist also states that the was "...no missing data" (point 14). This is extremely unlikely in

	any dataset, let alone a retrospective analysis of data collected during routine clinical care. The statement also appears at odds with the statement that respiratory status at initial assessment and hospital arrival were available for 85.5% of patients. I suggest the authors review this data and consider including the N for rows in the Tables where it does not match that given at the top of the column. In the unlikely event that complete data was available for all variables in all patients this is sufficiently unusual to be highlighted in the table legend and commented on in the text- were the variables the subject of mandatory reporting? There appear to be errors on a couple of rows in table 2. The number in the "Total" column should be the sum of the numbers in the two following columns. This is not the case for the rows "Any Salbutamol nebulisation" and "Three or more doses of inhaled salbutamol and at least one dose of ipratropium bromide", both of which are out by 1. I hope the authors find the above comments helpful in strengthening an interesting paper.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Michele Miraglia Del Giudice, University of Campania Luigi Vanvitelli

Comments to the Author:
Craig and coworkers' study shows that most children with asthmatic exacerbation do not require escalated therapy (in addition to standard treatment with systemic corticosteroids and inhaled bronchodilators) during their pre-hospital treatment from ambulance paramedics. The work itself is interesting. I have some comments and revisions to improve the manuscript.

1) Were the patients included in the study already treated for asthma? Provide information on the therapeutic background of the patients.

The ambulance data extract did not contain details of each patient's usual medications. I have added the following sentence to the results section: "Information on usual asthma medications was not available."

2) Most patients who were assisted in pre-hospital settings were school-age children. There were some risk factors (allergy, obesity, coexisting respiratory diseases, etc...) in this group of patients that made them more likely to develop an acute asthma attack than others?
We do not have information on children who did not have an asthma exacerbation.

3) Line 33-35 page 11 'For those receiving bronchodilators, a median (IQR) of 1 (1-2) doses was administered'. What do the authors mean by dose? Does this sentence mean that they were administered a median of 1-2 puffs? According to the GINA guidelines for the management of asthmatic exacerbations should be administered SABA 4-10 Puffs by pMDI + spacer, repeated every 20 minutes for 1 hour. https///ginasthma.org/wp-content/uploads/2020/04//Main-pocket-guide_2020_04_03-final-wms.pdf. Please explain.

We apologise, however, do not have information on exact medication doses for each patient. Our main focus for this study was the use of "escalated" care (beyond inhaled bronchodilators and systemic corticosteroids)

We have added the following sentence to the methods section: “Exact medication doses were not extracted, as treatment is highly protocolised (Box 1)” and have amended Box 1 to include Ambulance Victoria treatment protocols.

4) How many times has the administration of bronchodilators been repeated? Please specify.
We have changed the word “dose” to “administration” in table 1, and changed the wording in the text to “a median (IQR) of 1 (1-2) administrations were recorded.

5) Specify in the text the administered dose of inhaled and nebulised salbutamol, inhaled and nebulised ipratropium and systemic corticosteroids depending on the mild, moderate, and severe clinical condition.
We do not have information on the exact dose of each medication. A supplementary table has been added which provides high-level information on this matter, and a reference is made to it in the text: “With increasing severity of illness, children were more likely to be administered nebulised salbutamol, less likely to be administered salbutamol by a pMDI, more likely to receive ipratropium and more likely to receive systemic steroids (Supplementary Online Table).”

Reviewer: 2
Dr. Valentina Fainardi, University of Parma

Comments to the Author:
Interesting data. Only a minor comment. Surprisingly, most cases looked like mild but still required ambulance intervention. Might be useful adding a comment on this. Were children not on daily therapy despite a diagnosis of asthma (not sure if you have data on that)? no asthma plan to follow? need of more education about asthma?
We have added the following sentence to the discussion: “Although more than 60% had either mild or no respiratory distress, over 90% of all patients were transported to hospital.”
Unfortunately, we did not extract data on usual asthma medications, as the focus of our study was the administration of “escalated” (beyond inhaled bronchodilators and systemic corticosteroids) treatment.

