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TITLE PAGE

An economic evaluation of nasogastric versus intravenous hydration in infants with bronchiolitis

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ABSTRACT

Background:

Bronchiolitis is the most common lower respiratory tract infection in infants and the leading cause of hospitalisation. We aimed to assess whether intravenous hydration (IVH) was more cost-effective than nasogastric hydration (NGH), as a planned secondary economic analysis of a randomised trial involving 759 infants (aged 2 to 12 months) admitted to hospital with a clinical diagnosis of bronchiolitis and requiring non-oral hydration. No Australian cost data exist to aid clinicians in decision making around interventions in bronchiolitis.

Methods:

Cost data collections included hospital and intervention-specific costs.) The economic analysis was reduced to a cost-minimization study, focusing on intervention-specific costs of IVH versus NGH, as LoS was equal between groups. All analyses are reported as intention to treat.

Results:

Intervention costs were greater for IVH than NGH (\$113 vs \$74; cost difference of \$39 per child). The intervention-specific cost advantage to NGH was robust to inter-site variation in unit prices and treatment activity.

Conclusion:

Intervention-specific costs account for <10% of total costs of bronchiolitis admissions, with NGH having a small cost saving across all sites.

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INTRODUCTION

Bronchiolitis is the leading cause of hospitalisation during the first year of life and is a major cause of morbidity and mortality.¹⁻⁶ In the United States of America bronchiolitis accounts for 21% of all hospital admissions for infants, with an estimated annual cost of \$390 to \$700 million.⁷ As the efficacy of bronchiolitis treatments is limited, international guidelines, including those of the American Academy of Pediatrics, recommend only supportive care of breathing and maintenance of hydration.^{1,2,6,8-12} Maintaining hydration is therefore an important component of the care of infants with bronchiolitis, with fluid replacement therapy being required in approximately 30% of infants admitted.¹³ Evidence to determine the optimum route of hydration therapy for infants has been limited, while evidence to inform the cost-effectiveness of alternative therapy options is scarce.

A recent study comparing intravenous hydration (IVH) with nasogastric hydration (NGH) in the treatment of inpatients with bronchiolitis has been performed by our team.¹⁴ Mean LOS in the NGH group was 86.6 (SD 58.9) hours compared with 82.2 (SD 58.8) hours in the IVH group with an absolute difference in LOS of 4.5 hours (95% CI -3.9, 12.9). NGH insertion was successful at the first attempt in 85.3% compared with IV insertion success in 62.4% ($p < 0.001$). Switching treatments was less common in the NGH group (13.1%) compared with the IVH group (25.1%); absolute difference 12.0% (95%CI 6.5% to 17.5%) $p < 0.001$. Overall there was a difference in the length of fluid treatment between arms with an average length of fluid treatment of 41.05 hours (SD 38.91) for IVH and 48.28 (SD 48.84) for NGH groups; absolute difference of 7.23 hours (95%CI 5.21, 9.25). There was no difference in the ICU admission rate (NGH 5.5% and IVH 6.6%) $p = 0.53$. There was no difference in adverse events between the groups, including: the incidence and type of complications of hydration therapy; ventilatory support; adverse events including desaturation, bradycardia, apnoea and pulmonary aspiration; local complications of the insertion methods; need for intravenous cannula or nasogastric tube replacement.¹⁴

This paper reports the economic evaluation of this recent study, and is undertaken to determine whether intravenous fluid replacement is more cost-effective at treating children admitted to hospital with a clinical diagnosis of bronchiolitis than nasogastric fluid replacement, determined by the 'cost per child discharged' ratio.

METHODS

Patients

The study was a three-year, open, randomized trial comparing NGH and IVH in children between two months and 12 months of age, admitted to hospital with bronchiolitis and requiring non-oral fluid hydration. Inclusion and exclusion criteria are described elsewhere.^{14,15} Recruitment was at 7 hospitals in Australia and New Zealand during the bronchiolitis season (April-October) between 2009 and 2011. The study received approval from the research ethics committee at all participating sites. The trial protocol (described in detail previously)¹⁵ was developed by the study investigators. Data were collected by research nurses and the study was overseen by an independent data monitoring committee. Funding agencies had no role in study design, data analysis or manuscript preparation. The trial was registered with the Australian and New Zealand Clinical Trials Registry, registration number ACTRN12605000033640.

