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Towards evidence-based medicine for paediatricians

Edited by Bob Phillips

Slippage

We have gone on (at length) about the need to think carefully about populations where a diagnostic test is under investigation, and using those assessments in different clinical situations.[1] We have also banged home the difference between 'particularising' and 'generalising' from clinical trials—basically, do not ask 'would this patient be allowed to go into the study' and do ask 'what is so different about my patient that I think this treatment could act differently'.[2] What we have not spoken to too much is the way things change over time …

Back in the good old days, your average biochemistry laboratory could reliably measure methotrexate levels down to about 0.2 µmol/L. Lots of the paediatric oncology protocols using high-dose methotrexate kept rescuing the normal cells with folinic acid until levels of active drug could not be measured. With modern analysers, we can reliably go down to 0.1 µmol/L now, and potentially lower. Should we keep our old instruction—'until below the limit of detection'—or change what we do or say? (This is pretty easy—we just turned it to 'less than 0.2 µmol/L'—but not all are so obvious.)

What if the thing that has slipped is not the measurement of a drug level, but the ease of detection of a genetic change? Or the diagnostic criteria for a condition? How do we then know if a treatment which holds more good than harm for the 'old' diagnosis with significant symptoms will do the same in the broader definition? What is the prognosis in those who have an incidentally detected change, given the data were derived from an older setting?

We can hope for new studies, and those may come along. And while they do, we need to apply the same frameworks for thinking how to extrapolate from all the other studies we look at. How much does my patient differ? What are the important things for them? Where does the benefit seem to come from? And make sure we discuss the limits of our uncertainties with families.

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