Reply to: Cause or consequence?

Received: 14 Jan 2022
Accepted: 19 Jan 2022

Reply to F.M. Volpe:

We thank F.M. Volpe for questioning whether the results of the SABINA III study showing associations between short-acting β_2-agonist (SABA) prescriptions and poor asthma outcomes should be regarded as "cause or consequence." We agree that causation cannot be assumed and stated this clearly as follows "this cross-sectional study does not permit an assessment of a causal link between SABA prescriptions and asthma outcomes and does not discount reverse causality; the results simply represent an association" [1]. But implying that high levels of SABA use is simply a "consequence" is also an oversimplification of a complex issue. First, besides the consistent results from epidemiological studies, there are many mechanistic studies of the negative effects of regular SABA use on biomarkers of airway inflammation, airway hyper-responsiveness, asthma symptom control and exacerbation risk, so causation is not ruled out [2, 3]. Further, while logical to consider that high use of an as-needed medication for symptoms must represent poor control, we would point out that a central purpose of our paper was to assess not inhaler use, but SABA prescriptions by clinicians and purchase over the counter. These are systemic issues concerning physician behaviour and access to SABAs that, in the face of excessive use and poor asthma control, permit or even encourage SABA use, which is contrary to asthma guideline recommendations [4]. The "long list" of recommendations for addressing this situation is therefore highly pertinent to the objectives of the paper and we agree that these may, and in fact are intended to, have "profound implications… for clinical practice and public health" [4–6].

Shareable abstract (@ERSpublications)
SABINA III shows associations between SABA prescriptions and poor asthma outcomes and does not imply causation. However, implying that high SABA use is simply a "consequence" of poor asthma control is also an oversimplification of a complex issue. https://bit.ly/3rXKSGm

Cite this article as: Bateman ED, Price DB, Wang H-C, *et al*. Reply to: Cause or consequence? *Eur Respir J* 2022; 59: 2200103 [DOI: 10.1183/13993003.00103-2022].

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Conflict of interest: E.D. Bateman is a member of the Science Committee and Board of GINA and reports personal fees from ALK, AstraZeneca, Boehringer Ingelheim, Chiesi, Menarini, Novartis, Orion, Regeneron Pharmaceuticals and Sanofi Genzyme. D.B. Price has board membership with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Mylan, Mundipharma, Novartis, Regeneron, Sanofi Genzyme, Teva Pharmaceuticals and Thermofisher; consultancy agreements with Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline (GSK), Mylan, Mundipharma, Novartis, Pfizer, Teva and Theravance; grants and unrestricted funding for investigator-initiated studies (conducted through Observational and Pragmatic Research Institute Pte Ltd) from AstraZeneca, Boehringer Ingelheim, Chiesi, Circassia, Mylan, Mundipharma, Novartis, Pfizer, Regeneron, Respiratory Effectiveness Group, Sanofi Genzyme, Teva, Theravance and UK National Health Service; payment for lectures/speaking engagements from AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GSK, Kyorin, Mylan, Mundipharma, Novartis, Regeneron, Sanofi Genzyme and Teva; payment for the development of educational materials from Mundipharma and Novartis; payment for travel/accommodation/meeting expenses from AstraZeneca, Boehringer Ingelheim,

Mundipharma, Mylan, Novartis and Thermofisher; funding for patient enrolment or completion of research from Novartis; stock/stock options from AKL Research and Development Ltd, which produces phytopharmaceuticals; owns 74% of the social enterprise Optimum Patient Care Ltd (Australia and UK) and 74% of Observational and Pragmatic Research Institute Pte Ltd (Singapore); is a peer reviewer for grant committees of the Efficacy and Mechanism Evaluation programme and Health Technology Assessment; and was an expert witness for GSK. H-C. Wang reports no disclosures. P. Schonffeldt reports lectures on medical education and inclusion as a researcher on clinical study protocols funded by AstraZeneca, GSK, Teva, ITF Labomed, Boehringer Ingelheim and Sanofi Genzyme. A. Catanzariti and R.J.P. van der Valk are employees of AstraZeneca. R.J.P. van der Valk has shares in GSK and shares and options in AstraZeneca. M.J.H.I. Beekman was an employee of AstraZeneca at the time the study was conducted and has shares in AstraZeneca.

Support statement: AstraZeneca funded the SABINA III study; was involved in the study design, protocol development, study conduct and statistical analysis; and was given the opportunity to review this manuscript before submission. Publication support was provided by Michelle Rebello of Cactus Life Sciences and funded by AstraZeneca. Funding information for this article has been deposited with the Crossref Funder Registry.

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