Challenges in interpreting trends in testing for α_1-antitrypsin deficiency in COPD patients from UK primary care

To the Editor:

Soriano *et al.* [1] recently published data on trends in testing and diagnosis of α_1-antitrypsin deficiency in chronic obstructive pulmonary disease (COPD) patients using primary care data from the UK. This was a large population-based study reporting that only ~2.2% of patients diagnosed with COPD before the age of 60 years are tested for α_1-antitrypsin deficiency and suggests that α_1-antitrypsin deficiency may remain undiagnosed in many people with COPD. The study does highlight an important point that testing for this relatively rare but potentially important cause of COPD should be considered more widely among healthcare professionals.

In that article, the authors report that there was a significantly increasing trend in α_1-antitrypsin deficiency testing between the years 1994 and 2013 in UK COPD primary care patients and that the incidence of α_1-antitrypsin deficiency diagnosis generally increased. However, in order to provide a valid interpretation as to the meaning of these data, important aspects relating to data contained within UK primary care electronic medical records needs to be understood.

Compared to the apparent large increase in the trend of α_1-antitrypsin deficiency testing, the incidence of α_1-antitrypsin deficiency diagnosis, as reported in figure 2e of the study by Soriano *et al.* [1], is relatively limited, with the incidence of diagnosis remaining either fairly stable from ~2002 or falling depending on sex. In general, one could expect to see a more positive correlation in the incidence of α_1-antitrypsin deficiency diagnosis linked to the increase in α_1-antitrypsin deficiency testing in people with COPD, unless for example the wrong set of patients had been targeted for testing. If such a situation where to occur, it could be argued that routine testing in that specific COPD population may not be worthwhile.

However, it is likely that the observed increase in the trend of α_1-antitrypsin deficiency testing seen in that study is confounded by the evolution of electronic blood test requesting and recording in UK primary care electronic medical records. During the study period, electronic test requesting and laboratory-linked systems were introduced using systems to provide an integrated link directly from and to primary care electronic medical records of different UK electronic medical record providers, including INPS Vision, EMIS and System One [2]. It is now fairly standard that the results of blood tests requested by general practitioners in the UK are automatically populated within the patient's electronic medical record. However, this was not always the case and failure to account for this could lead to observed increases in the trend of blood testing requests, including for α_1-antitrypsin deficiency.

As part of a different project [3], descriptive analysis of blood test recording in a cohort of 204473 spirometry-confirmed COPD patients identified from the UK Clinical Practice Research Datalink (protocol 15_112) using a validated Read code algorithm [4] is shown in figure 1, together with trends in the frequency of new α_1-antitrypsin deficiency testing among the whole COPD population. Similar increases in all other common blood test recording occurred during this period, with a rapid uptake early on, particularly between 2000 and 2008.

Prior to electronic test requesting in UK primary care, blood test results would have been entered into the electronic medical record manually with little incentivisation to do so. The risk of unobservable test requests

@ERSpublications
Apparent increasing trends in blood test requesting observed using UK primary care electronic medical records (EMRs) may be confounded by adoption of electronic test requesting systems linked to EMRs rather than changes in clinical practice http://ow.ly/M3Er30mIsJq

Cite this article as: Morales DR. Challenges in interpreting trends in testing for α_1-antitrypsin deficiency in COPD patients from UK primary care. *Eur Respir J* 2018; 52: 1801986 [https://doi.org/10.1183/13993003.01986-2018].

