

Recently, there have been two letters published which imply data quality issues with The Health Improvement Network (THIN) database^{1,2}. Apart from the potential conflict of interest of the authors, we feel that their claims are not substantiated and we demonstrate this below.

Since public debate often degenerates into a long series of exchanges, we have decided to make researchers aware of our interpretation of the stated concerns via our website.

Letter 1: Van Staa, TP, Parkinson J. *Pharmacoepidemiology and Drug Safety*, 2007¹ in response to the publication by Arellano et al³.

Comment on: "... some of their results differ remarkably from data in the General Practice Research Database (GPRD)**; the database considered to be the UK gold standard. It raises again the issues of quality and completeness of The Health Improvement Network (THIN)"

- The differences they find to justify this statement are those presented in the table in van Staa's letter. They make comparisons between THIN and GPRD in terms of the percentage of patients with a "history of thrombotic [*sic*] events" and the percentage of patients with "history of gastrointestinal [GI] events". They calculated the figure for GPRD, whilst the rates from THIN were taken from the original article by Arellano et al. The table does indeed show rates of GI events that were around 10 times higher in GPRD, however they appear to have made a fundamental error: the "percentage history" in THIN was only calculated over a 6-month period prior to index date whilst for GPRD the "history" appears* to mean lifetime prevalence. Thus such a difference is natural and cannot imply data quality issues. Indeed, the expected incidence of GI events is in the order of 1/1000 patient years [Hernandez et al] and the rates in THIN, found over the 6-month period, exceeded this (0.2% to 0.7%). So again this is not likely to constitute evidence of missing data.
- The use of the word "again" was not qualified; as far as we are aware there has been no previous article that demonstrated data quality issues in THIN Data.
- We are not aware of any such thing as a "Gold Standard" primary care database, and hence it is difficult to imagine how differences between GPRD and another source imply that the latter is wrong.

Comment on: "A previous report has suggested considerable differences within THIN of the incidence rate of fractures" [*citing van Staa et al, Q J Med, 2005*]

- The article they cite contains no reference to differences in the incidence rate of fractures.⁴ To quote the only reference to THIN Data in that paper, "When

* If the GPRD rates were indeed correctly calculated using the 6-month period then the GPRD sample suffers GI events at a rate between 50 and 150 times higher than the expected 6 month incidence (1/1000 person years).

applying the risk score as developed in GPRD to another dataset (THIN), the risk score equally differentiated between high- and low-risk patients...”. Clearly this is in no way a criticism of THIN; indeed it indicates that the model derived on GPRD data was validated in THIN. This seeming misquote is curious given that the first author is also the author of the letter.

Comment on: “As an example of how GPRD ensure quality, 11% of the practices that sent data to the GPRD are not used as data do not meet quality standards”

- Since, as far as we are aware, GPRD’s “quality standards” have not been published, it is difficult to comment on how not meeting those standards determines “quality”.
- THIN provides most practices to researchers and also provides the necessary information for researchers to decide which practices can be included for individual studies. This information includes the Research Files, the AMR⁵ (Acceptable Mortality Reporting) date, the computerisation date, and the date of Vision software conversion. The AMR date, which is externally evaluated, indicates when the reporting of mortality is considered complete. The AMR is vital for determining accurate denominators – this approach has not been used in other primary care databases as far as we are aware.
- Stringent checks of data quality and completeness of reporting are part of the process for generating the THIN database. THIN also provides valued feedback to the practices and training for practices to optimise their use of the Vision software and increase their awareness of the research use of the data.

Letter 2: Van Staa TP, Parkinson J. *Pharmacoepidemiology and Drug Safety* 2008² in response to the publication by Lewis et al.⁶

Comment on: “There is now evidence that completeness of the data may be an issue with THIN...”

- This is not backed up by any references or evidence.

Comment on: “In a large study with THIN, it was found that the incidence of fractures was substantially lower in THIN compared to GPRD...” [Citing: van Staa QJM 2005⁴]

- As mentioned above there is no evidence of this given in the paper cited by van Staa. However, a similar paper by van Staa⁷ published a year later did state:

“There were also differences within THIN in fracture rates between practices that contributed both to GPRD and THIN vs. those contributing to THIN only: the rate of hip fracture was 31% higher in those contributing both to GPRD and THIN. For clinical vertebral fractures, the difference was +64% and for other clinical osteoporotic fractures +35%.”

