

The effect of gender-specific invitation letters on utilization of colorectal cancer screening

Der Einfluss von geschlechtsspezifischen Einladungsschreiben auf die Inanspruchnahme von Darmkrebsvorsorgeuntersuchungen

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ZUSAMMENFASSUNG

Hintergrund und Zielsetzung Darmkrebsvorsorgeuntersuchungen können die Krebs-assoziierte Mortalität wirksam reduzieren. In Deutschland haben Personen über 50 bzw. 55 Jahren Zugang zu spezifischen Vorsorgeuntersuchungen. Die Teilnehmerate am Darmkrebsvorsorgeprogramm ist jedoch persistierend niedrig, insbesondere in der männlichen Bevölkerung. Diese Beobachtungsstudie vergleicht den Einfluss von einfachen mit geschlechtsspezifischen Einladungsschreiben auf die Inanspruchnahme von Darmkrebsvorsorgeuntersuchungen.

Methodik Die Teilnehmerate am Darmkrebsvorsorgeprogramm wurde in einer Kohorte von Personen, die durch eine große, gesetzliche Krankenkasse in Bayern versichert sind, untersucht. Alle Personen, die während des Beobachtungszeitraums das 50. bzw. 55. Lebensjahr erreicht haben, erhielten entweder ein einfaches (2013–2014) oder geschlechtsspezifisches Einladungsschreiben (2015–2016). Die Inanspruchnahme von Vorsorgeuntersuchungen innerhalb von 6 Monaten nach Erhalt des Einladungsschreibens wurde verglichen.

Ergebnisse Es haben insgesamt 49 535 Personen ein Einladungsschreiben erhalten. Davon waren 48,8 % geschlechtsspezifische Einladungsschreiben. Die Teilnehmerate unterschied sich nicht zwischen Empfängern eines einfachen oder geschlechtsspezifischen Einladungsschreibens (11,6 % vs 11,1 %; RR 0,97 [0,92–1,02], $p = 0,19$). Die Inanspruchnahme von Vorsorgekoloskopien war jedoch signifikant höher bei Personen, die ein geschlechtsspezifisches Einladungsschreiben erhielten (2,9 % vs 3,5 %; RR 1,21 [1,04–1,39], $p = 0,01$). Hingegen war die Nutzung von Tests für okkultes Blut im Stuhl in der gleichen Gruppe geringer (10,4 % vs 9,7 %; RR 0,93 [0,88–0,99], $p = 0,016$).

Schlussfolgerung Geschlechtsspezifische Einladungsschreiben können die Präferenz von Patienten für spezifische Vorsorgeuntersuchungen verändern und die Inanspruchnahme von Vorsorgekoloskopien erhöhen.

ABSTRACT

Background and aim Colorectal cancer (CRC) screening can effectively reduce cancer-associated mortality. In Germany, individuals over the age of 50 or 55 have access to CRC screening services. However, utilization rates are persistently low, particular in the male population. This observational study investigates the effect of standard versus gender-specific invitation letters on utilization of CRC screening services.

Methods We analyzed utilization rates of individuals who were insured by a large health insurance fund in Bavaria, Germany. Persons who became eligible for CRC screening

received a standard (2013–2014) or a gender-specific invitation letter (2015–2016). We compared utilization rates within 6 months after receipt of the invitation letter using billing codes of the health insurance fund.

Results Invitation letters were sent to 49 535 individuals, of which 48.8 % were gender-specific. The overall utilization rate did not differ between recipients of the standard versus gender-specific invitation letter (11.6 % vs 11.1 %; RR: 0.97 [0.92–1.02], $p=0.19$). However, uptake of screening colonoscopy was significantly higher among recipients of gender-specific invitations (2.9 % vs 3.5 %; RR: 1.21 [1.04–1.39], $p=0.01$), whereas utilization of fecal occult blood tests declined (10.4 % vs 9.7 %; RR: 0.93 [0.88–0.99], $p=0.016$).

Conclusions Gender-specific design of invitation letters can modify the patients' preference for specific CRC screening services and increase the acceptance of screening colonoscopy.

Introduction

Colorectal cancer (CRC) is one of the main causes of cancer associated morbidity and mortality worldwide [1]. At the same time, effective screening methods such as colonoscopy [2, 3] or fecal occult blood tests [4, 5] are available, which can reduce the incidence and mortality of CRC [6]. Hence, national programs for CRC screening have been introduced in many countries [7]. Most programs follow an organized screening policy, with defined age categories, screening methods, and intervals for the target population. Furthermore, the majority of organized programs have a structured invitation procedure and perform quality assurance as well as validation of screening results [8]. In contrast, some countries offer an opportunistic screening system that is organized by a fee-for-service reimbursement policy. In such a system, participants can decide for a specific screening test on an ad hoc basis.

