LETTER TO THE EDITOR

Response to "Pharmacovigilance 2030: Invited Commentary for the January 2020 'Futures' Edition"

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To the Editor:

We agree with Arlett *et al*. that individual case safety reports (ICSRs) will remain an important element of front-end signal detection for the foreseeable future, though the authors may be overemphasizing the future relative importance of ICSRs.[1] Despite their severe qualitative and quantitative limitations, and the heterogeneity of quality, information content, and signal-to-noise ratio between ICSR report sources, their accessibility and geographic, demographic, and pharmacological scope are conducive to high-throughput, hypothesis-free signal detection. They contribute enormously to the safe use of drugs, and it is apt that we honor the contributions of those who report, collect, archive, and analyze ICSRs.

Nonetheless, the relative contribution of ICSRs, while still substantial, may be diminishing, as other more robust sources of real-world data (RWD) and emerging methods become available. Arlett *et al*. mention that these other sources of RWD, such as electronic medical records, are more applicable to signal evaluation than signal detection, because hypothesis should not be generated and tested in the same data. However, this is not a bright line, and research has highlighted potential utility of other RWD for high-throughput, hypothesis-free drug safety signal detection.[2] Further, the best data set for signal detection may be a function of an event's incidence, clinical phenotype, seriousness, latency, and overall drug-attributable risk.

Therefore, we have a more ambitious vision for Pharmacovigilance in 2030 that includes the continued fruitful shared effort by regulators, industry, and academia to develop, harmonize and/or refine e-standards, terminology, and analytic methodologies, applied to more robust RWD, including large distributed data networks, so that in addition to a premier role in signal refinement and evaluation, these will at least vie with ICSRs as an important source of signals.

Regardless of the differences in the relative emphasis of ICSRs in our predictions, we stress the importance of the statement of Arlett *et al.* of the need for evidence-based decisions and data quality monitoring. This is especially apt with an expanding inventory of data and methods. Common sense, practical experience, and queueing theory indicate that more data, including spontaneous reports, do not always improve signal detection performance. A case in point is ICSRs obtained via solicited reporting, which have been reported to be of low quality and degrade quantitative signal detection performance.[3,4] Further, we should be cognizant of, and attempt to dampen, the documented hype cycle effects associated with emerging quantitative pharmacovigilance methodologies regardless of study setting.[5]

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CONFLICT OF INTEREST

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