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# Commentary Time for integrating clinical, lifestyle and molecular data to predict drug responses — Authors' reply



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Thank you for an excellent and comprehensive commentary (Patrignani and Dovizio, 2016) that highlights the findings of our paper (Pottegård et al., 2016) and provides suggestions for the road forward in pharmacoepidemiologic studies. While "individualized therapy" is somewhat beyond the scope of the current study, utilizing an epidemiological/population-based analysis, we fully agree that research integrating clinical, lifestyle, and molecular data is an important step forward for improving drug therapy. In our opinion, our approach targeting multiple drug-cancer associations and the applied analyses can be considered a first step towards such integrated studies. However, the challenge lies in identifying data sources that can provide drug, clinical, lifestyle and genetic data for a sufficiently large population. In the context of the present study (Pottegård et al., 2016), we used prescription drug data dating back to 1995 (Kildemoes et al., 2011). Longterm data are necessary in the study of outcomes with long latency such as cancer (Umar et al., 2012). Importantly, the case might be different for acute events, such as bleeding or cardiovascular events. We believe that advances in the study of cancer risk associated with prescription drug use will require innovative methods that make use of detailed data on a subset of a population in ways that leverage the information for the analysis of the full population. One example in pharmacoepidemiology is propensity score calibration (Stürmer et al., 2007), which allows adjustment of confounding based on data that is only available for a subset of the study population, e.g. survey data of life-style factors. Another example is recursive partitioning (Seeger et al., 2006), which can be used to refine study variables (e.g., confounders or outcomes) in a subset of the population that can then be applied to the entire study population.

### **Declaration of interests**

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### References

- Kildemoes, H.W., Sørensen, H.T., Hallas, J., 2011. The Danish National Prescription Registry. Scand. J. Public Health 39, 38–41.
- Patrignani, P., Dovizio, M., 2016. Time for integrating clinical, lifestyle and molecular data to predict drug responses. EBioMedicine 7, 9–10.
- Pottegård, A., Friis, S., Christensen, R.D., Habel, L.A., Gagne, J.J., Hallas, J., 2016. Identification of associations between prescribed medications and cancer: A nationwide screening study. EBioMedicine 7, 73–79.
- Seeger, J.D., West, W.A., Fife, D., Noel, G.J., Johnson, L.N., Walker, A.M., 2006. Achilles tendon rupture and its association with fluoroquinolone antibiotics and other potential risk factors in a managed care population. Pharmacoepidemiol. Drug Saf. 15, 784–792.
- Stürmer, T., Glynn, R.J., Rothman, K.J., Avorn, J., Schneeweiss, S., 2007. Adjustments for unmeasured confounders in pharmacoepidemiologic database studies using external information. Med. Care 45, S158–S165.
- Umar, A., Dunn, B.K., Greenwald, P., 2012. Future directions in cancer prevention. Nat. Rev. Cancer 12, 835–848.

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