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Using preceding hospital admissions to identify children at risk of developing acute rheumatic fever

Original article

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Abstract

Aims

New Zealand (NZ) M ori and Pacific children have high rates of acute rheumatic fever (ARF). Around 150 new cases arise each year. As part of the national ARF prevention programme, funding is available to improve housing. To obtain maximum benefit from interventions, an effective tool is needed for targeting high-risk children. This study aimed to assess the effectiveness of using hospitalisations for identifying children at-risk of subsequent ARF.

Methods

Three potentially avoidable hospitalisation (PAH) groups were investigated, containing diseases thought to be influenced by housing. All were developed using expert opinion or systematic reviews. These were: 1. The PAH conditions associated with the housing environment (PAHHE) group, 2. The Crowding group, and 3. The Ministry of Health (MoH) group. We analysed NZ public hospital discharge data (2000-2014). The prevalence of ARF among patients hospitalised in each group was calculated to estimate sensitivity and potential effectiveness. The number needed to screen (NNS) to identify one ARF case was estimated as a measure of efficiency.

Results

Nearly one-third of ARF patients experienced a PAH as children (before developing ARF). Sensitivity for detecting future ARF ranged from <5% (MoH group) to 27% (PAHHE group). NNS ranged from 502.4 (PAHHE) to 707.5 (MoH).

Conclusions

Because ARF is relatively rare, observing hospitalisations is not particularly efficient for targeting prevention activities for this condition alone. However, housing interventions are

likely to improve multiple outcomes, thus the hospital setting is still useful for identifying at-risk children who could benefit from such programmes.

Introduction

Acute rheumatic fever (ARF) and its sequelae rheumatic heart disease (RHD) represent an important burden of disease throughout much of the world.(1) ARF is an inflammatory disease which presents in 0.3-3% of untreated people following an episode of group A *Streptococcus* (GAS) pharyngitis.(2, 3) GAS skin infection may also trigger ARF.(4) ARF incidence rates peak in 5-14 year old children and RHD typically presents in adulthood.

Once common across the world, ARF rates have declined dramatically in most Western countries over the last century.(5, 6) Improvements in socioeconomic conditions and increasingly widespread use of antibiotics to treat streptococcal infections may have contributed to the decline.(7-11) This view is supported by research showing that ARF is associated with socioeconomic and living conditions.(12, 13) Previous studies have identified associations between ARF/RHD and poor housing conditions,(14-17) sometimes including home crowding.(12, 13, 18, 19) It is possible that cold, damp living conditions promote GAS infection by weakening immune and respiratory defences.(20) Crowding could facilitate GAS transmission.(21) ARF remains an important public health problem in many low-income countries(22, 23) and persists in certain (predominantly indigenous-minority) populations in high-income countries.(24) ARF rates in Indigenous Australians and New Zealand (NZ) M ori and Pacific peoples are among the highest in the world.(5, 25, 26)

In NZ, ARF cases are almost exclusively M ori and Pacific.(27-29) M ori and Pacific peoples are also dramatically over-represented in RHD prevalence rates and early mortality statistics.(30) In 2012 the NZ Government set a goal of reducing ARF by two-thirds by mid-2017, hence ARF became the focus of an extensive national Rheumatic Fever Prevention Programme (RFPP), however the reduction target was not met.(27)

An opportunity to improve health outcomes involves identifying children at high risk of ARF and implementing targeted interventions.(31) Admission to hospital with a preventable condition provides an obvious intervention point, as these children are likely to go back into a similar high-risk environment once discharged.(32, 33) Housing interventions could prevent a significant burden of future child mortality and morbidity.(33) As part of the RFPP, funding

is available to improve housing for some children hospitalised with specific conditions, such as pneumonia, with the hope of preventing ARF.(27, 34)

To obtain maximum effectiveness from targeted interventions, an effective tool for screening patients at the time of hospitalisation is necessary. A number of disease groups have been developed with the aim of identifying potentially avoidable hospitalisations (PAH) in children that are influenced by the home, crowding, socioeconomic conditions and the physical environment.(35) One is the PAHHE group.(36) The Crowding group aims to identify PAH associated with household crowding.(37) A third group, currently in use by the NZ Ministry of Health (MoH), includes children with infectious and other PAH conditions thought associated with an increased risk of ARF.(34) All three groups are for use in the NZ child population and were developed based on expert opinion and published literature. Most other grouping systems hold more relevance to adult populations.(38) Our previous research indicated that children hospitalised in these three groups would likely benefit from housing interventions to prevent future poor health, especially those in the MoH group.(33)

The aim of this study was to assess the effectiveness of different screening groups for identifying children with an increased risk of ARF using national hospitalisation data. This information is important as it could enable effective targeting of ARF prevention interventions to children who would benefit significantly.

