



## Podcast transcript:

### Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis

---

#### *Methodological considerations*

“Our review aimed to investigate the effect of concomitant chemotherapy and radiotherapy (or chemoradiotherapy) for women with cervical cancer and, for reasons I’ll describe later, it allowed us to provide new and reliable estimates of these effects. Chemoradiotherapy is already widely accepted as the standard of care for many women with cervical cancer, but there were a number of important questions that neither the individual trials, nor a prior Cochrane review based on published data had been able to address. This was because outcome data were not available for all trials. Also, some trials had only reported the proportion of women having a recurrence or developing metastases, so it was not possible to determine the length of time between treatment and the reappearance of the cancer. Toxicity was also poorly reported and could not be assessed properly using the published data and the summary data available from the trials meant that the reviewers couldn’t look at the effects of chemoradiotherapy in different patient subgroups.

So, we decided to conduct a new systematic review using updated individual patient data (IPD) from all available randomised trials to try to overcome these problems. Systematic reviews and meta-analyses that use IPD have been described as the gold standard and yardstick of systematic review. They involve the central collection, validation and re-analysis of "raw" data, from the eligible trials. The methodology differs from a typical Cochrane Review only in terms of organisational structure, data collection and analysis, but the same basic methods still apply.

The benefits of collecting and analysing IPD are many. In this review in particular, it allowed us to address some of the questions about chemoradiotherapy that the trials and previous reviews had been unable to answer. We obtained the data needed to do time to event analyses for all survival and recurrence outcomes. We collected data on patient and

treatment characteristics so that we could assess whether the effect of chemoradiotherapy differed with the use of different drugs or doses of these drugs; different radiotherapy schedules, or in different patient subgroups. We asked the investigators to supply data on treatment related toxicity. However, although we were able to look at the short term side effects of chemoradiotherapy, many of the trials had not routinely collected or recorded late side effects so we weren't able to assess the impact of chemoradiotherapy on these.

Collecting IPD also meant that we could re-instate 202 patients who had been excluded from the original trial analyses and to use updated follow-up for survival and recurrence outcomes, so that we could look at the effects of chemoradiotherapy in the longer term. We were also able to check the data thoroughly and to validate the integrity of the randomisation methods, so that we could feel confident that we are only including properly randomised trials and had reduced or limited potential sources of bias.

All of the investigators who contributed data for the meta-analysis became part of a collaborative group, along with a small team of statistical and clinical experts in the field. This group helped to define the clinical questions and (importantly in this review), decide which trials to include and exclude; interpret the results and set them in context of current clinical practice.

Whilst this review demonstrates the many benefits of conducting IPD reviews, they do require considerable time and resource. But, for this review, that was worthwhile because the additional effort meant we could provide new evidence about chemoradiotherapy, helping to inform future treatment choices.”