In Germany, an opportunistic CRC screening program was introduced in 2002. Individuals ≥ 50 years have access to annual screening with a guaiac-based fecal occult blood (gFOBT) or fecal immunochemical test (FIT), which is reimbursed since April 2017 and has replaced gFOBT. In addition, individuals ≥ 55 years can either opt for a screening colonoscopy or a biannual gFOBT/FIT. Since the introduction of the program, the incidence of CRC was reduced by 17–26 % within 10 years, underlining its efficiency [9, 10]. However, annual utilization rates in Germany are persistently low and range between 1.9 and 4.4 % for screening colonoscopy [9, 11] and between 8.6 and 27.1 % for gFOBT use in relevant age groups [12]. In contrast, reported utilization rates are much higher in other European countries such as the United Kingdom [13] or the Netherlands [14], ranging between 54 and 71 %. To improve the utilization of CRC screening in Germany, the National Cancer Plan advocated the introduction of an organized screening system [15]. An important element of this reorganized CRC screening system are invitation letters. In fact, several pilot studies conducted in different German federal states demonstrated that the use of CRC screening services can be increased by personal invitation letters [16, 17]. However, these

and previous studies have demonstrated a major gender-specific difference in utilization of CRC screening in Germany, with significantly lower rates in males than females [11, 17, 18]. Since premalignant lesions in the colorectum occur more frequently and earlier in the male population [19], this gender gap is a major challenge for cancer prevention. To address this problem and to improve the overall utilization of CRC screening, the large statutory health insurance fund BARMER GEK introduced gender-specific invitation letters and information leaflets in the federal state of Bavaria starting in May 2015. These letters and leaflets are designed to inform the target population about CRC screening in a gender-specific context (e. g., by comparing the frequency of CRC with prostate or breast cancer). To investigate the effect of this program on CRC screening, we compared utilization rates of screening services between recipients of standard or gender-specific invitation letters. We show that the overall utilization of CRC screening services was not changed by gender-specific invitation letters. However, a higher proportion of individuals opted for screening colonoscopy, indicating that the preferences for specific screening services can be modulated by a gender-specific invitation procedure.

Materials and methods

Ethics approval

The study was approved by the local board of ethics (Medizinische Ethikkommission II, Heidelberg University, identifier 2014-614N-MA, date of approval: November 18, 2014). All principles outlined in the ethics guidelines of the 1975 Declaration of Helsinki were followed. The pseudomized data documentation was approved by the local board of ethics and no informed consent from each individual was required by the ethics committee due to the retrospective design of the study.

Health insurance database and invitation procedure

This study is based on billing data from the large statutory health insurance fund BARMER GEK in the federal state of Bavaria, Germany. The BARMER health insurance fund covers 10 % of all insured individuals in Bavaria, which has a population of 12.93 million inhabitants [20]. In 2016, 5.43 million inhabitants were ≥ 50 years and eligible for participation in the national CRC screening program [20]. Starting in July 2013, invitation letters were sent to all insured individuals within 1 month after they turned 50 or 55 years. From May 2015 on, the standard invitation letter was replaced by a gender-specific version. A small group of individuals did not receive invitation letters, including those who declined to be directly contacted by the insurance fund, had long-term nursery service, had limited capability to act, or had a legal supervision.

Design of invitation letters and leaflets

The standard invitation letter consists of a letter from the insurance company that provides information on the incidence of CRC, different methods of CRC screening, and lifestyle modifications that can prevent cancer. In addition, a leaflet is included, which delivers detailed information on the utility of fecal occult blood tests and screening colonoscopy, describing in plain language how the tests are performed. Furthermore, telephone numbers are presented in the leaflet, which can be used to obtain more information on general medical issues and further counseling on cancer screening. In contrast, 2 versions of the gender-specific invitation letter were developed, for both the male and female target population. These invitation letters deliver the same information as the standard version but are more concise and directly compare the incidence of CRC with other gender-specific cancers. Furthermore, they are supplied with a gender-specific information leaflet. The leaflet contains either an illustration of an elderly man or woman and informs about the incidence of CRC in relation to prostate or breast cancer, respectively. The leaflet also provides information on the utility of fecal occult blood tests and screening colonoscopy in plain language. Compared to the standard leaflet, the amount of information is reduced. Finally, the same telephone numbers are provided as in the standard leaflet. Examples of the standard and gender-specific leaflets can be found in ► **Fig. 1** (English translation) and ► **Fig. 1S** (German).

