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US cancer treatment guidelines 'often based on weak evidence'

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Cancer treatment guidelines produced by the US National Comprehensive Cancer Network (NCCN) are often based on low quality evidence or no evidence at all, finds a study published by *The BMJ* today.

The researchers, led by Dr Vinay Prasad at Oregon Health & Science University, say their findings "raise concern that the NCCN justifies the coverage of costly, toxic cancer drugs based on weak evidence."

NCCN guidelines are developed by a panel of cancer experts who make recommendations based on the best available evidence.

These recommendations are used by US private health insurers and social insurance schemes to make coverage decisions, and guide global cancer practice, but it is not clear how the evidence is gathered or reviewed.

In the US, the Food and Drug Administration (FDA) approves all new drugs and grants new indications for drugs already on the market. The NCCN makes recommendations both within and outside of FDA approvals, but patterns of NCCN recommendations beyond FDA approvals have not been analysed.

So Dr Prasad and his team compared FDA approvals of cancer drugs with NCCN recommendations in March 2016 for a contemporary sample of drugs. When the NCCN made recommendations beyond the

FDA's approvals, the evidence used to support those recommendations was evaluated.

A total of 47 new cancer drugs were approved by the FDA for 69 indications over the study period, whereas the NCCN recommended these drugs for 113 indications, of which 69 (62%) overlapped with the 69 FDA approved indications and 44 (39%) were additional recommendations.

Only 10 (23%) of these additional recommendations were based on evidence from randomised controlled trials, and seven (16%) were based on evidence from phase III studies. Most relied on small, uncontrolled studies or case reports, or no offered evidence.

And almost two years after their analysis, the researchers found that only six (14%) of the additional recommendations by the NCCN had received FDA approval.

"The NCCN frequently makes additional recommendations for the use of drugs beyond approvals of the FDA and when it does so, it often fails to cite evidence or relies on low levels of evidence," write the authors.

"Few of these additional recommendations subsequently lead to drug approval," they add. "If there is additional evidence in support of these recommendations the NCCN should improve its process and cite all evidence used."

This is an observational study, so no firm conclusions can be drawn about cause and effect, and the researchers point to some limitations. However, they say, given that NCCN endorsement is linked to reimbursement by many commercial insurers and social insurance schemes, "our results suggest that payers may be covering cancer drugs with varying and scientifically less robust justification."

Finally, they point out that 86% of NCCN guidelines members have financial ties to the pharmaceutical industry, with 84% receiving personal payments and 47% receiving research payments.

"The presence of conflicted physicians has been shown to lead to more optimistic conclusions regarding disputed practices," they say. "Thus our findings raise concern about the nature of the recommendations offered by these individuals."

More information: Frequency and level of evidence used in recommendations by the National Comprehensive Cancer Network guidelines beyond approvals of the US Food and Drug Administration: retrospective observational study, www.bmj.com/content/360/bmj.k668

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