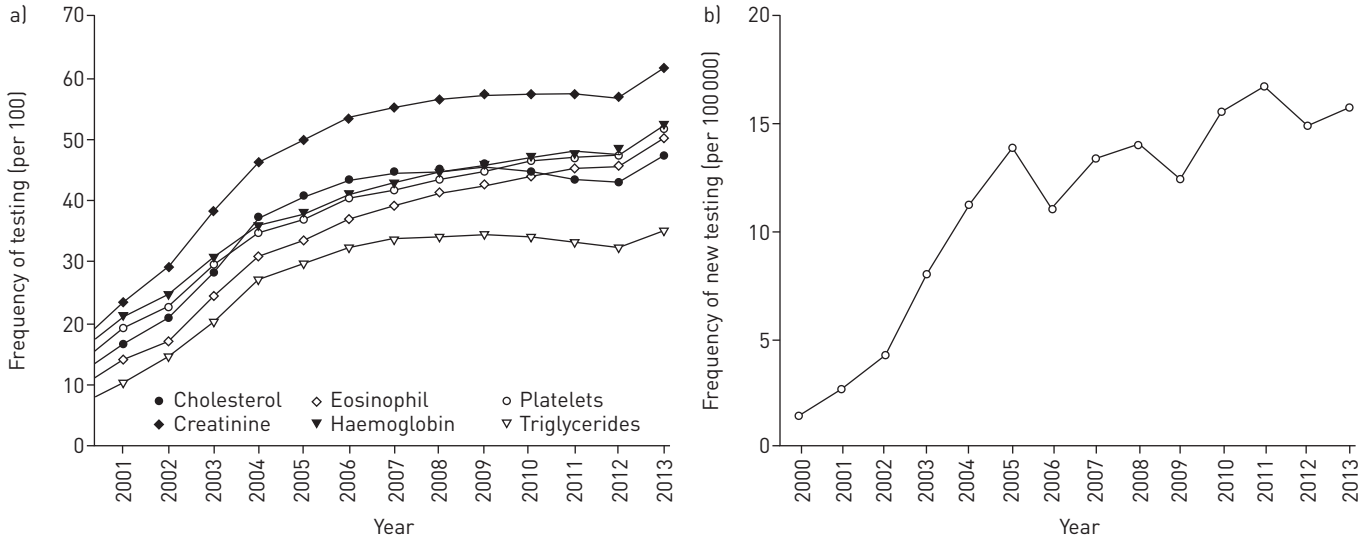

FIGURE 1 a) Trends for different blood tests recorded in a UK primary care cohort of people with chronic obstructive pulmonary disease (COPD). b) Trends in the frequency of new α_1-antitrypsin deficiency testing in a primary care cohort of people with COPD. Data are presented for the entire COPD cohort and are not restricted by age.

prior to electronic test requesting in such practices is, therefore, likely to be high. Although it is possible that the rate of all blood test requesting in UK primary care may have increased, it is perhaps more probable that standardised electronic test requesting has influenced the amount and type of lab data present in UK primary care electronic medical records. Failure to account for this makes it challenging to determine what the true trend in α_1-antitrypsin deficiency testing has been, although it is reasonable to suggest it is still low.

As correctly pointed out by Soriano *et al.* [1], trend data are based on tests that largely reflect only those requested from primary care and therefore will underestimate the true prevalence of α_1-antitrypsin deficiency testing, particularly if younger or nonsmoking patients with newly diagnosed COPD, unexplained respiratory symptoms or unexplained airway obstruction are referred directly to speciality clinics for further investigation. It must also be remembered that specific genotype testing may not routinely be available to be requested by primary care clinicians even if they would like to.

Lastly, when presenting data on incidence it is important to be consistent in the way data are presented. In this regard, Soriano *et al.* [1] note a fall in incidence in their data in 2014, due to data from only the first half of 2014 being included in their database. However, as presented data for 2014 is actually a period prevalence and it may have been more informative to have calculated and presented an incidence based upon person-years of follow-up for 2014 as seen with other data points, or simply to not have presented data for this time period in order to avoid any potential confusion.

Daniel R. Morales
Division of Population Health and Genomics, University of Dundee, Dundee, UK.

Correspondence: Daniel R. Morales, Division of Population Health and Genomics, University of Dundee, MacKenzie Building, Kirsty Semple Way, Dundee, DD2 4BF, UK. E-mail: d.r.z.morales@dundee.ac.uk

Received: Oct 17 2018 | Accepted: Oct 22 2018

Conflict of interest: D.R. Morales has nothing to disclose.

References

1 Soriano JB, Lucas SJ, Jones R, *et al.* Trends of testing for and diagnosis of α_1-antitrypsin deficiency in the UK: more testing is needed. *Eur Respir J* 2018; 52: 1800360.
2 INPS. Test requesting in Vision. London, INPS Ltd, 2011. www.inps.co.uk/sites/default/files/Test%20Requesting%20User%20Guide%20for%20ICE%20Users.pdf Date last accessed: October 12, 2018.
3 Morales DR, Flynn R, Zhang J, *et al.* External validation of ADO, DOSE, COTE and CODEX at predicting death in primary care patients with COPD using standard and machine learning approaches. *Respir Med* 2018; 138: 150–155.
4 Quint JK, Müllerova H, DiSantostefano RL, *et al.* Validation of chronic obstructive pulmonary disease recording in the Clinical Practice Research Datalink (CPRD-GOLD). *BMJ Open* 2014; 4: e00554.

