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**Efficacy and safety of extended duration to perioperative thromboprophylaxis with low molecular weight heparin on disease-free survival after surgical resection of colorectal cancer (PERIOP-01)**


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**Study question**
Does extended duration to perioperative thromboprophylaxis using subcutaneous low molecular weight heparin improve disease-free survival in patients undergoing resection for colorectal cancer?

**Methods**
614 adults (≥18 years) with invasive adenocarcinoma of the colon or rectum, without evidence of metastatic disease, and due to undergo surgical resection in 12 hospitals in Canada, from 25 October 2011 to 31 December 2020, were included. Patients received extended duration thromboprophylaxis using daily, subcutaneous, tinzaparin at 4500 IU, beginning at decision to operate and continuing for 56 days postoperatively or at inpatient postoperative thromboprophylaxis only. The primary outcome was three year disease-free survival, defined as survival without locoregional recurrence, distant metastases, second primary (same cancer), second primary (other cancer), or death. Analyses were done in the intention-to-treat population.

**Study answer and limitations**
The primary outcome occurred in 235 (77%) of 307 patients in the extended duration group and in 243 (79%) of 307 patients in the in-hospital thromboprophylaxis group (hazard ratio 1.1, 95% confidence interval 0.90 to 1.33; P=0.4). Postoperative venous thromboembolism occurred in five (2%) patients in the extended duration group and four (1%) in the in-hospital thromboprophylaxis group (P=0.8). The trial stopped recruitment prematurely after the interim analysis for futility.

**What this study adds**
These data suggest that extended duration to perioperative anticoagulation with tinzaparin does not improve disease-free survival in patients with colorectal cancer undergoing surgical resection.

**Trial registration**
ClinicalTrials.gov NCT01455831.

**Funding, competing interests, and data sharing**
See full paper on bmj.com for details.
Physician burnout undermines safe healthcare

ORIGINAL RESEARCH Systematic review and meta-analysis

Associations of physician burnout with career engagement and quality of patient care

Hodkinson A, Zhou A, Johnson J
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Study question What is the association of physician burnout with career engagement and the quality of patient care?

Methods Observational studies were included that assessed the association of physician burnout with career engagement (job satisfaction, career choice regret, turnover intention, career development, and productivity loss) and quality of patient care (patient safety incidents, low professionalism, and patient satisfaction). Data were extracted twice and checked with the study authors. Random effect models were used to calculate the pooled odds ratio; prediction intervals expressed the amount of heterogeneity; and meta-regressions assessed for potential moderators, with a significance set at P<0.10.

Study answer and limitations 170 observational studies with 239 246 physicians were identified. Physicians with burnout are up to four times more likely to be dissatisfied with their job (odds ratio 3.79, 95% confidence interval 3.24 to 4.43, I²=97%, k=73 studies, n=146 980 physicians), more than three times as likely to have thoughts or intentions to leave their job (turnover; 3.10, 2.30 to 4.17, I²=97%, k=25, n=32 271), and more than three times as likely to regret their career choice (3.49, 2.43 to 5.00, I²=97%, k=16, n=33 871). Physicians with burnout are twice as likely to be involved in patient safety incidents (2.04, 1.69 to 2.45, I²=87%, k=35, n=41 059) and show low professionalism (2.33, 1.96 to 2.70, I²=96%, k=40, n=32 321), and more than twice as likely to receive low satisfaction ratings from patients (2.22, 1.38 to 3.57, I²=75%, k=8, n=1002). Small diversity in the outcome definition might have led to some overestimation of the association with physician burnout.

What this study adds This meta-analysis provides compelling evidence that physician burnout is associated with poor function and sustainability of healthcare organisations, primarily by contributing to the career disengagement and turnover of physicians, and secondarily by reducing the quality of patient care.

COMMENTARY Urgent action is required to protect patients, physicians, and health systems

A substantial proportion of healthcare professionals report symptoms of burnout.1 2 In their paper adding to this work,3 Hodkinson and colleagues collate 170 observational studies of 239 246 physicians in a large systematic review and meta-analysis examining associations of physician burnout with career engagement and the quality of care provided to patients. The authors found that burnout was associated with a threelfold to almost fourfold increase in the odds of job dissatisfaction and regrets about career choice, that physicians with burnout were three times more likely to consider quitting than staying in their jobs, and that burnout was associated with significantly lower productivity. These findings are a compelling testimony to the pivotal role of burnout in physicians’ career disengagement. Burnout was also associated with doubled odds of patient safety incidents, low levels of professionalism, and significant decreases in patient satisfaction. Hodkinson and colleagues’ research adds to growing evidence that the poor mental health of healthcare providers jeopardises the quality and the safety of patient care.4 A notable strength of this review is the meta-regressions, which allow a deeper

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Physician burnout is a risk to patient safety and must be treated like any other patient safety risk. Understanding of contextual influences. These analyses support that relations vary with respect to specialty, age, career stage, clinical setting, and level of national income and resources. Hodkinson and colleagues' findings suggest that the consequences of burnout are exacerbated by acute healthcare environments, such as emergency departments and intensive care units.

