

1 Research letter

2 Title: Impact of using different predictive equations on the prevalence of chronic byssinosis in textile
3 workers in Pakistan

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1 Abstract

2 Objective: byssinosis remains a significant problem among textile workers in low- and middle-income
3 countries. Here we share our experience of using different prediction equations for assessing ‘chronic’
4 byssinosis according to the standard WHO classification using measurements of FEV₁.

5 Methods: we enrolled 1910 workers in a randomized controlled trial of an intervention to improve the
6 health of textile workers in Pakistan. We included in analyses the 1724 (90%) men who performed
7 pre-bronchodilator spirometry tests of acceptable quality. We compared four different equations for
8 deriving lung function percentage predicted values among those with symptoms-based byssinosis: the
9 third US National Health and Nutrition Examination Survey (NHANES-III, with “N. Indian and Pakistani”
10 conversion factor); the Global Lung Function Initiative (GLI, “other or mixed ethnicities”); a recent
11 equation derived from survey of a western Indian population; and one based on an older and smaller
12 survey of Karachi residents.

13 Results: 58 men (3.4%) had symptoms-based byssinosis according to WHO criteria. Of these, the
14 proportions with a reduced FEV₁ (< 80% predicted) identified using NHANES, GLI, Indian and Pakistani
15 reference equations were 40%, 41%, 14% and 12%, respectively. Much of this variation was
16 eliminated when we substituted FEV₁/FVC ratio (<LLN) as a measure of airway obstruction.

17 Conclusion: accurate measures of occupational disease frequency and distribution require approaches
18 that are both standardised and meaningful. We should reconsider the WHO definition of ‘chronic’
19 byssinosis based on changes in FEV₁, and instead use the FEV₁/FVC.

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21 **What this paper adds**

22 What is already known about this subject?

23 Byssinosis is a significant problem among textile workers in low and middle-income countries. It is
24 primarily identified by its characteristic symptoms, but more severe, chronic disease is accompanied
25 by airway obstruction. The current, WHO classification suggests that obstruction is measured through
26 FEV₁.

27 What are the new findings?

28 In the course of a large trial of a workplace intervention in Pakistani textile mills, the use of different
29 prediction equations for measuring reductions in FEV₁ led to widely varying estimates for the
30 prevalence of chronic byssinosis. Substitution of FEV₁ by FEV₁/FVC substantially reduced the variation.

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32 How might this impact on policy or clinical practice in the foreseeable future?

33 Since accurate measures of occupational disease frequency and distribution require approaches that
34 are both standardised and meaningful, we should reconsider the WHO definition of ‘chronic’
35 byssinosis based on changes in FEV₁ and replace it with FEV₁/FVC.

36 a. contributorship: AAN led this work in conceptualization, analysis, and write-up. MZM supported
37 its statistical analysis. SDM, PB, AA and PC provided supervision throughout this work. All authors
38 read and approved the manuscript before submission.

39 b. funding: Wellcome Trust (Ref: 206757/Z/17/Z)

40 c. competing interests: none declared.

41 d. Data Sharing/Data availability: data are available on reasonable request.

42 e. Ethics Approval: Aga Khan University, Pakistan (2019-0962-3710), National Bioethics Committee in
43 Pakistan (4- 87/NBC-402/19/483), and Imperial College London (19IC4968).

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1 **Introduction:**

2 Byssinosis remains a significant problem among textile workers in low and middle-income countries
3 where much global production is now located (1, 2). The disease is characterized by work-related
4 symptoms of chest tightness and dyspnoea and, in its chronic form, by reductions in FEV₁. There are
5 two classification systems currently in place for byssinosis: that produced by the World Health
6 Organisation (WHO) and the ‘Schilling criteria’ (3, 4). The most severe grade in the latter includes
7 decrements in FEV₁ in addition to presence of symptoms. The WHO approach, in contrast,
8 recommends that respiratory symptoms and chronic changes in lung function are considered
9 ‘together’, albeit as distinct health outcomes in epidemiological surveys, and that measurements of
10 FEV₁ should be compared with ‘data obtained from local populations or similar ethnic and social class
11 groups’ (3). Such data, however, are seldom readily available. Here we share our experience of using
12 different prediction equations for assessing ‘chronic’ byssinosis in Pakistani textile workers.

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14 **Methods:**

15 We recently completed the baseline survey of a cluster randomized trial of a multifaceted intervention
16 to reduce the incidence of byssinosis among textile manufacturers in Karachi, Pakistan (5). We
17 enrolled 1910 workers from 38 textile mills. Following ERS guidelines, trained technicians undertook
18 pre- and post-bronchodilator spirometry using EasyOne spirometers (ndd Medizintechnik AG) and
19 recorded up to eight measurements of FEV₁, FVC and their ratio (6). We reviewed all spirograms; the
20 analyses below include the 1724 (90%) men who performed pre-bronchodilator spirometry tests of
21 acceptable quality.