From the authors:

We sincerely thank D.R. Morales for his in-depth assessment of our results and methods [1]. We agree that recent improvements in the UK Optimum Patient Care Research Database and other databases, such as direct, automatic linkage of laboratory results to primary care electronic medical records increased during our period of study. This change for good, that also applies to other conditions [2–6], may partly explain an increased recording of α_1-antitrypsin deficiency testing in primary care in the UK, although trends in our Figure 2 [1] might be steeper than the one he presents for other blood tests or for α_1-antitrypsin deficiency testing in patients with chronic obstructive pulmonary disease (COPD) of all ages and both sexes. Indeed, our finding that new testing occurs most frequently in those COPD patients in the age band 45–65 years, in both males and females, points to the correct strategy of case-finding of α_1-antitrypsin deficiency in COPD, which should be a joint task for general practitioners and other medical specialists. Still, testing may have been originally conducted in specialist practices first, which could be looked at by proxies of referrals in younger COPD patients, and it might indeed be the focus for future research. The last point on how to report data for 2014 is reasonable.

Our conclusion that only ~2.2% of UK patients diagnosed with COPD before the age of 60 years are tested for α_1-antitrypsin deficiency, and that it is still necessary to explore the recording of α_1-antitrypsin deficiency testing (and diagnosis) in other large primary care populations and datasets, remains valid. Finally, we all concur on reinforcing and highlighting awareness and testing of these modifiable and treatable diseases.

@ERSpublications
It is still necessary to explore the recording of α_1-antitrypsin deficiency testing (and diagnosis) in other large primary care populations and datasets http://ow.ly/PANZ30mIvw7

Cite this article as: Soriano JB. Challenges in interpreting trends in testing for α_1-antitrypsin deficiency in COPD patients from UK primary care. *Eur Respir J* 2018; 52: 1802064 [https://doi.org/10.1183/13993003.02064-2018].

Joan B. Soriano, on behalf of all co-authors
Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Madrid, Spain.

Correspondence: Joan B. Soriano, Hospital Universitario de la Princesa, Universidad Autónoma de Madrid, Diego de León 62, 28005-Madrid, Spain. E-mail: jbsoriano2@gmail.com

Received: Oct 29 2018 | Accepted: Oct 30 2018

Conflict of interest: J.B. Soriano declares having received pharmaceutical company grants from GSK in 2011 and Chiesi in 2012 *via* CIMERA his former home institution, and grants from 2014 to date from Linde *via* Hospital Universitario de La Princesa. He has participated in speaking activities, advisory committees and consultancies during the period 2011–2018 sponsored by Almirall, AstraZeneca, Boehringer Ingelheim, CHEST, Chiesi, ERS, Esteve, GEBRO, Grifols, GSK, Linde, Lipopharma, Mundipharma, Novartis, Pfizer, RiRL, Rovi, Sandoz, SEPAR and Takeda, outside the submitted work.

Support statement: Funding was received from the Optimum Patient Care Research Database and Respiratory Effectiveness Group. Funding information for this article has been deposited with the Crossref Funder Registry.

References

1 Soriano JB, Lucas SJ, Jones R, *et al.* Trends of testing for and diagnosis of α_1-antitrypsin deficiency in the UK: more testing is needed. *Eur Respir J* 2018; 52: 1800360.
2 Moss S, Melia J, Sutton J, *et al.* Prostate-specific antigen testing rates and referral patterns from general practice data in England. *Int J Clin Pract* 2016; 70: 312–318.
3 Belhassen M, Nibber A, Van Ganse E, *et al.* Inappropriate asthma therapy-a tale of two countries: a parallel population-based cohort study. *NPJ Prim Care Respir Med* 2016; 26: 16076.
4 Tate AR, Dungey S, Glew S, *et al.* Quality of recording of diabetes in the UK: how does the GP's method of coding clinical data affect incidence estimates? Cross-sectional study using the CPRD database. *BMJ Open* 2017; 7: e012905.
5 Happich M, Kirson NY, Desai U, *et al.* Excess costs associated with possible misdiagnosis of alzheimer's disease among patients with vascular dementia in a UK CPRD population. *J Alzheimers Dis* 2016; 53: 171–183.
6 Halpin DM, Kerkhof M, Soriano JB, *et al.* Eligibility of real-life patients with COPD for inclusion in trials of inhaled long-acting bronchodilator therapy. *Respir Res* 2016; 17: 120.