Methods

Data and ethics

Ethics approval was obtained from the University of Otago Ethics Committee (No. HD15/046).

We obtained national hospitalisation data for the 15-year period 2000-2014 from the NZ National Minimum Dataset, including all acute, arranged and waiting list admissions. The encrypted National Health Index number (NHI) was used to identify and link individuals' hospitalisations over time. No entries lacked encrypted NHI numbers; consequently, patients' initial hospitalisations could be distinguished from later ones. Both principal and additional discharge diagnoses were used to identify ARF cases and preceding admissions.

The programme R 3.2.2(39) was used throughout the analysis.

Screening groups

The ability of three different condition groups to detect children who subsequently developed an initial episode of ARF was assessed. These groups were:

- The PAHHE group, which identifies PAH possibly avoided by "Central and local government policies which ensured that families with children had access to high quality housing and a safe physical environment (eg. availability, quality and affordability of state and other housing options)".(36)
- The Crowding group, which identifies a set of conditions associated with household crowding based on a systematic literature review.(37) The scope was further refined, based on published disease groupings.(40)
- Ministry of Health (MoH) group, which target conditions thought strongly associated with ARF.(34)

Individual diseases in each group are listed in Table III and were selected for further investigation. Only children hospitalised aged 1-15 years old were included. Children aged less than 1 year old were excluded due to the unique disease susceptibilities of this age

group.(41) Repeat hospitalisations for the same condition occurring within 30 days of last discharge were considered to be a single event.

Statistical methods

All cases where a principal diagnosis of ARF (ICD-10 codes I00-I02) had been applied during the 2000-2014 period were extracted. A subset of initial ARF hospitalisations was created by identifying and removing subsequent ARF hospitalisations for included individuals and including all admissions that remained. Any ARF patient who received a diagnosis of RHD prior to their initial ARF admission was then removed. No other exclusions applied. Demographic characteristics of individuals in the initial ARF hospitalisation dataset were described.

The number and proportion of ARF patients hospitalised in each of the three groups when aged 1-15 years old, before they received their initial ARF diagnosis, was noted. The effectiveness and efficiency of each group for detecting children who went on to develop ARF was calculated. The prevalence of ARF among patients hospitalised for individual diseases in each group was calculated. Denominator data were based on NZ census population estimates.(42)

All analyses were repeated on datasets containing only individuals of M ori or Pacific prioritised ethnicity. A subset of children hospitalisations from 2000-2004 was also created and analysed in the same way as the entire 2000-2014 cohort.

Prioritised ethnicity identifies individuals belonging to more than one ethnic group and allocates them to a single ethnic group based on a prioritised order of M ori, Pacific, Asian and Other. For example, a person who identifies as M ori and Pacific will be classified as M ori only.(43)

The 2006 New Zealand Index of Deprivation classification system measures the level of socioeconomic deprivation for people in each small area based on 2006 Census data.(44) Quintile 1 represents people living in the least deprived areas and Quintile 5 represents people living in the most deprived areas.

Screening effectiveness and efficiency

We used a standard screening approach to assess effectiveness and efficiency of the three groups. The sensitivity, specificity and PPV for detecting patients who subsequently developed ARF was calculated. We calculated the number needed to screen (NNS) to detect a single case of ARF as a measure of efficiency, and the mean number of cases that could potentially be prevented per year - with the assumption that, once hospitalised, a housing intervention would be delivered that would successfully prevent ARF.

Results

Total hospitalisations

Over the period 2000 – 2014, a total of 1,425,085 hospitalisations occurred in the 1-15 year old age group. This included 275,818 children hospitalised a total of 413,316 times for conditions in the PAHHE group (which comprised 29.0% of all hospitalisations for this age group). Slightly fewer admissions, 365,249 (25.6% of all hospitalisations) occurred for 243,791 children in the Crowding group. The smallest group, the MoH group, included 67,918 children, with 88,712 admissions (or 6.2% of total hospitalisations).

ARF hospitalisations

There were 2,035 patients hospitalised with initial diagnoses of ARF during the study period, 61% of whom were <16 years old. Table I describes key demographic characteristics of these patients.