Economic evaluation

The economic evaluation was designed to inform which of the treatment methods to use based on cost, rather than whether the treatment should be provided or not which may be influenced by many actors including treatment availability and family preference. As the intervention impacts primarily on the health sector, a health sector perspective was adopted focussing on the hospital as primary service provider (and government as '3rd party funder').

The primary study design was to be a cost-effectiveness analysis (CEA), where the outcomes were to be expressed in terms of 'cost per infant discharged' capturing both treatment-specific costs and associated LoS. Length of stay is of particular interest to health-care administrators, not only for its cost/revenue implications, but because it captures significant complications, case complexity and worsening of disease. In this case, as there was no statistical difference between the intervention and comparator in terms of the primary outcome (LOS), nor in the key secondary outcomes (Adverse Events and the rate of ICU admissions) a cost-minimisation analysis (CMA) was performed. This is the method of choice where equivalence in outcomes has been demonstrated and/or where researchers are prepared to accept there are no significant differences

in outcome. CMA is used to assess cost differences between arms of the trial, focusing on understanding associated cost drivers.

Outcomes

The primary outcome measured for this economic analysis is therefore the cost of each intervention arm and associated treatments.

Costs

All relevant resource costs to the hospital (the direct health care costs) associated with the NGH and IVH arms of the trial were identified through 'pathway analysis' and 'patient flowcharts'. Costs to the family or carers (the indirect health care costs e.g. child minding; travel expenses; time costs) were not included in this evaluation. All analyses are reported as 'intention to treat', with subsequent costs assigned to the allocated intervention group. All costs are reported in Australian dollars with New Zealand costs converted at the exchange rate of \$0.95.

Under the pathway costing approach all treatment activities are clearly specified (e.g. activity; staff involved; number of times activity occurs). All costs and events associated with the administering of each intervention and those that are a consequence of an adverse event were included. Prior to the start of the study a list of the likely resource cost categories (equipment, products, clinical staff time, etc.) was compiled (Table 1). An event series of activities involved with each intervention was then agreed between all investigators and sites (Table 2). Cost data including unit prices for all products, services and activities was collected from study hospitals using a costing template. The data was audited for any potential errors or significant variation across the 7 hospital sites. Staffing numbers and seniority were obtained from each hospital. An average procedure time was calculated from 20 procedures (10 of each intervention) at 5 different sites. An average cost per intervention (including equipment and staff time costs) was developed from this data.

The procedure (Nasogastric tube insertion or Intravenous insertion) were costed using the average cost per intervention. For the initial randomised intervention, a cost was allocated to each attempt at insertion. For patients crossing over to the alternate intervention the number of attempts at insertion were not recorded, so this is costed on all occasions as a single insertion attempt. Tests and unexpected interventions were costed individually with actual costs.

RESULTS

During the study period 759 infants were randomised to an intervention, 378 to the intervention (IVH) and 381 to the comparator (NGH). (Figure 1)

Cost of the treatment pathways

The costs of providing the assigned intervention were determined as a 'cost per child treated' to standardize total costs over the number of children per arm. The average cost per child treated was calculated using the average cost per procedure (confirmed in assessment of 20 procedures) with key elements set out in Table 2, and including equipment, staff grade, procedure time and the number of attempts at the procedures at randomisation. Group averages for the number of attempts, and number switching to the alternate intervention were used to calculate group intervention costs which were then divided by the number of infants in the group.

Using the 'cost per child assigned to treatment' result, there was a cost difference of \$39.01 in favour of NGH (Table 3). Subgroup analysis was conducted using the outcomes of each treatment arm stratified by age (2 months to <6 months and 6 months to <12 months) and by hospital site. The cost difference was lower in the 6-12 month age group (\$31.98 compared with \$45.60). The cost difference varied between sites, ranging from \$31.51 to \$67.08, with costs lower for NGH at all sites.

The largest drivers of cost were switching from one treatment arm to the other (25.1 IVH vs 13.1 NGH $p < 0.001$) and the failure of insertion of the intervention on the first attempt (62.3% IVH vs 85.3% NGH $p < 0.001$).

