



Why did so many women develop cancer?

The correspondence in this *Journal* regarding Linda Bryder's book *A History of the 'unfortunate experiment' at National Women's Hospital* serves a number of important functions.¹ First, it assists in focusing opinion on the scientific validity of Associate Professor Green's research into the natural history of carcinoma *in situ* (CIS) of the cervix. Second, it provides an opportunity to raise relevant issues which have not previously been reported. This is illustrated by Dr Bill McIndoe's failure to communicate his concerns regarding Green's flawed 1974 paper which was published in this *Journal*.²

Green's previous papers had been published in international medical journals and few if any readers would have been familiar with the emerging information and tensions within National Women's Hospital (NWH). The publication of Green's 1974 paper caused McIndoe considerable distress. He drafted a lengthy response outlining the details of the women who had developed invasive cancer and who had been excluded from Green's paper. However, he did not submit it for publication. Had he done so, the wider medical community may have responded (not that would I have confidence on this issue) and alarms may have been raised for others in New Zealand to speak out. If this had happened it may have prompted the 1975 internal NWH "whitewash" committee to take more definitive action.

Dr Overton states that "debate over [Bryder's] book has unfortunately centred on criticism of Professor Bryder". This is not so, the criticism is not personal, but on the evidence and conclusions she has reached. Professor Bryder and Dr Overton are advocates for that sector of the medical profession who remain aggrieved by the outcome of the Cartwright Inquiry. I am an advocate for the patients.

Dr Overton's analysis has focused on the treatment received by the two groups of women described in the 1984 McIndoe et al. paper but not on the adequacy of treatment.^{1,3} The object of writing our paper was to describe the natural history of CIS, provide alternative results to those previously published by Green and to further alert the medical authorities. This paper which "blew the medical whistle" on the 'unfortunate experiment' was an analysis of a cohort of women with CIS who had been followed prospectively as a consequence of the NWH Medical Committee's approval for Green's study of the natural history of CIS, entailing withholding treatment of curative intent.

We used similar techniques to Green, describing a group of women with CIS, who, irrespective of their treatment had cytology abnormalities consistent with continuing disease (showing that they had failed to receive adequate treatment). This group of women who illustrated the natural history of CIS was compared with a group of women who irrespective of their treatment, had normal cytology follow-up and who therefore did not represent the natural history of CIS. The women with continuing abnormal cytology were 25 times more likely to develop invasive cancer.

In the context of cancer or precancer the adequacy of treatment is paramount. Doctors and patients recognise that inadequate excision of cancer or precancer significantly increases the risk of recurrence of the disease.

It is a pity Professor Bryder and Dr Overton's supporters have not done their homework. Bryder cites the endorsement of Professor Sir Ian Chalmers who admits to having never read the Cartwright Report and Professor de Costa has failed to respond to this question. Professor Seber and Dr Mullins have failed to publish their 1990 "independent analysis" at all. In fact I understand that it was rejected by the *Lancet*.

If there was never an 'unfortunate experiment' as Professor Bryder and Dr Overton claim, can they explain why so many women with CIS in NWH developed cancer? If one ignores the groupings in our 1984 paper and bearing in mind the vast majority of women with CIS in NWH were treated adequately, why did one in 20 develop cancer? With adequate treatment, the proportion that will go on to develop invasive cancer should be approximately one in two hundred after 10 years.⁴ Failure to adequately answer this question totally undermines the credibility of the book.*

(* The correct answer is: because so many women with a known precancerous abnormality were either not treated or inadequately treated.)

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Response by Linda Bryder

As an historian I am not an advocate of any group, disaffected or otherwise, but rather assess the evidence. My research enables me to make a number of observations regarding Professor Jones's latest offering.

The 1975 Committee, which Professor Jones refers to, was not a 'whitewash' but rather a serious attempt to review the evidence. The members were well aware of the disputes between Green and McIndoe and McLean; another publication by McIndoe would not have altered their deliberations.

Professor Jones does not tell us how Green's 1974 paper was 'seriously flawed'. He does say that in dividing the patients into groups according to persistent disease for the 1984 paper they adopted a similar approach to Green; the similarity was that

Green too was reviewing patient data, drawn not from his own patients but from all patients with CIS at the hospital.

Professor Jones writes dismissively of Mullins and Seber's 'independent review'. Yet Mullins and Seber were not related to the hospital which qualifies them as independent reviewers. By contrast the same could not be said of the 1984 paper, described by the 2008 *Lancet Oncology* article, of which Jones was an author, as an 'independent review'; all three authors of the 1984 paper had worked at National Women's and with Green for many years. The third contributor to Mullins and Seber's review, Dr Graeme Overton, has confirmed after speaking with Mullins that their review was never sent to the *Lancet* nor was there ever any intent to publish it.

There continues to be a strange logic in the discussion of the 1984 paper. When Jones writes of the women who 'irrespective of their treatment had cytology abnormalities consistent with continuing disease (showing they had failed to receive adequate treatment)', one has to ask the question, 'How could doctors have ensured they received "adequate treatment" if the results were "irrespective of treatment"?' The point is, as Jones writes, women with continued abnormal cytology irrespective of treatment were 25 times more likely to develop cancer than those whose smears had returned to normal.

Curiously Professor Jones writes in his final paragraph, discussing the supposedly high rates of cervical cancer at National Women, that 'if one ignores the "groupings" in the 1984 paper'... But if one ignores the groupings then there was no experiment—the 'experiment' was supposed to have been based on treating some women differently, with 'Group 2' patients receiving 'limited or no treatment'. (This premise was of course false in any case as Group 2 received 228 major treatments according to the 1984 paper, as Dr Overton noted).

Professor Jones demands an answer to the question 'Why did so many women with CIS at National Women's Hospital develop cancer?' In order to answer this question one needs to place the hospital in its international context. The 1984 paper showed that 41 out of 948 women who presented at National Women's Hospital with a positive cervical smear over 21 years, between 1955 and 1976, developed cervical cancer and 12 died of the disease.

Was this worse than other institutions? At the Inquiry, the expert witness from Norway, Professor Per Kolstad, stated that in relation to treatment of cervical cancer, National Women's compared very favourably with other institutions. The International Federation of Gynecology and Obstetrics (FIGO) ranked National Women's among the top three in the world in the treatment of cervical cancer according to 5-year survival rates in 1981. National Women's Hospital clearly did better than most.

What's most interesting about the article cited by Professor Jones (Soutter et al) is the authors' conclusion that the risk of developing invasive cancer following treatment for CIN, regardless of the type of treatment, remains higher than among the general population for at least 10 years after treatment. In other words, there is still no certainty that 'adequate' treatment of CIN will avoid subsequent cancer.

Professor Jones claims that he is not being personal. Supporting the suggestion that I was possibly engaged in 'deliberate obfuscation' and stating that my 'response to

criticism has often been to reply with further factual errors', as he did in his February letter in this *Journal*, is tantamount to saying that I am a liar and is about as personal as it gets.

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