non and current smokers those with influential values, the ex-smokers, the obese, and the clinically abnormal. The number 486 agrees with the Miller paper, but the regression lines in table 2 and the figure in the Kilburn paper are those for the 193 subjects only. The Kilburn paper is positively misleading on this.

Before turning fully to the Kilburn paper, it is appropriate to comment further on the regression lines presented by Miller *et al*. The lines are linear relations of the lung function indices to age and height. They are based on women aged 18 to 82. For men, it is generally accepted that lung function continues to increase up to about age 25. Although the turning point may be lower for women, it will still probably be at least age 21. Thus the inclusion of younger women will bias the regression line to have a flatter age slope than it should be. Most influential data points will occur at the extremes of age or height, or both. This may have led to the exclusion of some of the youngest subjects but could also have excluded older subjects with relatively reduced lung function but still clinically normal for age. This again would have flattened the regression lines.

Kilburn studied histology technicians who attended four national conventions of the National Society of Histotechnology. The attendance rate varied between 22% and 42%. Kilburn argued that because "recruitment was directed at neurobehavioural symptoms and testing a biased selection for pulmonary function testing seems unlikely." Under the circumstances of a series of national conventions, it must be assumed that volunteers (except perhaps the first few) were aware that lung function testing was included. With such poor response rates, it cannot be concluded that the selection was unbiased. Kilburn *et al* also make the implicit assumption that attendees at national conventions are representative of all histology technicians.

The comparisons in table 2 and the figure of the Kilburn paper are used to argue that the relations to age are steeper for the histology technicians and so the technicians must have an adverse occupational environment. It has already been pointed out above that the comparison Michigan relations are not based on all 486 comparison subjects. Also, the comparison regressions probably have too low age coefficients. Yet, for FVC for example, the Miller *et al* age coefficient is −0·0232 with standard error 0·0024. The slope for the histology technicians is −0·0273 well within the 95% confidence interval for the Michigan sample. For $FEV_1$, the technicians age coefficient does lie outside that for the confidence interval for the Michigan group. But no standard error is given for the technicians, so it is impossible to determine what an appropriate statistical analysis would have shown. For $FEF_{25-75\%}$, Kilburn *et al* have compared age coefficients when one relation includes height as a covariate and the other does not. It only requires a small correlation between age and height, as occurs commonly, to invalidate this comparison. It is incorrect to conclude that the histology technicians have a significantly steeper age coefficient. This part of the analysis was statistically unsatisfactory.

There is also another implicit assumption—that differences between people of varying age reflect the change in an individual with increasing age. This is generally not fully true, because of changes in nutrition—for example, between people born in the 1940s and the 1960s, and because of changing occupational exposure circumstances, if there is an exposure effect.

Finally, Kilburn *et al* conclude that the reduced lung function is caused by exposure to low doses of formaldehyde. To draw that conclusion, comparison must be made between those with known exposure to formaldehyde to those without, standardising for other exposures. Only a little information on exposure levels in the Los Angeles area is provided. Such information showed wide variability for all substances analysed (formaldehyde, xylene, toluene, and chloroform). No exposure data for other parts of the United States were provided. There is no justification in ascribing any occupational effect to formaldehyde, or indeed to any of the four substances.

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*Author's reply:*

The regression equations listed for histology technicians in table 2 are misprints, whereas the Miller series of equations is correct. The equations used to calculate the data in the histotech column are listed below together with the Miller equations; the yearly decrements now match the age coefficients.

In addition, in response to Rossiter's comment concerning lack of a height coefficient for $FEF_{25-75}$ in the Miller equation, we have provided an equation from Morris *et al*,[2] with a height coefficient and calculated the $FEF_{25-75}$ at the same five age intervals. As can be seen, they show an annual decrement of 31 ml which is much nearer to the Miller one of 36 ml than the histotech decrement of 57 ml a year.

In table 3 and thus in the figure he has correctly noted that the comparison was made with the Michigan model population of Miller *et al*, not with all Michigan women.

