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Improving vaccination cold chain in the general practice setting

Background
This study compared temperature control in different types of vaccine storing refrigerators in general practice and tested knowledge of general practice staff in vaccine storage requirements.

Methods
Temperature data loggers were set to serially record the temperature within vaccine refrigerators in 28 general practices, recording at 12 minute intervals over a period of 10 days on each occasion. A survey of vaccine storage knowledge and records of divisions of general practice immunisation contacts were also obtained.

Results
There was a significant relationship between type of refrigerator and optimal temperature, with the odds ratio for bar style refrigerator being 0.005 (95% CI: 0.001–0.044) compared to the purpose built vaccine refrigerators. Score on a survey of vaccine storage was also positively associated with optimal storage temperature.

Discussion
General practices that invest in purpose built vaccine refrigerators will achieve standards of vaccine cold chain maintenance significantly more reliably than can be achieved through regular cold chain monitoring and practice supports.

In the past 10 years, Australia has achieved control of many vaccine preventable diseases with very high routine vaccination coverage. Internationally, there is considerable investment in the provision of cold chain guidelines and education for vaccine providers.[1] Breaks in the cold chain are not uncommon in the general practice setting,[2] with compliance to storage guidelines particularly unacceptable where vaccines are stored for more than 8 weeks.[3] Exposure to unacceptably cold temperatures is more common than overheating vaccines, even in hot climates[4–6] and as many as one-quarter of general practice refrigerators may be freezing vaccines.[7] The loss of potency for vaccines that are freeze sensitive is immediate, and hepatitis B vaccine has been identified as being most at risk.[8]

Maintenance of the cold chain is a vital component in ensuring an effective vaccine is administered. Vaccine stability varies dramatically by type. Bacille Calmette-Guerin (BCG), measles, mumps, rubella (MMR), and oral polio vaccine (OPV) vaccines are unstable at room temperature; diphtheria, tetanus and pertussus (DTPa), MMR, OPV, and meningococcal C conjugate vaccines need to be protected from light; and DTP, haemophilus influenza B, hepatitis A and B, meningococcal C conjugate, pneumococcal and influenza vaccines are all unstable if frozen.[9] Field evaluations of vaccine safety demonstrate an increased rate of local reactions associated with incorrectly stored vaccines.[10] Australia does not have a consistent approach to measuring vaccine wastage,[11] but failures were recorded across all 19 of the delivery areas in South Australia in 1 year.[12]

Electronic monitoring with direct feedback of storage temperatures is effective in correcting adverse storage at most suboptimal sites,[13] and is also a useful tool in achieving changed policy and practice.[14] Educating a staff member on correct vaccine storage conditions and nominating that person to be responsible for monitoring refrigerator temperatures improves adherence to vaccine storage guidelines.[15] This result is further improved if the staff member is senior, qualified, and

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has had recent contact with immunisation program providers.[16] Quality improvement activities with specific advice such as not storing vaccines in the refrigerator door can improve compliance, even when baseline compliance is high.[17] Vaccine vial monitors provide a continuous check on maintenance of cold chain preservation, but are limited in that they can't capture all micro climate temperature variations that can deactivate immunisation products.[18,19]

Domestic refrigerators are the most common choice for vaccine storage in general practice,[20] and are generally of three types: frost free, cyclic defrost, and bar refrigerators. Temperature control may be uneven in different areas of such refrigerators. In contrast, purpose built vaccine refrigerators feature a stable, uniform, and controlled cabinet temperature unaffected by ambient temperature. Their defrost cycle allows defrosting without rises in cabinet temperature.[21,22]

The Northern Rivers General Practice Network (NRGPN) in northern New South Wales was concerned about unacceptably high regional rates of vaccine preventable disease. In addition to commencing a multistrategy program to improve low vaccination rates, we performed an audit of standard practice procedures, including cold chain adherence, and initiated a continuous education and quality improvement program to support vaccine providers.

Methods

The aim of this study was to determine the predictors of optimum temperature control for vaccine storage in general practice settings, including refrigerator type and knowledge of vaccine storage. We obtained temperature recordings from refrigerators used to store vaccines in general practices in the NRGPN area and examined predictors of optimal temperature, including refrigerator type, frequency of practice contact with the NRGPN and vaccine knowledge, as assessed by a vaccine knowledge score using generalised estimating equations models.