DISCUSSION

Bronchiolitis is a significant cause of hospital admissions in infants and a large cost burden on the health system.³⁻⁵ The largest driver of the cost of bronchiolitis admission is the hospital-related and bed day costs, which are tenfold greater than the intervention-related costs. The lack of difference in LoS between groups therefore made it unlikely that any substantial cost savings would be associated with either intervention. As switching between treatments was a large driver of cost it is of little surprise that hospitals with the greatest intervention-related costs had a higher proportion randomised to IVH who changed to NGH. The other largest driver of intervention cost was the number of attempts at insertion of the randomised treatment and the rate of switching from the randomised to the alternative intervention. Both of these were higher in the IVH group. Hospitals with higher unit prices naturally experienced higher costs across both arms, but this did not necessarily impact the size of the cost differences between arms.

One of the strengths of this analysis is that the measurement of both the costs and activities is sourced directly from the treating hospitals and from a large sample of patients across a number of different hospitals. Actual treatment-related cost differences were relatively small, but were consistently in favour of NGH across all sites and by age sub-group. A health service at the upper end of the range in this cost difference with a large number of patients admitted with bronchiolitis needing fluid replacement could be driven toward NGH.

This is the first analysis published of the costs of one of the key interventions in care of infants with bronchiolitis, and reinforces the recommendations in new clinical guidelines that NGH is an acceptable alternative to IVH, and may have some benefits in allaying hunger and associated agitation.⁶

LIMITATIONS

Whilst the number of attempts at inserting the intervention was captured for the assigned intervention, if a patient switched intervention, the number of attempts at inserting the second or subsequent intervention was not captured. This denotes that any costs associated with multiple attempts at inserting the switched intervention were not captured or allocated to the randomised treatment. Length of treatment (fluid duration) for the assigned treatment was not captured for 76/378 (20.1%) IVH patients compared to 30/381 (7.9%) of

NGH patients. As a greater proportion of patients randomised to the IVH group switched treatment, and a larger proportion had multiple insertion attempts it is likely the cost difference between the two treatment arms has been underestimated.

Costs of the intervention were not directly captured for each patient. They were estimated based on a set protocol of delivering the interventions. The personnel time required to insert each intervention was estimated based on the average time taken to successfully insert the intervention (based on data from 20 insertion attempts). This means the personnel costs assigned to patients who had the assigned intervention inserted on first attempt were identical to those that required multiple attempts. This would have underestimated the cost of IVH where more insertions attempts were undertaken.

The set protocol for NGH in the trial included the use of gastrolyte for the first two hours of hydration. This is not standard practice at most institutions and likely represents an unnecessary intervention and cost.

These limitations represent an overall uncertainty around the estimated treatment-related cost difference and suggest that it may be an underestimate. However the base cost and treatment activities relating to IVH were higher than NGH and IVH was more costly across all sites.

CONCLUSION

Costs associated with the intervention make up a small proportion (<10%) of the overall costs of hospital admissions with bronchiolitis, which is dominated by LoS. NGH appears to have a small cost saving, taking fewer attempts, less switching to alternative treatment arm, and having a higher success rate of insertion. This study provides a valuable insight into the costs and activities associated with the methods of fluid replacement therapy used in infants with bronchiolitis, and given the large number of admissions may present significant health system savings.

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Conflicts of Interest

Stuart Dalziel and Franz Babl are Section Editor, Paediatric Emergency Medicine, for Emergency Medicine Australasia.

Author Contribution:

All authors contributed to the design and implementation of the study, or analysis and interpretation of the study results. EO, FB, MB, JA, JN, DK, MS, AD contributed to all stages of the study. SDa contributed to the implementation of the study. EO was the principal investigator. SDo, and KJ performed the statistical analysis. KJ controlled the database. RC and BM ensured appropriate data collection for and performed analysis of the economic evaluation. EO, FB, MB, SDa, DK, JA, BM, RC contributed to interpretation of the results. All authors contributed to the manuscript preparation and review, and approved the final version. The report was written by EO.

