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In reply to: “Antimicrobial defined daily dose adjusted by weight: A proposal for antibiotic consumption measurement in children”



En respuesta a: “Dosis diaria definida ajustada por peso: una propuesta para la medición de consumo antimicrobiano en pediatría”

Dear Editor,

We thank the authors of the letter¹ (AOL) for their interest in our manuscript.² They have correctly pointed out the importance of quantifying antimicrobial use (AU) for antimicrobial stewardship programs (ASP), recalling the lack of an optimal standardized metric for paediatric patients while reviewing current recommendations on approved metrics: Days of Therapy (DOT) and Daily Defined Dose (DDD). Further comments on the methods and the results interpretation in our article has been made.² We agree with their comments, which correctly summarized some of the challenges we have faced and mentioned in the manuscript and would like to further elaborate on some of the points stated.

We agree that the AU rate may possess different sources of variability that may not have been fully covered through the time period selected. The chosen 12-month period (which importantly includes the winter season) focused on setting up the methodology for the proposed metric, however validation will require an extended period.

We also agree that age and weight variability between different cohorts hampers the comparison between centres and benchmarking. As suggested in our manuscript, and supported by the AOL with additional references, weight-adjusted DDD would require the use of weight bands,³ which our group is in the process to establish for the validation phase. Dose based metrics with agreed doses for standardization indeed could obviate dose variability, however a harmonized set-up value is necessary to allow benchmarking and comparison.⁴ Aggregate metrics for ASP tackles patient's complexity and dose variability in real life practice by the distribution of cases through periods of time, although this may not be exact in all situations and interpretation of data deviation is required.⁴

Admittedly, antimicrobial inclusion and exclusion criteria are lacking in our methodology. Antibiotics were included based on available data between centres. Voriconazole (not widely used in all included hospitals) and antiviral drugs (data was not systematically recorded by all participants) were not included. Great efforts were made (Delphi methodology) in order to homogenize antibiotic doses. Nevertheless, and not surprisingly, discrepancies were

observed and are possibly more pronounced in non-study conditions as it is frequently observed in clinical settings.

The AOL state that DOT remains the metric of choice for all ages based on recommendations and guidelines from the United States of America (USA).^{5,6} It must be noted, that DOT is the measure recommended by the Center for Diseases Control and Prevention (CDC) and the Infectious Diseases Society of America (IDSA),^{5,6} therefore hospitals in the USA have adapted to report their results using this metric. The IDSA guideline recommendation for using DOT in preference to DDD has a weak recommendation and low-quality evidence level, nonetheless recognizing the advantage of DOT in children due to weight-based dosing.⁵ However, DOT also possess limitations for its use in children and require patient level antibiotic use data which may not be available in all settings.^{4–7}

The referenced study by Stanić Benić et al., gives a global approach to the issue, reviewing different settings by different professionals to identify inpatient quantity metrics (IQM) for AU.⁸ Their consensus procedure resulted in a set of 12 IQMs where DDD and DOT based metrics were included among others.⁸ One of the IQM proposed was to preferably express AU in at least two metrics simultaneously,⁸ as AOL suggest to overcome the disadvantages of individual metrics and get further information to correctly interpret AU data.

As mentioned in the manuscript, we agree that DDD has important disadvantages for monitoring AU in children and that DOT remains as the currently recommended option when available. Considering all this, we feel that our proposed metric, when refined and validated, may serve as a complementary option for DOT. Efforts should be directed not only to improve process metrics in our opinion, but also to develop impact metrics for paediatric ASP that would correlate with clinical outcomes and evaluate not only quantity but quality of AU.^{6,9,10} The quest for the best AU metric in children continues, and further data and investigation is needed.

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Conflicts of interest

None to declare.

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