The Royal Society of Medicine

Journal of the Royal Society of Medicine; 106(11)
459–460
DOI: 10.1177/0141076813507843

How dramatic were the effects of handwashing on maternal mortality observed by Ignaz Semmelweis?

Pierre La Rochelle and Anne-Sophie Julien

Département de médecine familiale et de médecine d'urgence, Université Laval, Québec, Canada G0R 1Z0

Corresponding author: Pierre La Rochelle. Email: pierre.la.rochelle@videotron.ca

Questions remain about how much evidence is needed to accept or at least to consider an observation as providing sufficiently strong evidence to justify a change in clinical practice,[1,2] even when the key outcome measure is objective, definitive and clinically very important.

Maternal death is one such outcome, and Ignaz Semmelweis' observation of the reduction in maternal deaths associated with the introduction of handwashing in a maternity hospital in Vienna provides an illustrative example.[3,4] A plot of the rate of maternal deaths every month from January 1841 until May 1847 shows substantial variability and some evidence of a pattern in the changes, possibly related to the seasons.[5] After handwashing was introduced in June 1847, deaths were less frequent and showed less monthly variability in the period up to February 1849. How much analysis is needed to convince people that this is an effect of handwashing and not a chance association, or a reflection of bias?[2]

Eyeballing the plot shown in Figure 1, many observers might consider the reduction in deaths following the introduction of handwashing to be real and significant. When considering the high risk of bias in studies using historical controls, Glasziou *et al.*[1] suggested considering an effect as likely to be real if a risk ratio of between 5 and 10 has been observed. In this case, a comparison of the average monthly mortality rate before the introduction of handwashing (10.65%, blue points) and after it (1.98%, red points) yields a risk ratio of 5.38. We can explore these data in more depth by analysing this interrupted time series with a Seasonal AutoRegressive Integrated Moving Average model. The monthly mortality rate can be formulated as follows:

$$MR_t = B \times H + AR \times MR_{t-1} + MA \times E_{t-12} + E_t$$

where MR = mortality rate, t = month, B = handwashing coefficient, H = 0 (before the introduction of handwashing), H = 1 (after the introduction of handwashing), AR = first-order autoregressive coefficient, MA = monthly moving average coefficient and E = random error.

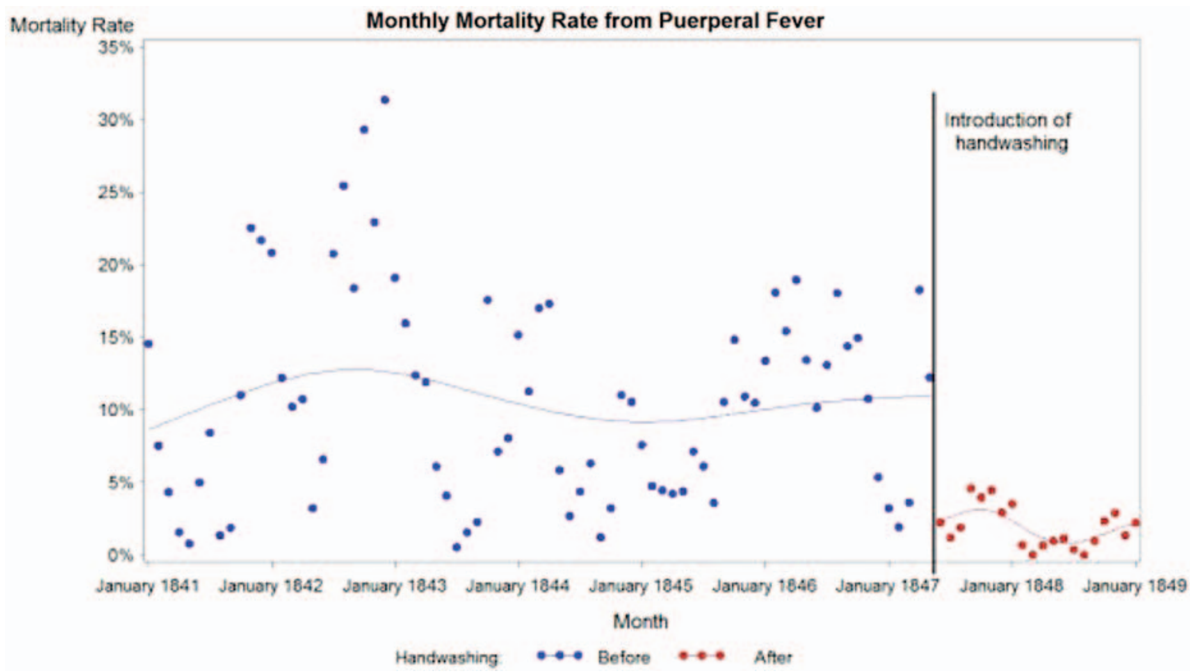
The estimations of the three coefficients of the model are presented in the table below.