In addition, we note that the small difference for $FEF_{25-75}$ l/sec in the first column under L Rock (60), is not statistically significant—the asterisk should be removed.

In modelling the Michigan women for pulmonary function values no increase or decrease with age was found to support the concept of a "turning point" between ages 21–25; thus the age slopes were linear from 18 to 82. This was confirmed by residual analyses which were clean. Thus inclusion of younger women did not bias the age slope. The exclusion of 23 women in modelling Michigan did not change the regression equations for FVC, $FEV_1$, or $FEF_{25-75}$ relied on in this paper.

The other issues raised by Rossiter are considered below.

(1) The comparison group is not a representative sample. The Michigan population probability sample studied for pulmonary function is one of the largest published probability samples. Age is normally distributed in the Michigan sample. The data are consistent with other published series as is shown in the table below for women adapted from Miller. Comparison of these age coefficients shows excellent agreement with Miller (Michigan), an average of the more recent non-smoking larger studies. If Crapo were adopted,[3] or Morris,[4] the results would not differ from those published in our paper. This agreement between series answers the question about bias by volunteers by showing great consistency in the pulmonary function behaviour of these population samples.

(2) The histology technicians are not representative of all histology technicians.

In the real world all samples are composed of volunteers as I am sure Rossiter realises. Perhaps one could

$$
\begin{aligned}
FVC &= \text{Histo} = -0{\cdot}916 + 0{\cdot}03497\ \text{Htcm} - 0{\cdot}0296\ \text{age},\\
&\quad\ \text{Miller} = -2{\cdot}198 + 0{\cdot}0414\ \text{Htcm} - 0{\cdot}0232\ \text{age},\\
FEV_1 &= \text{Histo} = 0{\cdot}0758 + 0{\cdot}0265\ \text{Htcm} - 0{\cdot}0349\ \text{age},\\
&\quad\ \text{Miller} = 0{\cdot}3801 + 0{\cdot}0268\ \text{Htcm} - 0{\cdot}0251\ \text{age},\\
FEV_{25-75} &= \text{Histo} = 1{\cdot}9425 + 0{\cdot}0213\ \text{Htcm} - 0{\cdot}0572\ \text{age},\\
&\quad\ \text{Miller} = \log FEF_{25-75} = 1{\cdot}55628 - 0{\cdot}0120\ \text{age},\\
&\quad\ \text{Morris} = 0{\cdot}551 + 0{\cdot}0236\ \text{Htcm} - 0{\cdot}0310\ \text{age},
\end{aligned}
$$

| Age | $FEF_{25-75}$ l/sec |
|---|---|
| 20 | 3·785 |
| 30 | 3·485 |
| 40 | 3·185 |
| 50 | 2·885 |
| 60 | 2·585 |

select a perfectly representative sample but the utility of doing so is questionable for the real world. By getting similar values across four samples of histotechs, we showed consistency across time and in multiple samples. The variations in flows probably reflect effects of air pollution in Anaheim (Los Angeles Basin) and in Washington DC.

(3) The comparison regression lines quoted by Kilburn *et al* are not based on all 486 women in the Miller study despite Kilburn's statements.

True, the comparisons are all based on the 193 women in the normal population selected to model pulmonary function. All factors consisted, this is the appropriate population for comparing in the search for subtle effects because the 486 also included those with pulmonary disease including asthma, cardiac disease, and obesity.

(4) The statistical analysis comparing the regression lines was inappropriate.

As pointed out earlier, the regression equations published in table 2 of the paper for histotechs were at slight variance with those used to calculate the age intervals data. Using the correct equations, now supplied, the comparisons of the numbers in table 2 and the figure which were correct remain robust.

(5) The information on exposure did not justify an attribution of any effect to low dose formaldehyde exposure.