Table I: Key demographic characteristics of all patients with new presentations of ARF hospitalised in New Zealand during the period 2000-14

Detecting previous hospitalisations

Of the total 2,035 ARF cases, n=1,306 (64.2%) had a previous hospitalisation recorded over the 2000-14 period. When admissions that were not specific to illness or injury were removed (ie. for maternal, perinatal or congenital conditions, ICD-10: O00-Q99 and Z00-Z99),(40) and admissions were restricted to patients aged <31 years old at the end of the study period, a total of 813 (40.0%) of patients were hospitalised >30 days before their initial ARF admission. Thus 40.0% sensitivity was the highest possible for identifying future ARF cases.

Performance of PAH groups for identifying future ARF

A smaller minority of children (n=617) were hospitalised for a condition in any of the three PAH groups and went on to develop ARF. These 617 patients comprised 30.3% of the total ARF cases arising over the study period. Table II summarises the performance of each group for detecting these children using a range of screening performance measures.

Table II: Screening performance of different PAH groups for detecting children who subsequently developed ARF, 2000-14

The PAHHE group demonstrated the best sensitivity for detecting children who went on to develop ARF (27%). Crowding group sensitivity was 22% and the MoH group demonstrated the lowest sensitivity (<5%). All groups demonstrated correspondingly higher specificity. The PAHHE group also demonstrated the best (lowest) NNS (502.4), compared with the Crowding group (547.8) and the MoH group (707.5). As ARF is rare, PPVs were correspondingly very low.

Efficiency rose when the analysis was limited to hospitalisations with at least 10 years of follow-up time (study period 2000-2004). Here the MoH group provided the lowest NNS (N=486.9). Sensitivity for all groups was low (<15%). When restricted to M ori and Pacific peoples, the sensitivity remained low, and the PAHHE group provided the lowest NNS (N=459.7, see: Appendix).

The mean number of ARF cases that could have potentially been avoided each year, had a successful intervention been delivered, was 5.0 for the PAHHE group, 3.8 for the Crowding group and 0.9 for the MoH group (based on screening performance presented in Table II).

Potentially avoidable conditions preceding ARF

Table III shows the prevalence of subsequent ARF in children who were hospitalised with individual diseases in the three PAH groups. GAS sepsis patients demonstrated the highest prevalence of future ARF (735 per 100,000 patients), followed by bacterial meningitis, and meningococcal disease patients. When restricted to M ori and Pacific, patients with GAS

sepsis again demonstrated the highest prevalence of ARF (1290 per 100,000), followed by patients with meningococcal disease, and acute nephritis. When restricted to children for whom we have at least ten years of follow up data for, bacterial meningitis patients demonstrated the highest ARF prevalence (652 per 100,000), followed by meningococcal disease and acute bronchiolitis patients.

None of the seven 'highest' prevalence conditions alone preceded more than a small (<8%) proportion of all ARF. These conditions were otitis media, skin infection, asthma, acute URTI, gastroenteritis, viral infection of an unspecified site and non-viral pneumonia. Collectively, these seven conditions preceded a total of 28% of ARF cases. The total number of admissions for these conditions was 510,127, so the number needed to screen to detect a single subsequent case of ARF was 895.

Table III: The prevalence of subsequent ARF hospitalisation in children hospitalised with individual diseases in PAHHE, Crowding and MoH groups, 2000-14

Discussion

To our knowledge, this study is the first to investigate the use of hospitalisations as a tool for identifying children at high risk of a subsequent disease event, in this case ARF. Many patients who develop ARF were admitted to hospital with another condition first in childhood – importantly, a condition considered potentially avoidable due to environmental factors. This hospitalisation provides a potential intervention point for preventing poor future health outcomes.(33) As prior hospitalisations were distributed over a large number of conditions, it is hard to specifically identify which children face the highest risk of ARF. Of the groups explored, the PAHHE group is the most sensitive (27%), but its efficiency is limited. Preventing these 549 children from subsequently developing ARF would require identification and successful intervention for all 275,818 hospitalised children, which implies a number needed to screen of 502.4 children (and a PPV <0.01). Despite limited efficiency for ARF prevention, a significant burden of child death and repeat hospitalisation might still be avoided through housing intervention targeted to this group.(33)

The study findings highlight the importance of addressing the social determinants of health (rather than the health determinates of health, such as prior illness) to achieve social justice and improve health outcomes overall. As expected, ARF is concentrated in the most deprived socioeconomic groups. Thus, short of a highly effective and widely available GAS vaccine (an important 'vaccine against poverty'), it appears likely that reducing poverty is the most important intervention to reduce ARF and other streptococcal diseases.(45)

