

Intended for healthcare professionals

🗨️Rapid response to:

Analysis

Modernising vaccine surveillance systems to improve detection of rare or poorly defined adverse events

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Rapid Response:

The New WHO Causality Assessment Algorithm Needs Revision to Restore Public Trust

It is commendable that Rebecca Chandler has highlighted the need to modernize vaccine surveillance to restore public trust in vaccine safety (1). She, however, cites the response to intussusception after RotaShield and narcolepsy in 2009 after Pandemrix, as evidence of the robustness of the 'current system'. This is factually inaccurate and needs correction in indexed literature.

The current system uses the 'WHO Causality Assessment of an Adverse Event Following Immunization (AEFI)' manual revised in 2013 (2) following the report of the CIOMS/WHO working group on vaccine pharmacovigilance in 2012 (3). Both these signals (intussusception and narcolepsy) were detected using the original Brighton classification of AEFI (4), before the current system was instituted. In the old system, reactions that were temporally associated with immunization, for which there was no alternate explanation, were classified as 'probably' related to immunization. It facilitated signal detection. This cannot be said for the currently used WHO causality assessment.

In the new causality assessment, only reactions that have previously been acknowledged in epidemiological studies to be caused by the vaccine, are classified as a vaccine-product-related-reactions. Reactions observed for the first time during post-marketing surveillance (Phase 4 clinical trial) are not considered as 'consistent with causal association with vaccine'. All new serious adverse reactions are labelled as coincidental events 'inconsistent with causal association,' or 'unclassifiable' and the association with vaccine is not acknowledged. (5). It has, in effect, made phase 4 trials redundant.

By definition, an AEFI implies an 'untoward medical occurrence which follows immunization and it does not

necessarily have a causal relationship with the usage of the vaccine' (2). However CIOM/WHO recommend that if "there is adequate evidence that an event does not meet a 'case definition' of a known adverse reaction, the event should be rejected and should be reported as 'Not a case of [AEFI]'" (3) (Page 170 Notes for guidelines: i). If it is 'not classifiable', the reactions will not be categorised as "Indeterminate" and so it will not be recognised as a potential signal that needs further investigation.

The new scheme also specifies that a "cause-and-effect relationship between a causative factor and a disease is considered only if there is no other factors intervening in the process". This definition exclude interacting causalities.

Given these apparent anomalies, the new WHO's algorithm for causality assessment of AEFI is not fit for purpose and it fails to inspire confidence that it can identify new, uncommon AEFI. It will erode faith not only in the immunisation programme but also the public's trust in their physicians.

Reference

1. Chandler RE. Modernising vaccine surveillance systems to improve detection of rare or poorly defined adverse events BMJ 2019; 365: l2268
2. WHO. The Causality assessment of an adverse event following immunization (AEFI): User manual for the revised WHO classification. WHO/HIS/EMP/QSS. March 2013. Available at https://www.who.int/vaccine_safety/publications/aevi_manual.pdf?ua51. Accessed on 1/6/19
3. CIOMS/WHO. Definitions and Application of Terms for Vaccine Pharmacovigilance Report of CIOMS/WHO Working Group on Vaccine Pharmacovigilance. Available at https://www.who.int/vaccine_safety/initiative/tools/CIOMS_report_WG_vacc... Accessed on 1/6/19
4. WHO. Adverse Events Following Immunization (AEFI): Causality Assessment (2005) Available at

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