22 We compared four different equations for deriving lung function: those established through the third
23 US National Health and Nutrition Examination Survey (NHANES-III; “Caucasian”) (7) with a conversion
24 factor of 0.9 recommended for N. Indian and Pakistani individuals (8); the Global Lung Function
25 Initiative (GLI, “other or mixed ethnicities”) equations (9); a recent equation derived from survey of a
26 western Indian population (n=1258) aged 19-88 years (10); and one based on an older and smaller
27 (n=504) survey of Karachi residents aged 16-65 years (11). We classified workers using the WHO
28 recommended FEV₁ cut-off for identification of workers at risk of developing permanent pulmonary
29 impairment: FEV₁ <80% predicted. We compared results based on this classification with one where
30 we replaced FEV₁ by FEV₁/FVC ratio considering values below the normal limit of normality (LLN) to be
31 abnormal. We undertook analyses in Microsoft Excel.

32 The study was approved by the ethics committees at Aga Khan University, Karachi (2019-0962-3710),
33 the National Bioethics Committee in Pakistan (4- 87/NBC-402/19/483), and Imperial College London
34 (19IC4968).

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36 **Results:**

37 Using symptom classification (alone) the prevalence of byssinosis was 3.4% (n=58) and 3.9% (n=67)
38 according to WHO and Schilling’s criteria, respectively – reflecting the grade ½ (9 workers) in the latter.
39 Of the 58 men with byssinosis according to WHO criteria, the proportion with a reduced FEV₁ (<80%
40 predicted) varied according to which set of predictive equations was used, from 40%-41% with those
41 from NHANES and GLI, to 12%-14% with the more locally derived models (Table 1). Much of this
42 variation was eliminated when we substituted FEV₁/FVC ratio (<LLN) as a measure of airway
43 obstruction; in particular, the estimates derived from using the GLI, and Indian reference equations

- 1 were very similar. We observed the same patterns when estimating the prevalence of airway
- 2 obstruction in the total mill population.

Table 1: proportion of workers with airway obstruction, by different criteria and reference equations, in those with symptoms of byssinosis and in the total mill population								
Metric of airflow obstruction	Workers with symptoms of byssinosis (n=58)				Total mill population (n=1724)			
	NHANES (7)	GLI (9)	Indian (10)	Pakistani (11)	NHANES	GLI	Indian	Pakistani
FEV ₁ <80% predicted	40%	41%	14%	12%	1.3%	1.4%	0.5%	0.4%
FEV ₁ /FVC ratio<LLN	12%	24%	21%	NA	0.4%	0.8%	0.7%	NA

NHANES: National Health and Nutrition Examination Survey III
 GLI: Global Lung Initiative
 NA: not available

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4 **Discussion:**

5 The substantial variation in the prevalence of abnormal FEV₁, consistent with standard classifications
 6 of ‘chronic’ byssinosis, resulting from the use of different lung function prediction equations in this
 7 population reinforces the WHO recommendation that reference data from ‘local’ populations be used.
 8 Whether the stipulation for data from ‘similar social class groups’ is met is more difficult to ascertain
 9 since these are seldom reported for the populations from which predicted values are derived. It is
 10 evident that the widely used GLI (in which there is a lack of representation of South Asian populations)
 11 and NHANES III equations (even after adjustment) give a very different picture of the prevalence of
 12 lung function abnormality when this is expressed by FEV₁, and therefore may not be useful in a
 13 local/regional South Asian context. Much textile manufacture now takes place in populations that are
 14 poorly served by spirometric norms, and the problem we have identified in Pakistan will be reflected
 15 in many other LMICs (1, 2). In contrast, substitution of FEV₁ with FEV₁/FVC ratio, with a LLN criterion
 16 of abnormality, produces estimates of airway obstruction that are relatively stable across different
 17 prediction equations, including the GLI. Since the FEV₁ is correlated with the FVC, it is not an
 18 unambiguous measure of obstruction, and for this the FEV₁/FVC, in which the FEV₁ is adjusted for lung
 19 size, is preferable for defining obstruction. In the current context this has the added advantage that it
 20 is largely independent of ethnicity, the ethnic differences in FEV₁ and FVC largely cancelling each other
 21 out.

22 A potential limitation of our work includes the effect of a ‘healthy worker effect’ and the consequent
 23 underestimation of the risk of byssinosis in this context; it is improbable that this will have affected
 24 our findings in relation to the relative merits of FEV₁ and FEV₁/FVC ratio. Reproducible measurements
 25 of FVC are more difficult than those of FEV₁ and require greater technical skill. Finally, the information
 26 provided by the authors of the reference equation for Pakistanis (11) was insufficient to calculate an
 27 LLN.

28 Notwithstanding this, all efforts should be made to reduce exposures to cotton dust to identify
 29 byssinosis early through periodic workplace surveillance for the presence, nature, and extent of
 30 characteristic symptoms and before lung function loss has occurred.

31 Exposures in the workplace may be important causes of respiratory disease (12) and especially so in
 32 LMICs where occupational health and safety measures may be poor. The basis for the prevention of

1 the important public health burden of occupational disease is accurate measures of its frequency and
2 distributions which requires approaches to its recognition and classification that are both standardised
3 and meaningful. We should reconsider the WHO definition of 'chronic' byssinosis based on changes in
4 FEV₁ and substitute it with the use of FEV₁/FVC.

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