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EDITORIALS

# Treatment or surveillance for CIN2?

## Women now have better data on regression and progression to help them decide

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When cervical screening is delivered systematically as an organised programme, cervical cancer rates have fallen.[1] Even with the introduction of vaccination against human papillomavirus (HPV), which can deliver high levels of protection against cervical cancer, and other HPV related cancers, screening remains important to reduce cervical cancer rates in unimmunised women as well as the risk of cancers attributed to non-vaccine HPV types in all women.

As screening has evolved over time and in different settings, so has our understanding of the clinical course of cervical disease. In this week's issue, a systematic review and meta-analysis by Tainio and colleagues (doi:10.1136/bmj.k499) provides a more robust prediction of the clinical course and risk of active surveillance for women with cervical intraepithelial neoplasia grade 2 (CIN2).[2] The results not only update the available evidence but take on the challenges of bias and other limitations in previous observational studies and trials.

Accurate figures for regression and progression are important for our understanding of the clinical course of CIN2 and for women who need the best possible information before choosing between immediate treatment and surveillance. Tainio and colleagues report that over two years, CIN2 will regress in 50% of women kept under surveillance, persist in 32%, and progress to CIN3 or worse in 18%. Outcomes were more favourable for women aged less than 30 (60%, 23%, and 11%, respectively).

Cervical screening offers a relatively non-invasive test with a reasonable performance profile that can detect early changes in the cervix; cervical intraepithelial neoplasia (CIN). Often called a "precancer," CIN may be better understood as HPV induced disease, which has the potential to progress to cancer but might also regress completely or persist as CIN.

Over time, screening has become more sophisticated and the bar for treatment has been raised to protect women, particularly young women, from the reproductive harms associated with local excision of CIN.[3,4] Tainio and colleagues conclude that CIN2 lesions should be below that bar, managed instead with active surveillance.

Within clinical practice, and in this review, we are reliant on a histological diagnosis to establish the grade of CIN: 1, 2, or 3. Programmes with inbuilt quality assurance aim to improve consistency, but variability in diagnosis within and between observers is well documented.[5] Hence the increasing interest in biomarkers to help distinguish truly progressive CIN from regressive disease.[6]

So what does this meta-analysis mean for women trying to decide which management option is best after a CIN2 diagnosis? Knowing that the chance of regression is 50-60%, still means taking a gamble that surveillance is simply delaying treatment. Even a small risk of cancer (0.5% in this study) may still be unacceptable to some.

Women may assume the diagnosis of CIN2 is accurate and that the risk profile presented here is reliable, but the review had limitations, seen with the heterogeneity of the studies included (which improved when the authors grouped studies by decade or continent), the likelihood of misclassification, and a high risk of bias in half the studies. The effects of local excision, such as pain, bleeding, or menstrual disturbance,[7] time off work, and the possibility of pregnancy complications, including preterm birth and mid-trimester miscarriage are also important considerations in decision making.

The authors looked at progression of cervical lesions from three months after diagnosis, but data on the duration of "active surveillance" was limited. Active surveillance is inconvenient for women, who must attend clinics for repeat assessments and colposcopy. We do not yet have a clear definition of active surveillance in the context of CIN2; which interventions and at what frequency are needed to confirm regression, identify persistence, or recommend treatment for progression?

In practice, there will be a range of approaches, including "passive surveillance," and surveillance strategies that use cytology, HPV testing, colposcopy, or repeat biopsies either alone or in combination. The intensity of surveillance on offer will vary among healthcare settings and might reflect patient or clinician preference, local policy, or local resources. It might also depend on women's ability to access surveillance and attend clinics. Where women cannot afford choice, a 50% rate of persistence or progression may justify immediate treatment of CIN2 in women aged more than 30 years.

Inevitably, the known outcomes studied in the meta-analysis by Tainio and colleagues do not always reflect the concerns

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most important to women. Knowledge of the rates of regression from CIN2 are reassuring but they must be presented in a meaningful way alongside clear information about the effects of both surveillance and treatment, so women can make fully informed choices. Although this meta-analysis might not have all the answers, it does provide the best information to date on likelihood of regression or progression after a diagnosis of CIN2.

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