

**Editorial for “Development and validation of risk prediction equations to estimate survival in patients with colorectal cancer: cohort study.”**

Dr Juliet Usher-Smith, Clinical Senior Research Associate, The Primary Care Unit, Institute of Public Health, University of Cambridge School of Clinical Medicine, Box 113 Cambridge Biomedical Campus, Cambridge CB2 0SR

Mr Richard Miller, Consultant Colorectal and General Surgeon, Cambridge Colorectal Unit, Addenbrooke’s Hospital, Cambridge CB2 0QQ

Prof Simon Griffin, Professor of General Practice, The Primary Care Unit, Institute of Public Health, University of Cambridge School of Clinical Medicine, Box 113 Cambridge Biomedical Campus, Cambridge CB2 0SR

Correspondence to: Juliet Usher-Smith [jau20@medschl.cam.ac.uk](mailto:jau20@medschl.cam.ac.uk)

Word count: 748

By estimating the probability of given outcomes for individuals based on a combination of clinical and socio-demographic characteristics the growing number of risk prediction models have the potential to support clinician and patient decision making.

In the linked paper, Hippisley-Cox and Coupland add to their suite of risk prediction models by using data from a large UK primary care database (the QResearch® database) to develop models to estimate survival in men and women following a diagnosis of colorectal cancer[ref]. They then validated them in a separate set of patients within the same database and in the Public Health England cancer registry. Using established statistical measures of performance, they show that the models are reasonably good at ranking individuals according to their survival and the predicted survival estimates closely match those observed in the study populations and other studies.

Compared to existing models, these new ones have a number of advantages(1,2). Firstly, existing models apply to patient sub-groups while these models are applicable to all patients. Secondly, the survival estimates can be updated conditional on the number of years survived since diagnosis, allowing patients and clinicians to obtain dynamic survival estimates annually up to 9 years after diagnosis. Thirdly, the models provide estimates for both all-cause mortality and colorectal cancer specific mortality.

The authors provide a web based calculator (<http://qcancer.org/colorectal-survival/index.php>) and suggest this could be used by patients and clinicians to inform discussions regarding cancer treatment and follow-up. Currently, discussions about treatment are based mainly on stage at diagnosis and trial evidence of effectiveness(3). Although other co-morbidities and overall performance status are taken into consideration, this is largely through subjective assessments. By providing more objective estimates of mortality risk from other causes alongside colorectal cancer specific mortality, these new models help put the risks from colorectal cancer into context for individual patients and so facilitate more individualised and informed discussions and decisions. For example, patients with a low risk of dying from colorectal cancer and a high risk of dying from other causes may be more inclined to decline aggressive treatments compared with those whose risk of death is predominantly due to colorectal cancer. The more accurate and longer term estimates of overall survival may also help with future planning and inform decisions around follow-up. A recent review(4) highlighted the on-going controversy around optimal surveillance protocols and suggested a need for risk models to enable personalised follow-up. Ideally such models would include additional risk factors known to influence recurrence rates, such as postoperative infection. However, being able to obtain dynamic survival estimates may facilitate such discussions.

Inevitably, however, there are limitations. The risk models were developed using observational data collected retrospectively from electronic patient records across England from 1998. The observed effects of treatment are therefore a reflection of both the effect of the treatment administered at the time and the characteristics of the individuals who were offered, and subsequently accepted, that treatment. The result is that, for example, surgery for colorectal cancer appears to decrease risk of death from non-colorectal cancer causes, presumably because surgery was undertaken on those with less co-morbidities, and chemotherapy appears to increase mortality in those with stage 1 or 2 disease which may reflect, among other things, the use of chemotherapy among patients with stage 2 disease and other poor prognostic indicators(5). Radiotherapy is also missing from the risk models as it did not reach statistical significance and all chemotherapy regimens are included together as a binary yes/no variable. Additionally, molecular features are increasingly used to classify tumours and guide response to adjuvant chemotherapy(6) and these are absent from the models. Finally, the models do not consider impact on morbidity and quality of life which influences treatment decisions.

The new models therefore cannot be relied on to accurately demonstrate to individual patients the effects on mortality of contemporary chemotherapy and surgery. Instead, clinicians should continue to apply estimates of treatment effects from trials, or decision aids designed for that purpose(7), to estimates of mortality derived from these new models. Patients would then see estimates of the absolute benefits of treatment in the context of their other co-morbidities. Used in this way, these models might enable more individualised discussions about prognosis both before treatment and in those who have completed treatment, and enhance the consent processes(8). Used incorrectly they may complicate an already difficult decision. As with all risk models, development and validation is only the first step in implementation(9) and research is now needed to assess the impact of these models in practice.

## References

- 1 Weiser MR, Gönen M, Chou JF et al. Predicting survival after curative colectomy for cancer: individualizing colon cancer staging. *J Clin Oncol* 2011; **29**: 4796–802.
- 2 Renfro LA, Grothey A, Xue Y et al. ACCENT-based web calculators to predict recurrence and overall survival in stage III colon cancer. *J Natl Cancer Inst* 2014; **106**. DOI:10.1093/jnci/dju333.
- 3 National Institute for Health and Care Excellence. Colorectal cancer: diagnosis and management Clinical guideline [CG131]. 2014. <https://www.nice.org.uk/guidance/CG131>.
- 4 van der Stok EP, Spaander MCW, Grünhagen DJ et al. Surveillance after curative treatment for colorectal cancer. *Nat Rev Clin Oncol* 2016; **14**: 297–315.
- 5 Meyers BM, Cosby R, Quereshy F et al. Adjuvant systemic chemotherapy for stages II and III colon cancer after complete resection: a clinical practice guideline. *Curr Oncol* 2016; **23**: 418.
- 6 Müller MF, Ibrahim AEK, Arends MJ. Molecular pathological classification of colorectal cancer. *Virchows Arch* 2016; **469**: 125–34.
- 7 Miles A, Chronakis I, Fox J et al. Use of a computerised decision aid (DA) to inform the decision process on adjuvant chemotherapy in patients with stage II colorectal cancer: development and preliminary evaluation. *BMJ Open* 2017; **7**: e012935.
- 8 Sokol DK. Update on the UK law on consent. *BMJ* 2015; **350**: h1481.
- 9 Steyerberg EW, Moons KGM, Windt DA Van Der et al. Prognosis Research Strategy (PROGRESS) 3 : Prognostic Model Research. *PLoS Med* 2013; **10**: e1001381.

## Competing interests

We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None

## Copyright statement

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, a worldwide licence to the Publishers and its licensees in perpetuity, in all forms, formats and media (whether known now or created in the future), to i) publish, reproduce, distribute, display and store the Contribution, ii) translate the Contribution into other languages, create adaptations, reprints, include within collections and create summaries, extracts and/or, abstracts of the Contribution, iii) create any other derivative work(s) based on the Contribution, iv) to exploit all subsidiary rights in the Contribution, v) the inclusion of electronic links from the Contribution to third party material where-ever it may be located; and, vi) licence any third party to do any or all of the above.