Erratum to be care the risk of under fit in dose-response metaanalysis when using cubic spline

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Erratum to: Ann Transl Med 2016;4:388

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In the article entitled "Be care the risk of under fit in dose-response meta-analysis when using cubic spline" that appeared on Page 388 of Vol 4, No 19 of *Annals of Translational Medicine* (1), there are some errors. The full text should be replaced by the following content.

Be care the risk of over fit in dose-response meta-analysis when using cubic spline

Dose-response meta-analysis (DMA) plays a vital role in investigating the potential causality between continuous variable and binary outcome. An increasing number of DMAs have been published during the past several years. In this letter, we aim to discuss a hypothesis of over fit when using cubic spline.

We searched Medline, Embase, and Wiley online Library for published DMAs between Jan-2011 to Dec-2015 and 427 publications were identified. We found that 187 DMAs used restricted cubic spline and 2 DMAs used natural cubic spline to fit the potential non-linear trend, with 143 (76.47%) of them used 3 knots (the minimum number). Our argument is that whether 3 knots is adequate representing the potential non-linear trend.

Stone (1) suggests using 5 knots for it flexibility enough representing the potential non-linear trend. While Durrleman (2) claims the number of knots may need to refer to the sample size that a reasonable large sample size can consider more knots. Such advisory opinions are valuable for us to select the number of knots. But is more knots better?

We took the recent published DMA (3) as an example (relevant data can be obtained by contacting the authors). The authors used restricted cubic spline with 5 knots $(1^{th}, 25^{th}, 50^{th}, 75^{th}, and 99^{th})$ to approximate the relationship between 24-hour sleep duration and risk of all-cause mortality and they found both shortened and prolonged sleep duration were associated with increased risk of all-cause mortality (J-shaped). We re-analyzed part of their data by insetting 3 knots $(1^{th}, 50^{th}, and 99^{th})$ and found a J-shaped trend with the value of Goodness of fit of 96.58 (*Figure 1A*); while when we used 5 knots, we got a more sharply trend at the cutoff point of 7 hours. However, the value of Goodness of fit is 76.5 (*Figure 1B*). Theoretically, with the

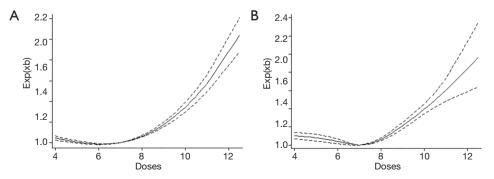


Figure 1 The approximated non-linear trend between sleep duration and risk of all-cause mortality by using restricted cubic spline: (A) using 3 knots; (B) using 5 knots.

Page 2 of 2

numbers of knots increase, the approximating effects will more close to the "true value". But in this example, we showed that more knots may get a poorer fit.

The authors of that DMA used 5 knots to fit the trend that the results may also at risk of over fit. However, their results and conclusions conform well to clinical practice.

Hypothetically, the results or conclusions of DMAs which uses 4 or more knots may be at risk of over fit whether the sample size is large or not. When approximating non-linear relationship between exposure and outcome by cubic spline, we should take both theory and clinical practice into consideration. For DMA with cubic spline, 3 knots may be enough, however we recommend a Goodness of fit should be reported (4) or an additional analysis should be done by using 4, even 5 knots to check whether the trend is accurately and realistically. We also recommend that at least one clinician should be advised when preparing a systematic review or meta-analysis.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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The publisher regrets the error.

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