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Back to the future in cervical screening: applying a contemporary lens to an old controversy

A paper for submission to:

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The case of Herb Green and the National Women's Hospital makes for uncomfortable reading;¹ while, over the years, it's been held up as an exemplar of unethical research, we have to wonder whether Dr. Green has suffered an injustice. The case does raise a number of issues which have contemporary relevance. Screening over the last 60 years or so has been a changing landscape; it has been influenced by science and public health, changing priorities and developments in our societal and ethical perspectives on screening.² So, in many ways, it is unsurprising that judgements made on a case so many years ago are now coming under scrutiny.

Our approach to potentially pre-cancerous lesions has, of course, changed. Nowadays we are much more likely to be content with 'watch and wait' approaches for lesions which may, or may not, develop into cancer (eg early prostate cancer, small lung nodules etc) and apply our decision-making with multiple test results, and screenee characteristics, in mind. In the 1960's our approaches didn't have these levels of nuance; there was much more of an inclination to remove any traces of pre-cancerous lesions, even if it meant quite radical treatments with significant potential harmful effects. Unsurprisingly, in that clinical paradigm, Herb Green's research was widely condemned.

The principals of avoiding harm and supporting autonomy are much more prominent in contemporary approaches to screening.³ For the benefits of screening programmes to outweigh harms, the many complex components of the process need to be all working well. There needs to be meticulous attention to technical detail, continuous quality improvement, reporting and follow-up, patient information and informed consent as well as an IT infrastructure that facilitates monitoring and evaluation of the whole screening pathway. We are more aware of institutional and societal pressures in favour of screening and their potential to undermine the autonomy of screening invitees. There has also been a much closer scrutiny of the way we do screening – for example, our target age groups, and frequency of screening. We seek that 'sweet point' where we are confident the right people are being screened with the best available methods and screening regime – in a way we can safely assume benefits will outweigh risks. Many screening commentators advocate a much expanded and more sophisticated approach to cancer screening policy and practice taking into account scientific, social and ethical perspectives;² cancer screening is a complex social process, which brings together people, organisations and technologies in a very unique way. There is a contemporary emphasis on accountability to people whose lives are changed by screening (for better or for worse) and a rather rigorous societal and ethical analysis of screening approaches is about the only way of ensuring this.

The Green case causes us to think about informed choice. We now emphasise that population benefits may not translate to an individual - we seek a well-informed population to invite to screening, provided with sufficient information to make an informed choice about whether or not they will participate. Some argue we've gone too far in our transparency - presenting people with too much information (particularly conflicting expert opinions) carries with it the potential for decisional anxiety. Other screening commentators believe we are still not sufficiently focused on avoiding harm and supporting autonomy in our programmes – so our emerging culture of open-ness is very much work in progress. Nevertheless we have come to expect a set of values to guide decision making in cancer screening and more explicit and

transparent inclusion of these values. Measuring informed choice has become a significant academic and public health endeavour.⁴ The process of informed choice, it is argued, needs to be underpinned by more robust methods and theoretical frameworks. Simply supplying invitees with wads of informational materials doesn't really measure up any longer. Of course, few of these considerations were part of the public discourse in the 1960's and it's always difficult to apply a contemporary lens to controversies from a different era.

The issue of over-diagnosis wasn't discussed as much back then either; it has been prominent in the cancer screening literature for the last couple of decades and has been at the heart of some significant disputes within the public health community. Over-diagnosis of indolent breast, prostate, thyroid and lung cancers, chronic kidney disease, depression and ADHD has been well documented in the literature. We know that over-diagnosis can cause harms in terms of anxiety, depression, labelling, financial burden and treatment side effects. There is a strong push through initiatives such as *realistic medicine*⁵ to reduce over-diagnosis and make clinicians and organisers of screening programmes more aware of the issues.⁶ In many ways over-diagnosis is an inevitable feature of healthcare systems which seek to diagnose and mitigate disease before it has any clinical relevance; the Herb Green case prompts us to think about the way we view pre-cancerous lesions and our natural instinct to treat them, even when the evidence for doing so doesn't measure up. In primary care, we are nowadays encouraged to think about our inbuilt diagnostic thresholds and the consequences of those thresholds for over-diagnosis - and balancing harms from the disease with harms from the treatment. And it's worth noting that these thresholds can differ between countries and health systems. Community understanding of the concept of over-diagnosis and the extent to which it should be tolerated within a screening programme is low - these are difficult concepts for patients (and health care providers) to fully comprehend. Nevertheless, we are encouraged to reduce over-diagnosis through more thoughtful and conservative management of indolent disease and we know that these approaches, with suitable education, are often entirely acceptable to patients. Again, these are conversations between doctors and patients which probably happened less frequently in the 1960's.

We are now more inclined to think about risk stratification in cancer screening, based on the premise that those at high risk stand to benefit more from screening programmes - and, specifically, programmes that apply more stratified approaches to both detection and follow-up. It could be argued that Herb Green was pioneering this kind of approach; accepting that risk of cancer can never be entirely eliminated but making a judgement about who might need aggressive treatments and who may be more likely to be harmed by these approaches. Nowadays conservative management for women under 30 with CIN2 lesions is gaining traction⁷ and more and more programmes are considering partial genotyping and/or other markers of risk to better stratify. HPV testing wasn't a feature of cervical screening in the 1960's and it is interesting to speculate how that might have changed things in the Herb Green case. HPV testing gives us the potential to risk stratify in a fairly accurate manner - it may raise anxiety in the short term, but this is generally short-lived. Of course, HPV testing comes with its own set of issues; labelling someone HPV positive carries a degree of stigma not associated with a positive smear test - nothing is ever straightforward in cancer screening!

We hope that as a screening community we are more inclined nowadays to learn from our mistakes and share information. Organisations such as the International Cancer Screening Network (ICSN) have an important role in promoting this global accountability and willingness to share data.⁸ The ICSN holds regular international meetings at which organisers of cancer screening programmes come together and compare and contrast the various approaches to cancer screening in their own countries. There is a culture of openness and data sharing in this and similar screening networks which, hopefully, helps to mitigate against bad screening practice. The EU's reports on screening across Europe have been a further important mechanism for information sharing.⁹ Perhaps the biggest lesson from the National Women's Hospital case is that in screening we must have a culture of openness, information sharing and best practice. We must compare and contrast the societal and ethical lenses we are using in our programmes and constantly look out for new approaches, which might lead to better outcomes - and better-informed patients. By promoting international dialogue and collaborative cancer screening, we can hopefully avoid the mistakes of the past and continually improve outcomes in patients who invest their time, effort and faith in the programmes we offer.

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