IRoSiE

Training Materials for Responsible Open Science

Case study

Data sharing and reanalysis in medicine

SOURCE: LeNoury, J., Nardo, J. M., Healy, D. et al. (2015). Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. *BMJ,* 51:h4320. https://doi.org/10.1136/bmj.h4320

In 2015 a team of scientists published a paper "Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence" in the British Medical Journal. The study aimed to reanalyse SmithKline Beecham's Study 329 published by Keller and colleagues in 2001. The primary objective of Study 329 was to compare the efficacy and safety of paroxetine and imipramine with placebo in the treatment of adolescents with unipolar major depression. The conclusion was that paroxetine is well tolerated and effective for major depression in adolescents.

In the reanalysis of data, researchers found out that neither paroxetine nor imipramine showed efficacy for major depression in adolescents. Moreover, with both drugs, there was an increase in harm. The researchers identified several potential barriers to accurate reporting of harms in the original study:

- "Use of an idiosyncratic coding system
- Failure to transcribe all adverse events from clinical record to adverse event database
- Filtering data on adverse events through statistical techniques
- Restriction of reporting event to that occurred above a given frequency in any one group
- Coding event under different heading for different patients (dilution)
- Grouping of adverse events
- Insufficient consideration of severity
- Coding of relatedness to study medication
- Masking effects of concomitant drugs
- Ignoring effects of drug withdrawal"

In the conclusions of the reanalysis, the authors wrote: "Access to primary data from trials has important implications for both clinical practice and research, including that published conclusions about efficacy and safety should not be read as authoritative. The reanalysis of Study 329 illustrates the necessity of making primary trial data and protocols available to increase the rigour of the evidence base."

Questions for discussion:

1) What is the role and significance of open data in scientific research? What are the benefits and risks of reanalysis of open data sets?
2) If you would perform a reanalysis of an openly accessible data set and discover similar problems, what would/should you do?
3) Should the original publication of the study be retracted in this case?

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