For measurement of refrigerator temperatures, two types of continuous electronic temperature data loggers were used, randomly distributed to participating general practices: Hobo® and Tinytag® ultra. All loggers were in the range of 0.2°C of each other when tested for calibration in an ice slurry test before data collection. Loggers were placed in the middle of the refrigerator in the vicinity of the thermometer probe used by the practices. Refrigerator temperatures were monitored at 12 minute intervals over a period of 10 days. Loggers were placed on the top and bottom shelf of each refrigerator tested in order to assess refrigerator variation in temperature by refrigerator type.

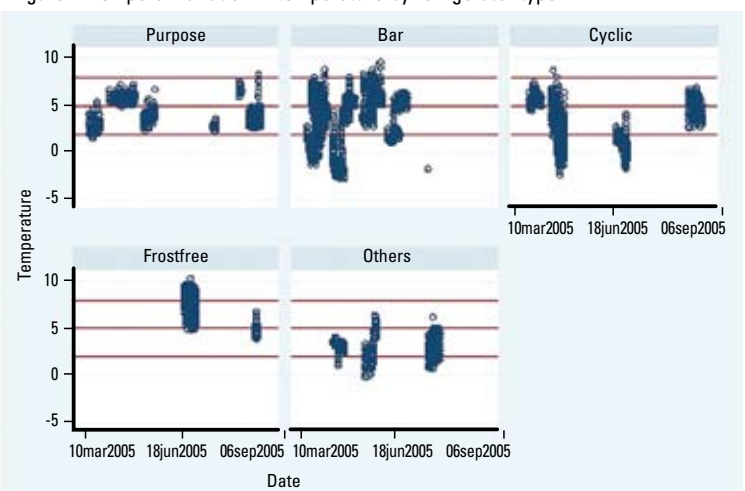
All 32 general practices in the NRGPN local area were approached to participate. One practice refused while three practices commenced logging temperatures but removed the loggers after a couple of days; one because the refrigerator had been disturbed during a burglary, and two for concerns about the inaccuracies of refrigerator thermometer readings against the data loggers – the practice thermometers were proved to be malfunctioning.

Of the 28 practices completing the study, 10 (36%) had bar style refrigerators (one changing to purpose built during the study), six (21%) cyclic, two (7%) frost free, eight (29%) purpose built, and three (11%) had other refrigerator types, including a display refrigerator and a top loading refrigerator.

Practices were categorised by frequency of contact with the NRGPN as a proxy for awareness of vaccine storage guidelines. Seventy-five percent had three or more contacts with the NRGPN, 11% had one or two previous contacts, and 14% were first contacts, for the division.

The main outcome measure was optimal temperature, being coded for 2–8°C. As there was serial autocorrelation in the data, and temperature readings expected to be clustered within the various general practices, we used generalised estimating equations (GEE) models to analyse the data. The primary feature of this method is that it estimates the correlation structure in the data from replications across practices and time periods. Ignoring this correlation can give estimates with an incorrect standard error and spurious significant results. We ran several univariate GEE models examining the impact of each of the covariates on the outcome. Odds ratios and their corresponding 95% confidence intervals were computed as estimates of effect size. We used the GEE model to compare the difference between the two readings (for the same refrigerator) across the various practices.

Figure 1. Temporal variation in temperature by refrigerator type



For the multivariate analysis, we added covariates sequentially, and reported the adjusted effect size for refrigerator type. Data analysis was performed in Stata V9.2. All tests were conducted at the 5% level of significance.

A secondary analysis was performed on knowledge of vaccine storage required temperatures in the general practices in the study. The vaccine storage score point system was based on a survey consisting of 10 questions assessing knowledge of cold chain recommendations according to the guidelines in the 8th edition of the *Australian Immunisation Handbook*.[9] They included questions such as designation of a person responsible for vaccine care, knowledge of recommended temperature range, recording of temperature, protection of power supply, policy regarding breach of recommended temperature, and policy regarding follow up after power interruption.

Results

Figure 1 shows the temporal variation in temperature, by refrigerator type, over time. The variation in temperature for the purpose built vaccine refrigerator shows the least variation, with most readings falling within the 2–8°C range.

Compared with the purpose built vaccine refrigerators, all other refrigerators were significantly less likely to keep temperature at an optimal level (*Table 1*). For instance, the odds ratio of a commercial grade purpose built refrigerator, as opposed to a consumer grade bar type refrigerator, being able to maintain optimal temperature was 0.005 (95% CI: 0.001–0.044).

There was no significant difference in vaccine storage score between established practices with numerous contacts and those with one or two previous contacts with the NRGPN (p=0.353). Knowledge of vaccine storage score was positively associated with optimal storage temperature, the odds ratio increasing by 1.69 (95% CI: 1.15–2.49) for every unit increase in score (p=0.008).

