US government website for collecting adverse events after vaccination is inaccessible to most users

Enhancing Community Confidence in Vaccines Safety

The Global Advisory Committee on Vaccine Safety (GACVS) met on 7 and 8 June 2017.

WHO's Executive Board, meeting in January, discussed the report of the mid-term review of the Global Vaccine Action Plan (GVAP) by WHO's strategic advisory group of experts on immunisation (SAGE). It acknowledges the achievements of the GVAP but offers strongly worded recommendations regarding accountability, equity, the integration of immunisation programs within general health system development and other areas of weakness. We note that there is no mention of 'community confidence' in the SAGE report, despite its being flagged earlier as a key parameter to be monitored (1), nor is there any discussion of weaknesses in post-marketing surveillance in many countries. Clearly effective post-marketing surveillance and causality assessment of adverse events following immunization are crucial for community confidence.

In this context we note that Tarfuri et al (2) who recommend use of the WHO's revised guidelines on causality assessment, the AEFI Manual (3), found that there appear to have been no reports which used those guidelines. We suggest that part of the reason maybe that the Manual itself is in places poorly worded to a degree which can be quite confusing and allow for certain ambiguities. We would like to highlight these before the GACVS meeting. In particular we cite three areas which we suggest need to be reviewed.

Causal association
In the Glossary (page viii of the Manual), 'causal association' is defined as "A cause-and-effect relationship between a causative factor and a disease with no other factors intervening in the process". This definition is very narrow. If the vaccination of an infant was reported to have been followed by sudden death but the child was malnourished or otherwise unwell does this mean that causality assessment should conclude no cause and effect relationship between the vaccine and the death? Why does this definition exclude interacting causalities?

It might also be clearer if the reference to 'disease' in this definition was replaced by 'adverse event' as defined to make it clear that causal assessment is not restricted to 'diseases'.

Case definition
The description of Step 4, 'Classification', in the Manual (page 20), is close to incomprehensible. The passage refers to the 2012 CIOMS/WHO Working Group report (4) and goes on to refer to 'cause-specific definitions' which suggests that case definitions are somehow 'cause specific'. It is our understanding that case definitions are designed to specify a diagnosis regarding the AEFI and to specify different levels of diagnostic certainty. Whether they are cause-specific is for the epidemiology to establish.
However, having been referred to the CIOMS/WHO WG report (4), the analyst will be further confused by the footnote on page 170 of the CIOMS/WHO Working Group report which states that "If there is adequate evidence that an event does not meet a case definition, such an event should be rejected and should be reported as 'Not a case of [AEFI]'". This is at odds with the advice on page 11 of the manual which is that a case definition can be adopted from the standard literature or by the reviewers themselves; not necessarily 'an existing case definition'.

It is our understanding that the purpose of the case definition is to draw on previous epidemiological research or undertake further research in order to confirm or exclude a causal link. Excluding causality in relation to an individual event is not dependent on that event conforming to a pre-existing case definition.
In passing we note the pejorative use of the term 'rejected' which suggests a somewhat defensive posture. Reports of AEFIs are not to be 'rejected'; they are to be assessed for causality and classified accordingly.

Strong evidence against a causal association
The description of Step III, on page 16 of the Manual and also depicted in Figure 4, could be much clearer. A clear distinction is needed at this point between individual assessment and population level assessment.
We understand that this passage is intended to convey that if the case definition adopted for this AEFI corresponds to a previously conducted epidemiological study and that study (or studies) found no statistical association with vaccination this will be treated in the algorithm as strong evidence against concluding that there is an association in this case.

The text of the para on p16 with the example is quite confused. First the reference to an 'AEFI that is initially thought to be due to a vaccine' is a misuse of the term; there need be no expectation that the AEFI was due to a vaccine; it is a report of an adverse event following vaccination which is to be investigated. Secondly the focus of the initial sentence is on finding a different cause but the MMR/autism 'example' illustrates a completely different issue; it is a case where a statistical association was sought but not observed. It is not an example of an alternative cause.

Conclusion
Community confidence depends on thorough, objective and practicable post-marketing surveillance. We hope the GACVS will revisit the guideline to make it easier to use.

David G Legge
Associate Professor Emeritus
School of Public Health
La Trobe University, Melbourne

Jacob Puliyel
Head of Pediatrics
St Stephens Hospital, Delhi.
Member of the National Technical Advisory Group on Immunization of the Government of India

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Jacob Puliyel
Pediatrician
David G Legge
St Stephens Hospital
Tis Hazari