We presume that this is the criticism that they wished to level against THIN. However the next sentence states:

“When stratifying within each dataset by deciles of fracture risk, a good concurrence was found between the predicted and observed risks of fracture”,

- In other words the lower incidence rates in THIN-only practices were explained by differences in the underlying risk of fracture between the samples.
- It is worth noting that van Staa was Head of Research at GPRD when the 2006 publication was submitted, revised and published.⁷ However this was not mentioned in his accreditations.

Comment on: “there are differences in the incidence between GPRD and THIN-only practices. The ratio of the number of cases in GPRD practices over THIN-only practices varied from 3.1 for colon cancer to 4.4 for myocardial infarction.”

- They are comparing numbers; numbers are lower in the THIN-only practices as there are less patient-years in this sample. Importantly, in order to compare groups they should have used age and sex adjusted incidence rates. Any such inference is dangerous as noted by Lewis et al in their reply.⁸

Comment on: “The other likely reason for lower completeness of THIN data is that practices solely contributing to THIN may be new to the VISION IT software and that the clinical data from their previous software are not coded as well and do not convert correctly to the VISION IT software. Researchers should be made aware of these issues.”

- The assertion of lower completeness is not backed up with references or data. With regards to the software, all THIN and GPRD practices are Vision software users. We agree that conversion to Vision may incur differing degrees of problems according to the coding systems and data structure of the previous software. However, we indicate the practices for which there have been issues with data conversion and data gaps so that researchers may apply the Vision date. These are specifically highlighted in the THINPRAC file available to researchers and are explained in the free training given to all researchers using THIN Data.
- THIN comprises both practices that are new practices, and hence their historical data had not been used for research purposes, and practices that had been part of the GPRD network. Any issues of lower completeness are more likely to be related to how long the practices had been contributing data for research purposes rather than a GPRD vs. THIN dichotomy. Therefore these issues will be exactly the same for the current MHRA GPRD practices in that those that joined the scheme more recently will not have been contributing data for research purposes in the past i.e. those that were not in the original panel of practices contributing to the VAMP Research Databank – the precursor to GPRD.

References:

¹ Van Staa TP, Parkinson J. Re: Use of cyclo-oxygenase 2 inhibitors (COX-2) and prescription non-steroidal anti-inflammatory drugs. *Pharmacoepidemiol Drug Saf*, 2007; 16:1253-4

(NSAIDS) in UK and USA populations: implications for COX-2 cardiovascular profile

² Van Staa TP, Parkinson J. Response to: validation studies of the health improvement network (THIN) database for pharmacoepidemiology research by Lewis et al. *Pharmacoepidemiol Drug Saf*, 2008; 17:103-4

³ Arellano FM, Ulcickas Yood M, Wenworth CE, Oliveria SA, Rivero E, Verma A, Rothman KJ. Use of cyclo-oxygenase 2 inhibitors (COX-2) and prescription non-steroidal anti-inflammatory drugs (NSAIDS) in UK and USA populations. Implications for COX-2 cardiovascular profile. *Pharmacoepidemiol Drug Saf*, 2006; **15**:861-72.

⁴ van Staa TP, Geusens P, Pols HA, de Laet C, Leufkens HG, Cooper C. A simple score for estimating the long-term risk of fracture in patients using oral glucocorticoids. *QJM* 2005; **98**(3): 191–8

⁵ Maguire A, Blak B, Thompson M, Hall G. The importance of defining periods of complete mortality reporting in automated patient databases. *Pharmacoepidemiol Drug Safe* 2008;17:S250

⁶ Lewis JD, Schinnar R, Bilker WB, Wang X, Strom BL. Validation studies of the health improvement network (THIN) data base for pharmacoepidemiology research. *Pharmacoepidemiol Drug Saf* 2007; **16**: 393–401

⁷ van Staa TP, Geusens P, Kanis JA, Leufkens HGM, Gehlbach S, Cooper C. A simple clinical score for estimating the long-term risk of fracture in post-menopausal women. *QJM* 2006; **99**:673-82

⁸ Lewis JD, Schinnar R, Bilker WB, Wang X, Strom BL. Response to van Staa and Parkinson. *Pharmacoepidemiol Drug Saf* 2008; **17**:104.