As ARF is a rare disease, it is not useful as an outcome measure when evaluating housing improvement programmes – the successes of which are likely to be far-reaching and spread across the entire life-course. An outcome measure with a much higher incidence, such as PAHHE, may be much more useful to measure the effectiveness of interventions.(33) Such conditions should be relevant to the population of interest, and thus may vary according to the country income level and other socio-demographic factors. The ability of the NZ Government sector to effectively deliver housing interventions on a large scale has been clearly demonstrated. The Healthy Housing Programme in Auckland reduced rates of paediatric infectious disease hospitalisations by one-third,(46) and the Warm Up New Zealand: Heat

Smart programme provided free or subsidised insulation to over 300,000 homes with an estimated net savings benefit of nearly $1 billion (NZD).(47)

A major strength of this study is the ability to investigate the risk of ARF in a full national cohort of hospitalised children. Additionally, most diagnosed ARF cases would have been included because hospitalisation is the standard of care. As complete count data were analysed, not study samples, there is no random error in our calculations, or any need for confidence intervals. That the PAHHE group (which contains the largest number of conditions) accounted for nearly 30% of total hospitalisations for children over this observation period is consistent with previous estimates that a quarter to half of all NZ child hospitalisations are potentially preventable.(35)

ARF risk estimates using previous hospitalisations are likely under-estimates. Some children, particularly those of Pacific ethnicity, will have spent time living in other countries so would not have previous hospitalisations recorded in NZ. Furthermore, admissions in infancy (<1 year) were excluded. Conditions affecting this age group may have different associations with environmental factors than in older age groups. However, exposures during infancy might also have long-term effects on immune function and could therefore operate as risk factors for ARF. Future research could investigate this association and other possible effects of PAH in the first year of life. Additionally, many ARF cases are not diagnosed or hospitalised and only become apparent when they present with established RHD later in life.(48)

One limitation in the causal logic of this analysis concerns the association of included diseases with poor quality housing.(36) While the PAH groups were developed by child health experts or were based on systematic reviews, the extent to which housing influences the occurrence rates of these diseases (including ARF) has not been thoroughly quantified.(33)

Similarly, this analysis has not considered the temporal association between PAH and ARF. Both left- and right-censoring issues are apparent. ARF cases diagnosed in 2000 had little time for a PAH to be captured, while cases aged >29 years in 2014 were >15 years old in 2000 – and their PAH were excluded. This is defensible as the PAH criteria were specifically

designed for use in child populations and housing interventions that target children can produce beneficial effects across the entire life course.(36, 45) The 2000-2004 dataset attempted to reduce right-censoring by allowing PAH cases at least 10-years of follow-up time in which to develop ARF. Despite this, low sensitivity for ARF was still apparent. False negative cases could potentially be reduced by following a birth cohort aged 1 year-old in 2000 and observing PAH and ARF admissions. However, this approach could reduce case finding sensitivity further as it would remove around a quarter of ARF cases (those born before 2000), some of whom would have prior PAH admissions. The only criteria considered in this analysis were that the PAH admission needed to occur prior to the ARF hospitalisation, so the interval between these events could be a few weeks up to almost 15 years. The likely effectiveness and practicality of intervening to improve housing conditions to prevent ARF and other conditions is likely to be strongly influenced by the causal pathways and temporal relationships that operate. Another measurement issue is that some children diagnosed as initial ARF cases will have been recurrences that had not been previously clinically detected.(5).

A limitation around the use of the NNS is that it refers to absolute, not relative, risk and thus may only be generalisable to populations where ARF and RHD are prevalent, such as sub-Saharan Africa, India and Pakistan.(49)

Interventions that improve housing quality and reduce crowding may reduce the risk of ARF. Such interventions may enhance immunity and reduce transmission of GAS infections.(20, 21) However the NNS in the NZ hospital setting to prevent one ARF case are high, because ARF is much less common than hospitalisations for many other conditions. Nevertheless, housing and other broad, multi-sectoral interventions are likely to provide an effective means of reducing childhood deprivation and improve multiple social, educational and health outcomes. Consequently, the hospital setting is still likely to provide a useful base for identifying at-risk children who could benefit from a range of interventions.(33)

Conclusion

The hospital setting provides an opportunity to identify vulnerable children and provide them with housing interventions which could prevent future poor health, including ARF. Because

ARF is relatively rare, this approach is not particularly efficient for targeting prevention activities for this condition alone. Effective, large-scale housing interventions have good potential to reduce the burden of a wide range of preventable diseases, if judiciously targeted to high-risk (ie. deprived M ori and Pacific) children. Scoping for such programmes could begin in areas with a high incidence of ARF, with an emphasis on incorporating well-integrated referral pathways, and delivering timely intervention to children at highest need. Useful outcome measures should be pre-defined and used to periodically evaluate the programme success.

