



## Can insulin response patterns predict metabolic disease risk in individuals with normal glucose tolerance? Reply to Crofts CAP, Brookler K, Henderson G [letter]

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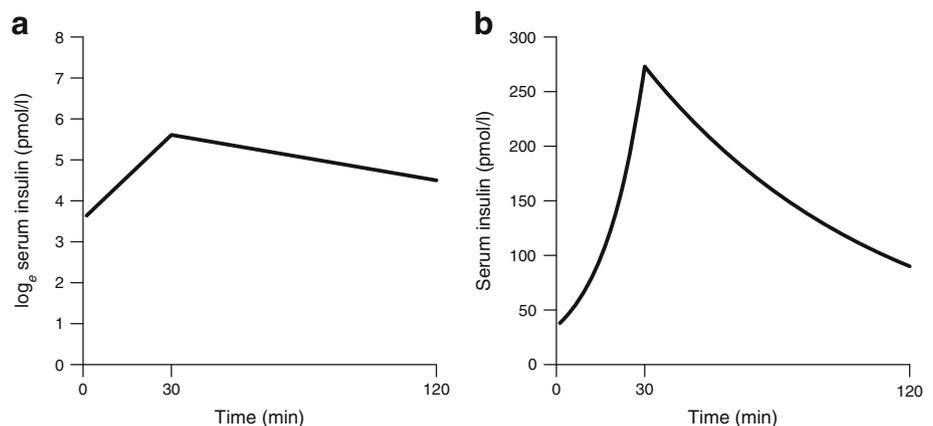
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*To the Editor:* We would like to thank Crofts et al [1] for their positive and constructive comments regarding our article [2]. The main reason why we have not explored insulin response in the Danish Inter99 cohort using the latent class trajectory approach is fairly technical. Serum insulin values are usually log-transformed before analysing them as continuous outcomes because of their skewed distributions. In our study, this would mean we would model a piecewise-linear trajectory on the log-scale (Fig. 1a), which results in a rather unrealistic shape when transformed back to the original scale (Fig. 1b). Imposing the peak at 30 min is already a big restriction;

therefore, we did not want to put this further constraint on the shape of the insulin response curve.

Furthermore, insulin levels are highly variable, and their analysis is laboratory-dependent and expensive, limiting their utility for clinical purposes. Their potential use in prediabetic substratification is the subject of another investigation that we are planning to pursue in the EGIR-RISC (European Group for the study of Insulin Resistance: Relationship between Insulin Sensitivity and Cardiovascular disease risk) cohort [3], using glucose and insulin measurements at more than three time-points during a 2 h oral glucose tolerance test.

**Fig. 1** Serum insulin trajectory on the (a) logarithmic and (b) original scale. The curves represent a fictional participant for the purpose of demonstration



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**Contribution statement** AH was responsible for drafting the response. All authors contributed to critical revision and approved the final version to be published.

## References

1. Crofts CAP, Brookler K, Henderson G (2018) Can insulin response patterns predict metabolic disease risk in individuals with normal glucose tolerance? *Diabetologia* <https://doi.org/10.1007/s00125-018-4581-7>
2. Hulman A, Vistisen D, Glümer C, Bergman M, Witte DR, Færch K (2018) Glucose patterns during an oral glucose tolerance test and associations with future diabetes, cardiovascular disease and all-cause mortality rate. *Diabetologia* 61:101–107
3. Hills SA, Balkau B, Coppock SW et al (2004) The EGIR-RISC STUDY (the European group for the study of insulin resistance: relationship between insulin sensitivity and cardiovascular disease risk): I. Methodology and objectives. *Diabetologia* 47:566–570