When adjusted for frequency of NRGPN contact and vaccine storage knowledge survey score, there were slight changes in the magnitude of the odds ratios for refrigerator type. For instance, the odds ratio for bar style refrigerators changed from 0.005 to 0.012, and the relationship was less significant (p=0.001).

The variation in temperature between loggers placed in different shelves of the various types of refrigerators was examined. The purpose built vaccine refrigerators had the lowest mean difference of 0.26°C. As shown in *Table 2*, both bar style and frost free refrigerators had a large difference compared with the purpose built refrigerators; however the cyclic refrigerators did not show a significant difference (difference of 0.39, 95% CI: –1.44 to 2.23), p=0.673. Practices with numerous contacts with the NRGPN showed lower variation in refrigerator temperature.

Discussion

This study is unique in simultaneously examining a number of the factors – refrigerator type, knowledge about vaccine storage (as measured by vaccine storage knowledge score) and frequency of contact with educational provider (as measured by division contact) – identified in the literature as influencing cold chain adherence for vaccine products in the general practice setting. Analysis of this data allows recommendations for improvement based on the comparative benefit of available refrigerator types.

Purpose built vaccine refrigerators offer greater benefits compared to each of the other types of refrigerators in terms of maintaining temperature at an optimal range and showing smaller variations in temperature within the refrigerator. These benefits remain after adjustment for potential confounders such as establishment type, knowledge of vaccine storage score point, and taking into account the serial temporal autocorrelation in the data. Whatever type of refrigerator is used, it is important that the operating condition of the refrigerator be monitored regularly. Even if the refrigerator is equipped with an integral thermometer, a stand alone thermometer should still be placed within the refrigerator to ensure proper operation.

The vaccine purpose built refrigerator involved in this study had been purchased within a year of the study. Concerns have since been

Table 1. Factors associated with optimal storage temperature

Covariates	Odds ratio	95% CI		*p* value
Type of refrigerator				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	0.005	0.001	0.044	<0.001
Cyclic refrigerator	0.008	0.001	0.080	<0.001
Frost free refrigerator	0.006	0.001	0.071	<0.001
Others	0.009	0.001	0.070	<0.001
Adjusted for establishment type and knowledge of vaccine storage score				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	0.012	0.001	0.166	0.001
Cyclic refrigerator	0.013	0.001	0.193	
Frost free refrigerator	0.015	0.001	2.649	0.112
Others	0.001	0.001	0.021	<0.001

Table 2. Factors associated with difference in temperature between loggers placed in different shelves

Covariates	Coefficient	95% CI		*p* value
Type of refrigerator				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	–2.54	–5.02	–0.07	0.044
Cyclic refrigerator	0.39	–1.44	2.23	0.673
Frost free refrigerator	–1.96	–3.68	–0.25	0.025
Others	NC			
Establishment type				
Established practices with numerous contacts with NRGPN	Reference			
One or two previous contacts with NRGPN	–5.15	–5.99	–4.31	<0.001
First contact with NRGPN	–2.16	–3.00	–1.31	<0.001
Knowledge of vaccine storage score	0.61	0.20	1.01	0.004
Multivariate analysis				
Type of refrigerator				
No adjustment				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	–2.54	–5.02	–0.07	0.044
Cyclic refrigerator	0.39	–1.44	2.23	0.673
Frost free refrigerator	–1.96	–3.68	–0.25	0.025
Others	NC			
Adjusted for establishment type				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	–1.57	–2.98	–0.17	0.028
Cyclic refrigerator	0.39	–1.44	2.21	0.678
Frost free refrigerator	–1.43	–2.95	0.09	0.065
Others	NC			
Adjusted for establishment type and knowledge of vaccine storage score				
Purpose built vaccine refrigerator	Reference			
Bar style refrigerator	–1.57	–2.99	–0.16	0.029
Cyclic refrigerator	0.47	–1.50	2.45	0.638
Frost free refrigerator	–1.07	–2.60	0.45	0.168
Others	NC			

Note: Generalised estimating equation models used, together with robust standard errors, for the calculation of the confidence intervals and *p* values; NC = not computable

raised about variation of performance over time and further studies will be required to clarify if this relates to particular brands or to smaller size refrigerators.

For individual practices, the cost of owning a purpose built refrigerator is disproportionately large. Practice infrastructure is currently less likely to be subsidised by government than are educational and other support programs. Potential strategies might include the addition of reimbursement schemes, thought to deliver a 24 month return on investment,[23] or sanctions for repeated temperature violations, including losing access to subsidised vaccines.

