Canadian rotavirus vaccine effectiveness data

We read with interest and enjoyed Dr Goldman's recent Child Health Update on the effectiveness of rotavirus vaccines.[1]

In Australia, there are 4 states currently using the multiple-strain vaccine (ie, RV5), and the remaining 2 states and 2 territories are using the single-strain vaccine (ie, RV1).[2] Dr Goldman attributes our decline in rotavirus notifications and hospitalizations[3] to RV1, but in Queensland we have always used RV5.[4] Since mid-2007, we saw a rapid decline in rotavirus notifications in both vaccinated and older, unvaccinated age groups, and a fall in the proportion of laboratory tests positive for rotavirus in all age groups.[5]

Canada's experience with rotavirus vaccines provides a wonderful opportunity to observe the effects of rotavirus vaccines, particularly in indigenous children living in harsh arctic and subarctic regions. In the pre-vaccine era in Queensland, we found rotavirus disproportionately affected aboriginal and Torres Strait Islander children with higher rates of notification and hospitalization, and hospitalization earlier in life with a longer average length of stay.[6] Recent outbreak data from the Northern Territory, where RV1 has been used since late 2006, suggests effectiveness wanes rapidly after infancy in indigenous children.[7] To date, we have no equivalent data from a state that uses RV5, but we are collating these data in Queensland. Of note, middle-income Latin American countries have seen blunted effectiveness values, compared with efficacy data, with both vaccines.[8]

We look forward to Canadian effectiveness data, particularly from Canada's aboriginal population, as they become available to aid our understanding of rotavirus epidemiology in the vaccine era.

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Competing interests

Dr Lambert has previously been a co-investigator on clinical trials sponsored by Merck, CSL, and GlaxoSmithKline—manufacturers or distributors of rotavirus vaccines in Australia. Merck paid an honorarium to his institute for 2 rotavirus presentations to international meetings. **Dr Grimwood** has, in the past 10 years, been a member of a Rotavirus Advisory Board and received support for conference attendance, lecture fees, and a research grant from GlaxoSmithKline. He has also received a research grant from Merck.

References

1. Goldman RD. Effectiveness of rotavirus vaccine in preventing severe acute gastroenteritis in children. *Can Fam Physician* 2012;58:270-1.
2. Buttery JP, Lambert SB, Grimwood K, Nissen MD, Field EJ, Macartney KK, et al. Reduction in rotavirus-associated acute gastroenteritis following introduction of rotavirus vaccine into Australia's National Childhood vaccine schedule. *Pediatr Infect Dis J* 2011;30(1 Suppl):S25-9.
3. Field EJ, Vally H, Grimwood K, Lambert SB. Pentavalent rotavirus vaccine and prevention of gastroenteritis hospitalizations in Australia. *Pediatrics* 2010;126(3):e506-12.
4. Grimwood K, Lambert SB. Rotavirus vaccines: opportunities and challenges. *Hum Vaccin* 2009;5(2):57-69. Epub 2009 Feb 8.
5. Lambert SB, Faux CE, Hall L, Birrell FA, Peterson KV, Selvey CE, et al. Early evidence for direct and indirect effects of the infant rotavirus vaccine program in Queensland. *Med J Aust* 2009;191(3):157-60.
6. Campbell SJ, Nissen MD, Lambert SB. Rotavirus epidemiology in Queensland during the pre-vaccine era. *Commun Dis Intell* 2009;33(2):204-8.
7. Snelling TL, Andrews RM, Kirkwood CD, Culvenor S, Carapetis JR. Case-control evaluation of the effectiveness of the G1P[8] human rotavirus vaccine during an outbreak of rotavirus G2P[4] infection in central Australia. *Clin Infect Dis* 2011;52(2):191-9.
8. Sheridan S, Lambert S, Grimwood K. Impact of rotavirus vaccination on childhood gastroenteritis. *Microbiol Aust* 2012;33(2):56-60.

Canadian trial data?

The recent RxFiles by Kosar et al[1] is an excellent and helpful review of oral anticoagulant management in atrial fibrillation (AF). However, some serious questions arise when looking at the "unexpected" high hemorrhagic stroke rates in the warfarin arms of these trials (RELY [Randomized Evaluation of Long-term Anticoagulation Therapy], ROCKET-AF [Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonist for Prevention of Stroke and Embolism Trial in AF], and ARISTOTLE [Apixaban for Reduction in Stroke and Other ThromboembolLic Events in AF]), all of which were conducted multinationally with 39 to 45 countries participating, as opposed to a very low rate of hemorrhagic stroke experienced in the warfarin arm of the SPORTIF V (Stroke Prevention using an ORal Thrombin Inhibitor in atrial Fibrillation V) trial (2 events in 1962 patients), which was a North American–only trial of the first novel oral anticoagulant, ximelagatran. Perhaps it would be helpful if the Canadian data from these subsequent trials were published. Is the difference in hemorrhagic stroke rates owing to the change in settings of these studies from North America (the most relevant context for Canadian family physicians) to a multinational arena? What are the differences in the elements of the HAS-BLED score between these studies? What are the ranges of these elements as well?

It only takes a few outlier patients taking acetylsalicylic acid, with uncontrolled hypertension and poor warfarin control, to create large differences in bleed rates. Second, the hemorrhagic stroke issue aside, warfarin is demonstrated to be superior to dabigatran for all other major end points using RELY's own data when warfarin is managed properly and the average proportion of time the international normalized ratio is in therapeutic range is greater than 72.6%.[2] Why is so little attention paid to sensitivity analyses when discussing warfarin?