Hong Kong Journal of Paediatrics

香港兒科醫學雜誌 (New Series)
An Official Publication of
Hong Kong College of Paediatricians &
Hong Kong Paediatric Society
c/o Hong Kong College of Paediatricians, Room 801, Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen,Hong Kong.

Publisher
Hong Kong Journal of Paediatrics is published by Medcom Ltd, Flat E8, 10/F, Ka Ming Court, 688-690 Castle Peak Road, Kowloon, Hong Kong SAR. Tel: (852) 2578 3833, Fax: (852) 2578 3929, Email: mcl@medcom.com.hk

Indexed in EMBASE/Excerpta Medica, Science Citation Index Expanded (SCIE) and Scopus

Website: www.hkjpaed.org

ISSN 1013-9923

Editorial

Real-World Clinical Evidence versus Randomised Controlled Trials in Paediatrics: The Competition has Begun

The amount of data created on a daily basis is estimated to be 2.5 quintillion bytes.[1] With 17 zeros that follow '25', this number represents a quarter of the total number of all insects alive on this planet at any time.[2] For data related to healthcare, industry analysts estimate their growth to about 2,300 quintillion bytes (exabytes) by 2020.[1] Review of microfilms of scanned clinical records is a moment of analogue nostalgia. Those were the days. Health data currently stored in the hospital administrative database, electronic healthcare systems, clinical registry, laboratory and medical imaging database, insurance claim records, and biometric data are the digital realities. How to make sense of these big data for the generation of evidence to improve healthcare has become a focus of attention.

The clinical wisdom in the practice of paediatrics is based on knowledge acquired through real-world clinical encounters, dissemination and discussion of interesting case reports, sharing of collective experience by publication and analysis of prospectively or retrospectively collected clinical data, and conducting of randomised controlled trials, the latter being ranked the top of the hierarchical level of evidence generated for evidence-based clinical practice. In this issue of the *Journal*, Karakayali et al. performed a randomised double-blind placebo-controlled trial to determine to the efficacy of ondansetron and metoclopramide in managing children who presented to the emergency department with acute vomiting.[3] Included in this issue are also two cross-sectional studies, one assessing the vitamin D and nutritional status of lean, normal weight and obese children,[4] and the other is a questionnaire survey assessing depression and eating disorders in children with type 1 diabetes mellitus.[5] Another original article explored the associations between infant feeding modalities and metabolic risk factors for urolithiasis in infants.[6]

The 1989 United Nations General Assembly "Convention on the Rights of the Child" acknowledges the right of the child to the enjoyment of the highest attainable standard of care,[7] which includes without doubt the right to benefit from the highest level of evidence generated from research for management of paediatric diseases. Nonetheless, the unique challenges in paediatric trials including the concern of testing new interventions in children, recruitment logistics and success, and consent seeking cannot be overemphasized. The inconvenient truth of a high probability of discontinuation and nonpublication of randomised clinical trial conducted in children is shown recently by the retrospective cross-sectional study of Pica and Bourgeois.[8] They found that 19% of the 559 trials registered in ClinicalTrials.gov from 2008 to 2010 were discontinued early, with difficulty in patient accrual and conduct of the trial[5] being the most common given reasons for trial discontinuation. Additionally, they found that 30% of the complete trials were not published.[8] These findings inevitably translate to the disappointing fact that thousands of children have been exposed to behavioural, pharmacologic, device, procedural, dietary and other types of interventions, who had accepted certain degree of potential harm and may not directly benefit from the study findings, but without leading to findings to improve paediatric healthcare.

Even beyond the unique paediatric challenges, limitations of randomised controlled trials have been witnessed over the past seven decade since formalisation of the methodology in the 1940s. It is beyond the scope of this editorial to elaborate on the limitations and lessons learnt from the history of randomised controlled trials. Interested readers can refer to recent discussions on this topic.[9,10] Some have argued that evidence based medicine may already be in a crisis for a number of reasons: the evidence based quality mark has been misappropriated by interest, the volume of evidence has become unmanageable, statistically significant benefits may be marginal in clinical practice, inflexible rules and technology driven prompts may produce care that is management driven rather than patient centred, and evidence based guidelines often map poorly to complex multimorbidity.[11] These advocates suggest refocusing on the provision of usable evidence that can be combined with clinical context and professional expertise for optimal care of individual patients.[11] Incorporation of personalised clinical data, patient and physician-wise, for the generation of this type of evidence seems to be a logical move.

Increasingly, headlines in media and debates in meetings have hinted on the possibility of real-world clinical performance and medical big data eclipsing or replacing the role of randomised controlled trials. While sparking controversies and being met with skepticisms, the big data technology has found its way to the medical arena, albeit in its nascent stage. Rumsfed et al have described for example eight potential areas of applications of big data analytics in cardiovascular care, including predictive modeling for risk and resource use, population management, drug and medical device safety surveillance, disease and treatment heterogeneity, precision medicine and clinical decision support, quality of care and performance measurement, public health, and research applications.[12]

The use or reuse of health data for generation of research data are nonetheless met with challenges and controversies. Strong evidence of the benefits of big data analytics over traditional medical research methods is lacking at this moment. Issues on data quality, heterogeneity, and inconsistency are important obstacles. Peek and Rodrigues recently discussed the important controversial issues on whether: i) data shall be used only for the purpose for which they well collected, ii) big data can replace traditional medical research methods, and iii) to protect the privacy of patients, health data should not be reused for research without explicit consent of the patients concerned.[13] These controversies remind us of the latest scandals related to data breach of the social media.

In this era of digital transformation, there is always special feeling of nostalgia on memorable analogue moments. Equally, the special moment of unleashing the potential of data analytics in paediatric healthcare is here and we have to stay ahead of the game of competition between the digital data of real-world clinical evidence and the analogue medical research methodologies.

YF Cheung
Chief Editor

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