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Table 1: Preliminary identification of cost categories

Study arm	Cost categories
IVH	<ul style="list-style-type: none">• Time taken to insert IV/ (mins)• Number and type of people assisting (e.g. nurse, doctor)• Disposables used (e.g. dressing packs, cannulas, tubing, Tegaderm™, Micropore™ tape etc.)• Other equipment or products used (e.g. fluid bag, IV line, Infusion pump, local anaesthetic cream etc.)• Additional tests (e.g. laboratory tests for electrolytes)• Any complications
NGH	<ul style="list-style-type: none">• Time taken to insert NGT (mins)• Number and type of people assisting (e.g. nurse, doctor)• Disposables used (e.g. tubing, Tegaderm™, Micropore™ tape, pH strips, syringes etc.)• Other equipment or products used, (e.g. gastrolyte solution, formula, pump, anaesthetic spray)• Additional procedures or tests (e.g. chest X-ray to confirm NGT placement)• Any complications

Table 2: Pathway analysis – specification of activities involved in fluid replacement

Intravenous Hydration (IVH)
<ul style="list-style-type: none">• Local anaesthetic cream applied to IV site and covered with Tegaderm™ patch for 30 minutes.• The skin then cleaned with chlorhexidine wash and cannula placed.• 10cm extension tube attached to cannula and saline used to flush IV tubing. Cannula then taped and bandaged to a backboard.• The extension tubing is then attached to 1000mL fluid bag containing 0.45% saline with dextrose (2.5%, 4%, or 5%) via an IV line, burette and I-MED pump. Fluids given continuously at 80% of daily maintenance• Laboratory tests, measuring electrolytes, urea and creatinine levels are costed to individuals as performed in the study• Bandage is changed daily• Tubing is replaced every 3 days requiring new tubing and disposables.
Nasogastric Hydration (NGH)
<ul style="list-style-type: none">• Local anaesthetic spray applied to nostril 2 minutes prior to NGT insertion.• Tubing, size 6 French <6 months of age and 8 French 6-12 months of age, is measured against child from nares to epigastrium to determine depth of insertion. Tubing then inserted to correct depth.• Tube placement confirmed by aspiration of stomach contents using 5mL syringe to draw sample of stomach contents which are applied to pH strip. If pH less than 4, tubing secured to face using Micropore™ tape and Tegaderm™. If pH greater than or equal to 4, aspiration is repeated after 30 minutes. If unable to confirm placement, abdominal/chest X-ray performed to confirm position of tube prior to use. If any doubt of placement, tubing removed and replaced, and procedure repeated. X-ray and replacement tubes costed to individuals as performed in the study.• Oral rehydration powder, prepared using single sachet added to 200mL boiled water; given

continuously for 2 hours.

- Infants then given normal feed of either formula or expressed breast milk (EBM), continuously or 2 hourly bolus with the total volume of fluid being 80% of daily maintenance.
- Tubing replaced every 3 days requiring new tubing and disposables as above.

Table 3: Cost results presented as ‘cost per child treated’ for each arm and by age group

	N		Estimated cost of treatment*		Cost
	NGH	IVH	NGH	IVH	Difference
Total population	381	378	\$74.30	\$113.31	\$39.01
By Age					
<6 months	201	196	\$75.75	\$121.34	\$45.60
6-12 months	180	182	\$72.68	\$104.66	\$31.98

Notes

*Costs associated with a patient switching from one intervention to the other and all subsequent treatment costs were assigned to the original randomised treatment group to give the real cost of each treatment arm.

Prices are reported in ‘real prices’ for the reference year of the clinical trial (2009). All cost estimates are ‘intention-to-treat’.

Table 4: Variation in ‘cost per child treated’ across the participating hospital sites

	N		Estimated cost of treatment		Cost difference
	NGH	IVH	NGH	IVH	
Total population	381	378	\$74.30	\$113.31	\$39.01
By site					
Hospital 1	109	107	\$76.11	\$116.16	\$40.05
Hospital 2	25	25	\$82.02	\$125.24	\$43.22
Hospital 3	36	37	\$59.53	\$119.43	\$59.90
Hospital 4	20	18	\$64.17	\$104.27	\$40.10
Hospital 5	103	102	\$76.28	\$107.78	\$31.51
Hospital 6	24	25	\$58.89	\$103.87	\$44.98
Hospital 7	64	64	\$48.31	\$115.39	\$67.08

Notes

All cost estimates are ‘intention-to-treat’. Prices are reported in ‘real prices’ for the reference year of the clinical trial (2009) and converted to \$Australian for the New Zealand sites.

FIGURE LEGEND

Figure 1: Eligibility and Randomisation

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