Conclusion

In the future we may see greater reliance on vaccines expressed in transgenic plants, including grains,[24] or stored in desiccated sugar beads,[25] which can be transported at room temperature. Alternatively we may see an increase in the use of cold chain dependent vaccines such as tetravalent and pentavalent vaccines. However, for the foreseeable future, general practices will be dependent on refrigerators to maintain vaccines at the required storage temperatures. This study supports the use of purpose built refrigerators as the best method for vaccine storage.

Implications for general practice

- Practices should upgrade their refrigerators to purpose built models.
- Educating practice staff on vaccine storage has a positive and significant effect on vaccine cold chain standards.
- Practice staff should have a formal monitoring routine in place to ensure proper equipment operation.

Conflict of interest: none declared.

References

1. Weir E, Hatch K. Preventing cold chain failure: vaccine storage and handling. CMAJ 2004;171:1050.
2. Finn L, Crook S. A distinct survey of vaccine cold chain protection in general practitioners' surgeries. Commun Dis Public Health 1999;2:47–9.
3. Haworth EA, Booy R, Stirzaker L, et al. Is the cold chain for vaccines maintained in general practice? BMJ 1993;307:242–4.
4. Wawryk A, Mavromatis C, Gold M. Electronic monitoring of vaccine cold chain in a metropolitan area. BMJ 1997;315:518.
5. Burgess MA, McIntyre PB. Vaccines and the cold chain: is it too hot... or too cold? Med J Aust 1999;171:82.
6. Guthridge SL, Miller NC. Cold chain in a hot climate. Aust N Z J Public Health 1996;20:657–60.
7. Lewis P, Reimer R, Dixon A. Evaluating the efficacy of vaccine storage in the general practice setting. Aust N Z J Public Health 2001;25:547–50.
8. Reimer RF, Lewis PR. Vaccine storage in pharmacies on the Central Coast of New South Wales. Aust N Z J Public Health 1998;22:274–5.
9. The Australian Immunisation Handbook 8th Edition: National Health and Medical Research Council 2003.
10. Tozzi AE. Field evaluation of vaccine safety. Vaccine 2004;22:2091–5.
11. Watson M. The cost of vaccine wastage. National Vaccine Storage Workshop 2004; Brisbane, 2004.
12. Lovell I. Establishing performance standards and benchmarks for pharmaceuticals through cold chain logistics. The cold chain distribution for pharmaceuticals conference, Sydney 2004.
13. Gold M, Martin L, Naydia CL, et al. Electronic temperature monitoring and feedback to correct adverse storage in general practice. Med J Aust 1999;171:83–4.
14. Weeks RM, Svetlana F, Noorgoul S, et al. Improving the monitoring of immunization services in Kyrgyzstan. Health Policy Plan 2000;15:279–86.
15. Jeremijenko A, Kelly H, Sibthorpe B, et al. Improving vaccine storage in general practice refrigerators. BMJ 1996;312:1651–2.
16. Bell KN, Hogue CJ, Manning C, Kendal AP. Risk factors for improper vaccine storage and handling in private provider offices. Pediatrics 2001;107:E100.
17. Gazmararian JA, Oster NV, Green DC, et al. Vaccine storage practices in primary care physician offices: assessment and intervention. Am J Prev Med 2002;23:246–53.
18. Samant Y, Lanjewar H, Block L, et al. Relationship between vaccine vial monitors and cold chain infrastructure in a rural district of India. Rural Remote Health 2007;7:617.
19. Arya S, Agarwal N. Re: Relationship between vaccine vial monitors and cold chain infrastructure in a rural district of India. Rural Remote Health 2007:7;730.
20. Hazelton K, Balcomb A, Bowd K, Hazelton-Parsons D, Liddle J. The immunisation cold chain. Why is it so hard to get right? Aust Fam Physician 2002;31:939–42.
21. National Vaccine Storage Guidelines: Strive for 5. Canberra: Commonwealth of Australia, 2005.
22. Miller NWM, Albances S, Anuf N. Technical issues with refrigerators. National Vaccine Storage Workshop 2004; Brisbane, Queensland Health.
23. Terrell-Jenkins M, Wong D. White paper: Use of new intelligent automated IT systems to prevent administration of ineffective vaccines and reduce vaccine wastage E2E IT Solutions Pty Ltd 2005. Available at www.temptrack.com.au/reports.htm [Accessed 17 March 2008].
24. Streatfield SJ. Delivery of plant-derived vaccines. Expert Opin Drug Deliv 2005;2:719–28.
25. Das P. Revolutionary vaccine technology breaks the cold chain. Lancet Infect Dis 2004;4:719.

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