Reviewer: 3
Dr. James Fingleton, Asthma Foundation Queensland and New South Wales Sydney

Comments to the Author:
The authors present the findings or a retrospective observational study looking at pre-hospital asthma care in Victoria, Australia. The main focus of the manuscript is the proportion of children requiring "escalated care", defined as need for respiratory support of parenteral adrenaline. The topic is of interest and the manuscript is well written.

The study is clearly reported and in line with the STROBE guidelines. The analysis is descriptive and appropriate to the data available- the small number of patients receiving escalated care precludes a more detailed analysis. Limitations are appropriately acknowledged.

Thank you for these positive comments

Comments:
The authors don't comment on whether there was any form of ethics review. If one occurred details should be provided and if they believe it was not required a statement to that effect would be reasonable.

We have included acknowledgement of ethics approval in the manuscript.

The authors do not specify if the protocol/analysis plan was finalised and shared publicly prior to analysis but as this is an exploratory/descriptive analysis this is not a major issue.
We did not publicly share the protocol / analysis plan prior to analysis.

The inclusion of all, or virtually all, ambulance call outs for the state is a strength of the dataset on which the paper is based. However there is relatively limited data presented about the details of care and outcomes. For example there is no information given on the range of medication doses administered and no information on final observations, e.g. respiratory rate and heart rate. It may be that this is a limitation of the dataset but if they are available the authors could consider including this data as it would strengthen the paper.

The lack of exact medication doses is a limitation of the extracted dataset (see response to Reviewer 1 above)
We have now added final observations and final respiratory status to Table 1.

The STROBE checklist contains a statement "Funding disclosures provided". I am unable to identify a funding statement in the manuscript and one should be provided, even if it simply states that this was an unfunded study.
Funding disclosures have been added to the main manuscript (they were originally included in the online submission, but not in the manuscript itself).
The checklist also states that the was "...no missing data" (point 14). This is extremely unlikely in any dataset, let alone a retrospective analysis of data collected during routine clinical care. The statement also appears at odds with the statement that respiratory status at initial assessment and hospital arrival were available for 85.5% of patients. I suggest the authors review this data and consider including the N for rows in the Tables where it does not match that given at the top of the column. In the unlikely event that complete data was available for all variables in all patients this is sufficiently unusual to be highlighted in the table legend and commented on in the text- were the variables the subject of mandatory reporting?
Thank you for pointing this out. We have identified the relevant missing data in Table 1 (there was some data missing for final observations), and mentioned this as a limitation of our paper: “There was some missing data on final observations on arrival to hospital, however, this was not a primary objective of our study.”
We have amended the STROBE checklist (item 14b) accordingly

There appear to be errors on a couple of rows in table 2. The number in the "Total" column should be the sum of the numbers in the two following columns. This is not the case for the rows "Any Salbutamol nebulisation" and "Three or more doses of inhaled salbutamol and at least one dose of ipratropium bromide", both of which are out by 1.
Thank you. We have corrected these typographic errors in the table.

I hope the authors find the above comments helpful in strengthening an interesting paper.

VERSION 2 – REVIEW

REVIEWER	Giudice, Michele Miraglia Del University of Campania Luigi Vanvitelli
REVIEW RETURNED	10-May-2023

GENERAL COMMENTS	The manuscript is improved and in its revised version can be accepted.

REVIEWER	Fingleton, James Te Whatu Ora Health New Zealand Capital Coast and Hutt Valley
REVIEW RETURNED	21-May-2023

GENERAL COMMENTS	The revisions have strengthened the paper and I recommend acceptance subject to one data check. I suspect there has been a transcribing error in the update to Table 1 as under final physiological parameters the respiratory rate and pulse rate are identical in the first and second columns, even down to the IQR. This is highly improbable. As long as this data is checked and amended where necessary I would recommend acceptance without further review.