Coefficient	Estimate	Standard error	*T* statistic	*P*
Handwashing	−0.0887	0.0310	−2.8639	0.0042
First-order autoregressive	0.6974	0.0761	9.1687	<0.0001
Monthly moving average	−0.7741	0.1299	−5.9581	<0.0001

This yields an estimated absolute reduction in maternal mortality of 8.87%, which is highly statistically significant ($P = 0.0042$). The reduction is also of great human significance: for every 11 women examined after handwashing, one fewer died. The analysis could be extended to take into account the data from the two clinics concerned, and to cover an earlier period, during which postmortem examinations were not done routinely.[6] This discovery happened before the germ theory take off with the work of Louis Pasteur in the early 1860s. The miasma theory was prevalent and no strong explanation was available to support this impressive observation.

These different levels of analysis strongly support the existence of a beneficial impact of handwashing on the risk of maternal mortality. This is not to suggest that data of this level of confidence are sufficient to introduce changes in clinical practice, which is influenced by medical tradition and cultural and other factors.[4,6] In Semmelweis' case,

Figure 1. Monthly mortality rate from puerperal fever.



the evidence of an important impact of handwashing on maternal mortality should at least have led traditional medical practices to have been questioned.

Declarations

Competing interests: None declared

Funding: None declared

Ethical approval: Not applicable

Contributorship: PLR is the main author of the article; A-SJ worked only on the statistical analysis and the presentation of the results.

Acknowledgements: The authors are grateful to Prof Paul Glasziou and Dr Irvine Loudon for helpful comments on an earlier draft of this article

Provenance: Invited contribution

References

1. Glasziou P, Chalmers I, McCulloch P and Rawlins M. When are randomised trials unnecessary? Picking signal from noise. *BMJ* 2007; 334: 349–51.
2. Guyatt GH, Oxman AD, Sultan S, et al. *The GRADE Working Group*. See http://www.jclinepi.com/article/S0895-4356(11)00184-3/fulltext. GRADE guidelines: 9. Rating up the quality of evidence. *J Clin Epidemiol* 2011; 64: 1311–6.
3. Semmelweis I. *Die Aetiologie, Der Begriff und Die Prophylaxis des Kindbettfiebers* [The Etiology, Concept, and Prophylaxis of Childbed Fever]. Budapest and Vienna: Hartleben, 1861.
4. Loudon I. *Ignaz Phillip Semmelweis' Studies of Death in Childbirth. JLL Bulletin: Commentaries on the History of Treatment Evaluation, 2002*. See www.jameslindlibrary.org (last checked 19 September 2013).
5. Carter KC. *Ignaz Semmelweis, The Etiology, Concepts and Prophylaxis of Childbed Fever*. Madison, WI: University of Wisconsin Press, 1983, 72 and 90–1.
6. Noakes TD, Borresen J, Hew-Butler T, Lambert MI and Jordaan E. Semmelweis and the aetiology of puerperal sepsis 160 years on: an historical review. *Epidemiol Infect* 2008; 136: 1–9.