What is already known on this topic:

- ARF and RHD cause an important and preventable global burden of disease.
- Associations between ARF and poor housing conditions have been reported.
- A number of condition groups can be used to identify potentially avoidable hospitalisations associated with the home environment (PAHHE).

What this study adds:

- Nearly one-third of ARF patients experienced a PAHHE as children, before they developed ARF.
- The hospital setting provides an opportunity to identify vulnerable children and provide them with housing interventions which could prevent future poor health, including ARF.
- ARF is a rare disease, so a more common health outcome, such as repeat hospitalisation for certain conditions, could be useful for evaluating the success of housing intervention programmes.

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Contributors' Statements:

Jane Oliver: Carried out the analyses, drafted the initial manuscript and carried out revisions, and approved the final manuscript as submitted.

Tim Foster: Assisted with carrying out the analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Deborah Williamson: Critically reviewed the manuscript, and approved the final manuscript as submitted.

Nevil Pierse: Conceptualized and designed the study, provided guidance on the statistical analyses, critically reviewed and revised the manuscript, and approved the final manuscript as submitted.

Michael Baker: Assisted in the study design and guided the write up, critically reviewed and revised the manuscript, and approved the final manuscript as submitted.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Tables

Table I: Key sociodemographic characteristics of all initial ARF hospitalisations in New Zealand during the period 2000-2014[1]

<5	10	0.5
5-14	1194	58.7
15-29	521	25.6
>29	310	15.2
Male	1094	53.8
Female	941	46.2
Māori	928	45.6
Pacific	802	39.4
European/Other	305	15.0
Quintile 1	74	3.6
Quintile 2	86	4.2
Quintile 3	174	8.6
Quintile 4	390	19.2
Quintile 5	1287	63.1
Missing	24	1.2

[1] Patients described are all those who received an initial diagnosis of ARF, regardless of whether they experienced a PAH prior to developing ARF.

Table II: Effectiveness analysis by group

		27.0%
		81.7%
		0.002
		502.4
		21.9%
		83.8%
		0.002
		547.8
		4.7%
		95.5%
		0.001
		707.5

Table III: The prevalence of subsequent ARF hospitalisation in children hospitalised with individual diseases in the PAHHE, Crowding and MoH groups over a 15 year period (2000-14)

Acute bronchiolitis	J21	PAHHE, Crowding & MoH	14	0.7	10388	134.8	184.3
Acute nephritic syndrome	N00, N05	MoH	13	0.1	2905	447.5	452.1
Acute upper respiratory tract infection excluding croup	J00-J03, J06	PAHHE, Crowding	70	3.4	75703	92.5	86.8
Asthma	J45, J46	PAHHE, & Crowding	84	4.1	78941	106.4	188.3
Bacterial meningitis	G00, G01	PAHHE, Crowding & MoH	5	0.2	992	504.0	285.3
Bronchiectasis	J47	PAHHE, Crowding & MoH	0	0.0	4804	0.0	0.0
Croup, acute laryngitis,	J04, J050	Crowding	0	0.0	621	0.0	0.0

tracheitis							
GAS sepsis	A400	Crowding & MoH	1	0.0	136	735.3	1298.7
Gastroenteritis	A00-A09, R11, K529	Crowding	50	2.5	74899	66.8	201.9
Meningococcal disease	A39	PAHHE, Crowding & MoH	10	0.5	2133	468.8	641.9
Non-viral pneumonia	J13-J16, J18	PAHHE, Crowding & MoH	47	2.3	41412	113.5	213.8
Otitis media	H65-H67	PAHHE & Crowding	160	7.9	126906	126.1	313.4
Skin infection	L00-L05, L08, L980, J340, H010, H000	PAHHE	107	5.3	52673	203.1	299.8
Tuberculosis	A15-A19	PAHHE & Crowding	0	0.0	330	0.0	0.0
Viral / other / unspecified meningitis	A87, G02, G03	Crowding & MoH	4	0.2	2244	178.3	237.9
Viral infection of unspecified site	B34	PAHHE	52	2.5	59593	87.3	182.3
Viral	J12,	PAHHE,	0	0.0	4343	0.0	0.0

pneumonia	J100, J110	Crowding & MoH					