Challenges and solutions

The challenges for patients, practitioners, researchers, and leaders in healthcare management and policy fall into three broad themes. First, burnout undermines professional engagement and results in loss of commitment and high turnover and absenteeism. Physicians’ wellbeing must be prioritised in all efforts to resolve these problems. Second, burnout is an indicator of a dysfunctional workplace. A broad evidence base in occupational health research has detailed various related adverse characteristics in work clinical environments. Excessive workloads, and work intensity in particular, have been shown to increase physician fatigue and deplete both motivation and engagement. Burnout is the inevitable result of physicians coping with exceedingly high workload caused by understaffing, inadequate support, and poor leadership, combined with imbalances between effort and reward, and moral injury stemming from the inability to provide adequate standards of care. Third, healthcare provider burnout is a risk to patient safety and must be treated like any other patient safety risk. Effective, evidence based interventions to reduce burnout are available at individual, workplace, and organisational levels. Work design and organisation level interventions are often neglected but are the key to meaningful progress on burnout. Reducing any preventable harm requires understanding the underlying causes of that harm, changing practices and culture, promoting staff engagement through peer learning, and aligning policy efforts around common goals and measures. Systems engineering approaches are needed to successfully design and secure these improvements, in full partnership with healthcare professions. Advocacy and policy changes that address burnout on a societal level are also pivotal. A deeper understanding of how burnout contributes to unsafe care is needed. Patient care is complex and suboptimal outcomes are multifactorial. Therefore, better research methods are needed to explore and quantify the specific contribution of physician burnout. Long term investigations with sophisticated designs will improve our understanding of how work stress influences physicians’ experiences of engagement over time. Research is needed that goes beyond observational studies and self-reported safety outcomes to establish effects of burnout and disengagement on patient outcomes. Discrepancies between physicians’ perceived functioning and their actual performance in terms of reliability and safety are a further challenge. Finally, qualitative studies are also required to explore the complex relationships between physicians and their working environments.

The mental wellbeing of physicians is vital for safe healthcare systems. The pervasive nature of physician burnout indicates a defective work system caused by deep societal problems and structural problems across the sector. Urgent action is imperative for the safety of physicians, patients, and health systems, including interventions that are evidence based and system oriented, to design working environments that promote staff engagement and prevent burnout.

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Funding, competing interests, and data sharing

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Study registration PROSPERO CRD42021249492.
**Study question** What is the diagnostic accuracy of three widely available commercial rapid antigen tests with unsupervised nasal self-sampling during and after the emergence of omicron and what is the effect of adding combined oropharyngeal plus nasal self-sampling on these performances?

**Methods** This prospective cross sectional diagnostic test accuracy study was performed at three public health service covid-19 test sites in the Netherlands. 6497 people with symptoms or signs of covid-19 aged 16 years presenting for SARS-CoV-2 testing were included and a swab sample was taken for reverse transcription polymerase chain reaction (RT-PCR) testing (reference test). Participants received one rapid antigen test to perform unsupervised with either nasal self-sampling (during the emergence of omicron, and when omicron accounted for >90% of infections, phase 1) or with combined oropharyngeal and nasal self-sampling (subsequent phase 2; omicron >99%). The evaluated tests were Flowflex (Acon Laboratories; phase 1 only), MPBio (MP Biomedicals), and Clinitest (Siemens-Healthineers). Diagnostic accuracies (sensitivity, specificity, positive and negative predictive values) of each self-test were assessed, with RT-PCR testing as reference.

**Study answer and limitations** When transitioning from when omicron accounted for 29% to >95% of SARS-CoV-2 infections, sensitivities decreased from 87.0% to 80.9% for Flowflex (P=0.16 by $\chi^2$ test), 80.0% to 73.0% for MPBio (P=0.60), and 83.1% to 70.3% for Clinitest (P=0.03) when performed with nasal self-sampling. Differences in RT-PCR positivity percentages and test performances were large between confirmatory testers (previously tested positive by a self-test at own initiative) and individuals who attended the test sites for other reasons. When combined oropharyngeal and nasal self-sampling was compared with nasal self-sampling, sensitivities for MPBio and Clinitest were found to be slightly higher in confirmatory testers (87.4% and 86.1% v 83.6% and 85.7%, respectively) and substantially higher in those testing for other reasons (69.3% and 59.9% v 51.5%, and 49.5%, respectively).

**What this study adds** Sensitivities of the three rapid antigen tests with nasal self-sampling decreased during the emergence of omicron but were only statistically significant for Clinitest. The addition of oropharyngeal sampling to nasal self-sampling could improve test performance.

**Funding, competing interests, and data sharing** Funded by the Dutch Ministry of Health, Welfare, and Sport. No competing interests declared. Participant data will be available, after deidentification, by submitting a research proposal to the corresponding author.

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**Table: Diagnostic accuracy variables for three rapid antigen tests in participants with covid-19 symptoms in the omicron period**

<table>
<thead>
<tr>
<th>Test</th>
<th>Sampling method</th>
<th>RT-PCR test positivity (%)</th>
<th>Sensitivity (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flowflex</strong></td>
<td>Nasal</td>
<td>620</td>
<td>66.0</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>341</td>
<td>42.5</td>
</tr>
<tr>
<td><strong>MPBio</strong></td>
<td>Nasal</td>
<td>820</td>
<td>48.2</td>
</tr>
<tr>
<td></td>
<td>OP-N</td>
<td>543</td>
<td>67.2</td>
</tr>
<tr>
<td><strong>Clinitest</strong></td>
<td>Nasal</td>
<td>726</td>
<td>59.1</td>
</tr>
<tr>
<td></td>
<td>OP-N</td>
<td>653</td>
<td>64.6</td>
</tr>
</tbody>
</table>

*RT-PCR=reverse transcription polymerase chain reaction; OP-N=combined oropharyngeal and nasal sampling.*

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**ORIGINAl RESEARCH** Cross sectional study

Diagnostic accuracy of covid-19 rapid antigen tests with unsupervised self-sampling in people with symptoms in the omicron period

Schuit E, Venekamp RP, Hooft L, et al

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