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The Effects of Different Invitation Schemes on the Use of Fecal Immunochemical Tests for Colorectal Cancer Screening

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Colorectal cancer is the worldwide third most common cancer. Screening with fecal occult blood tests and endoscopic methods has been shown by randomized, observational and modeling studies to effectively reduce incidence and mortality of colorectal cancer. Still, participation rates are low, especially in opportunistic screening programs without targeted invitations. The aims of the dissertation were to evaluate effectiveness of various types of general invitation schemes in increasing adherence to offers of colorectal cancer screening by fecal occult blood tests (guaiac-based fecal occult blood test or fecal immunochemical tests) through a systematic literature review and to investigate in an own randomized controlled trial the effects of various invitation schemes on use of fecal immunochemical tests in the German routine practice healthcare system.

The systematic literature review identified 33 randomized controlled trials or cluster randomized controlled trials, which reported on general screening invitations for fecal occult blood test in the general population. Invitations with attached, that means mailed fecal occult blood test, consistently increased test usage, with a maximum of almost 20% points. Likewise, the introduction of advance notification consistently led to a higher usage rate, with a maximum increase of 11% points. Reminders showed positive but varying effects by method (text message < call < letter/email), up to an increase of 10-16% points for letters or emails. Mixed results were observed for financial incentives and for added or changed invitation material. The implementation of multifaceted invitation, that means several interventions at the same time, increased fecal occult blood test usage in all respective studies, and up to almost 25% points. Compared to screening offers without personal invitation, the comparative invitation schemes consistently achieved a higher usage rate.

The own randomized controlled trial was conducted in 50-54-years-old insurance clients of AOK BW. 17,532 participants were randomized to receive: (A) an invitation letter including a fecal immunochemical test (n=5,850); (B) an invitation letter including an option to request

fecal immunochemical test to be sent by post (n=5,844); or (C) an invitation letter only (n=5,838, control group, routine practice). Reminders were sent to random samples of group A and B participants after four weeks. The primary endpoint was the use of fecal immunochemical tests within one year of the date of the invitation letter. Variant (A) - invitation including fecal immunochemical test, increased usage from 10% to 29.7% (+19.7% points, $p < 0.0001$) as compared to control (men: +19.4% points, women: +18.8% points). Variant (B) - invitation letter + fecal immunochemical test request option, increased usage from 10% to 27.7% (+17.7% points, $p < 0.0001$; men: +17.7% points, women: +17.4% points). Reminders increased usage within (A) by 7.5% points and (B) 8.5% points. Participation among women was higher than among men in all arms. The fecal immunochemical test positivity rate was at 6.9%. For 64.3% of fecal immunochemical test positive participants, a subsequent colonoscopy reported, and among these, advanced neoplasia was found in 21.3% of cases.

Results from the own trial confirmed the positive effects of mailed fecal occult blood test and reminders that were observed in the systematic review and further indicated the feasibility of effective request options. In the own trial, mailed fecal immunochemical test increased usage by almost 20% points, which, as compared to studies from the systematic review, ranges among the strongest changes. However, based on the observations from the systematic review, it can be suggested that an even greater increase of test usage could be achieved by additional measures to optimize adherence, such as the implementation of advance notification.

In conclusion, the findings from this dissertation show the great potential of personal invitations for fecal occult blood tests in colorectal cancer screening. Previous randomized studies reported a tremendous increase in participation for invitations with mailed fecal occult blood test, but also for advance notification and reminders. Additionally, it was demonstrated in an own randomized study that letters of invitation which either include, or offer low-threshold access to, fecal immunochemical test increase usage of fecal immunochemical test-based colorectal cancer screening, in ways which are strong and comparable. This dissertation thus summarizes and provides empirical evidence that could potentially contribute to a further improvement of colorectal cancer screening.