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How are we assessing the safety and quality use of medicines used by young people in Australia?

Viewpoint

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How are we assessing the safety and quality use of medicines used by young people in Australia?

Regulatory and subsidy approvals for medicines rely heavily on outcomes from randomised controlled trials. However, as an evidence base for safety assessment, trials data are limited[1, 2] and are rarely conducted in paediatric populations.[2] Safety data cannot be extrapolated from studies in adult populations. Children's physiological development may affect the bioavailability of medicines, making them potentially more vulnerable to adverse drug events.[3, 4] The impact of adverse events during growth and development may also be different, more serious, and longer term compared with adults.[5]

Safety monitoring of medicines for the entire population, and particularly for children, relies heavily on the post-regulatory approval period. Spontaneous reporting systems, such as adverse event reports to the Therapeutic Goods Administration, are useful for signalling safety issues, but are subject to selective under-reporting or stimulated reporting[2] and cannot quantify the incidence or rates of adverse events in the community or in population subgroups. Other data sources include calls to poisons hotlines, presentations to hospital emergency departments and admissions to hospital. For paediatric populations, these data sources have been underutilised, and have mainly addressed the burden of pharmaceutical poisonings.[6]

The Pharmaceutical Benefits Scheme (PBS) database comprises prescribed subsidised medicines dispensed in Australia (currently around 300 million dispensings a year).[7] Despite its potential to evaluate medicines use, this resource has been underutilised for children and young people. In a systematic review of studies using PBS data in the period 1987-2013, only four of the 228 identified studies focussed on children and young people.[8] Moreover, national annual reports of medicine use are often not stratified by age.[9] The PBS however, may not capture the use of off-label medicines, which is common in children.[10-14] While off-label use may be appropriate, children may be dispensed medicines that lack efficacy or present safety concerns.[11]

The importance of monitoring the use of medicines in children is highlighted by a recent review suggesting that childhood is the optimal period for detecting familial hypercholesterolaemia (FH), and that treatment involving statins is safe and effective.[15] In

selected adults, the benefits of statin treatment[16] (reducing major cardiovascular disease events and all-cause mortality) may outweigh the increased risks of serious adverse events (new-onset diabetes mellitis, myopathy, and possibly haemorrhagic stroke).[16-19] However, in children, the risk of cardiovascular disease events is close to zero, and screening and treatment for FH may lead to costs and harms without benefit.[18] The potential increased risk of diabetes and obesity from decades of treatment beginning in childhood has been described as alarming.[18] In addition, the suggestion of an association between statins and cognitive dysfunction in adults[20-22] demands assessment in children and adolescents before use in this young and vulnerable population. Proponents of the safety of statin treatment for children base their evidence on a ten-year follow up of 214 children enrolled in one randomised controlled trial. This trial lacked power to detect rare events, and its authors concluded 'the safety of statin therapy is supported by extensive evidence in adults'.[23]

The Australian Commission on Safety and Quality in Health Care has identified the evaluation and development of initiatives to ensure safety and quality of medicines use as a priority.[24] In the USA, the National Institute of Child Health and Development is required annually, to update a priority list of medicines requiring further study in children. This list of medicines is compiled from suggestions from the United States Food and Drug Administration and experts in paediatric medicine, and the prioritisation process considers the affected target populations, the level of available evidence and the feasibility of subsequent studies.[25]

Despite one quarter of Australia's population, around six million people, being younger than 20 years,[26] we know very little about the safe use and long term outcomes of all medicines, in this age group. With Australia's policy of assessing medicines prior to approval and availability of population-based data sources with the potential to assess safety and quality issues, we need to use current resources more effectively to build an evidence base for the safety and quality use of medicines in our young people. While monitoring the off-label use of medicines at a population level will require novel strategies, our potential to link medicines use (PBS) with health outcomes data would contribute to identifying adverse consequences that may otherwise escape detection. To detect rare outcomes in children and young adults, data linkage at a national level, or national state-based collaborative projects of linkage between PBS and other health data collections (such as hospital admissions and deaths data) would be ideal. Improved data linkage arrangements within, and across states,

would benefit all Australians by strengthening evidence-based policy making and health service delivery.[27]

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