Sampling for formaldehyde and solvents at the time the study was done was tactically and economically impossible. We did next best by adopting a sampling strategy applied to 10 Los Angeles area laboratories. The results underscored the variability in doses which corresponded with diary and questionnaire data provided by technicians based on odour and irritation. Our unpublished data on variability during the nine hours of two days sampling with a spectrophotometer (Miran) in one large participating laboratory convinced us that any expression of mean levels of formaldehyde was impossible. Rossiter is correct, a Los Angeles sample probably underestimates dosage because windows are open more days of the year due to moderate temperatures and less air is recirculated through laboratories.

Rossiter raises a point as to whether differences between people of varying age in cross sectional studies of normals adequately predict changes in an individual with increasing age. One major study has addressed this recently.[2] They found that 15 year decrements for FVC and $FEV_1$ in the original Oregon population matched those calculated from regression equations. Increases in stature (height) which is what I think Rossiter refers to as "changes in nutrition in people born in the 1940s and the 1960s" are admirably adjusted for by the regression equations.

In summary, we correct small errors in table 2 because the wrong regression equations and two small typographical errors in table 3 were included in the paper. Nevertheless, the data were and are correct. Certain generic issues raised about population representativeness have been dealt with and do not bear on this paper to any greater extent than to all other studies of self selected groups from large populations. It is doubtful that knowledge that lung function would be measured would bias outcomes of spirometry or selection in working women attending a series of national conventions and volunteering for neurobehavioural studies.[5]

*Age coefficients for FVC and $FEV_1$ using various regression equations (normal white adults)*

| | *FVC women* | *$FEV_1$ women* |
|---|---|---|
| Miller | −0·023 | −0·025 |
| Knudson | −0·017 | −0·020 |
| Crapo | −0·022 | −0·026 |
| Black | −0·014 | −0·018 |
| Bass | −0·019 | — |
| Ferris | −0·029 | −0·028 |
| Higgins | −0·018 | −0·021 |
| Schmidt | −0·022 | −0·027 |
| Cherniak | −0·015 | −0·019 |
| Morris | −0·024 | −0·025 |
| (Mean) | −0·020 | −0·023 |


1 Miller A, Thornton JC, Warshaw R, Bernstein J, Selikoff IJ, Teirstein AS. Mean and instantaneous expiratory flows, FVC and $FEV_1$: prediction equations from a probability sample of Michigan, a large industrial state. *Bull Eur Physiopathol Respir* 1986;**22**:589–97.

2 Morris JF, Koski A, Johnson LC. Spirometric standards for healthy non-smoking adults. *Am Rev Respir Dis* 1971;**103**:57–67.

3 Crapo RO, Morris AH, Gardner RM. Reference spirometric values using techniques and equipment that meet ATS recommendations. *Am Rev Respir Dis* 1981;**123**:659–64.

4 Morris JF, Koski A, Temple WP, Clarement A, Thomas DR. Fifteen year interval spirometric evaluation of the Oregon. *Chest* 1988;**93**:123–7.

5 Kilburn KH, Warshaw RH, Thornton JC. Formaldehyde impairs memory, equilibrium and dexterity in histology technicians: effects which persist for days after exposure. *Arch Environ Health* 1987;**42**:117–20.


# NOTICE

**Seventh International Symposium on Inhaled Particles,** Edinburgh, 16–20 September 1991

The symposium aims to promote the presentation and discussion of the results of the recent research on inhaled particles and their effects. It will be concerned primarily with advances in understanding the basic mechanisms of deposition and clearance of dusts, their biological reactions, and epidemiological studies. Topics will include: factors affecting the measurement of inhaled fraction; new models of deposition, clearance, and retention including overload effects and application to submicron and hygroscopic particles; biological reactions, including carcinogenicity, of dusts in the lung; synergistic effects of gases and dusts; exposure response studies of fibres, silica, and other dusts; role of different minerals in mixed dust pneumoconiosis; dust or chemical exposure in relation to occupational asthma; and effects of radon exposure and indoor air quality.

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