Measurement of utilization rates of CRC screening

To evaluate the effect of invitation letters on CRC screening, we determined the utilization rate of individuals who turned 50 or 55 years between 2 time periods: July to December 2013 and 2014 for the standard invitation and July to December 2015 and 2016 for the gender-specific invitation. We reviewed the data of the BARMER insurance fund for billing codes relevant to CRC screening, which are based on the physician's fee scale (Einheitlicher Bewertungsmaßstab). The following codes indicated utilization of CRC screening and were selected for our analysis: 01734 for gFOBT use, 97734, 01737, 01738 for FIT use, and 01741 for screening colonoscopy. Individuals insured by BARMER Bavaria

had access to FIT since November 2013 as part of the special cancer prevention program "Aktiv gegen Krebs". For each individual, we determined whether any relevant code was recorded within 6 months after receipt of the invitation letter. For individuals who utilized multiple screening methods within the observation period, only 1 method per person was selected according to the following priority: screening colonoscopy > FIT or gFOBT. All patients who had had a colonoscopy within 5 years before they became eligible for CRC screening were excluded from our analysis. In addition, we also determined the sex of individuals and the medical specialty of the physician proving the CRC screening tests.

Statistical analysis

Rate ratios of utilization rates between the years 2013/2014 and 2015/2016 were tested using the exact rate ratio test including corresponding 95 % confidence interval. All p-values are 2-sided, and p-values below 0.05 were considered statistically significant. All analyses were performed with software R and the add-on package `rateratio.test` [21, 22].

Results

Utilization of screening services

Between July to December 2013 to 2016, a total of 49 535 individuals received an invitation letter and an information leaflet. Of those, 51.2 % were standard and 48.2 % gender-specific invitation letters. The distribution of gender was the same between the 2 groups, with the majority of recipients being female (60.2 % in both groups) (► **Table 1**). Half of the recipients in both groups turned 50 years and the other half 55 years. The semiannual utilization rate for all CRC screening services ranged between 11.2 and 11.6 %. As observed in previous studies, the rate was much higher in the female than in the male population (14.7–15.4 % vs 5.8–5.9 %) (► **Table 2**). Most individuals opted for screening with gFOBT/FIT (9.4–10.2 %) and only a minority selected screening colonoscopy (2.9–3.5 % of individuals who turned 55 years). Although gFOBT use declined after FIT became a reimbursed screening service, it was still commonly used (see ► **Table 2**). In Germany, CRC screening with gFOBT/FIT can be offered by many different medical specialties, whereas screening colonoscopy can only be provided by physicians with specific qualifications (gastroenterologists, colorectal surgeons, or physician specialized in internal medicine with colonoscopy board certification) and extensive experience (at least 200 colonoscopies and 50 polypectomies within the last 2 years). To identify the most common providers of CRC screening in our study population, we determined the relative contribution of different medical specialties. Our analysis demonstrates that CRC screening is mostly provided by gynecologists (7.0–7.7 %), followed by general medicine practitioners/family physicians (2.0 %), internal medicine specialists (0.7–0.8 %), and gastroenterologists (0.7–0.9 %) (► **Table 3**).

► **Table 1** Basal characteristics of the study population.

characteristic	group – standard invitation	group – gender-specific invitation
gender (% of all individuals in the group)		
▪ male	10 089 (39.8 %)	9615 (39.8 %)
▪ female	15 283 (60.2 %)	14 548 (60.2 %)
age (% of all individuals in the group)		
▪ 50 years old	13 112 (51.7 %)	12 274 (50.8 %)
▪ 55 years old	12 260 (48.3 %)	11 889 (49.2 %)
total	25 372 (100 %)	24 163 (100 %)

► **Table 2** Characteristics of individuals participating in colorectal cancer screening.

characteristics	group – standard invitation	group – gender-specific invitation
total participation rate (% of all individuals in the group)	2938 (11.6 %)	2702 (11.2 %)
gender (% of all individuals with the same gender in the group)		
▪ male	587 (5.8 %)	571 (5.9 %)
▪ female	2351 (15.4 %)	2131 (14.7 %)
age (% of all individuals with the same age in the group)		
▪ 50 years old	1521 (11.6 %)	1364 (11.1 %)
▪ 55 years old	1417 (11.6 %)	1338 (11.3 %)
screening method (% of all individuals in the group)		
▪ gFOBT	1647 (6.5 %)	1070 (4.4 %)
▪ FIT	936 (3.7 %)	1217 (5.0 %)
▪ screening colonoscopy (% of all 55 years old)	355 (2.9 %)	415 (3.5 %)

Effect of gender-specific invitation letters on screening utilization

To assess the impact of the gender-specific invitation procedure on CRC screening, we compared utilization rates between recipients of the standard (2013, 2014) versus gender-specific invitation letter (2015, 2016). Our analysis shows that the overall utilization rate did not change after the introduction of the gender-specific invitation letter (11.6 % vs 11.1 %; RR: 0.97 [0.92–1.02], $p = 0.19$) (► **Table 4**). We then analyzed the effect on the level of different screening methods and observed that the rate of gFOBT/FIT use

► **Table 3** Medical specialties of physicians providing colorectal cancer screening.

medical specialty (% of all individuals in the group)	group – standard invitation	group – gender-specific invitation
gynecology	1958 (7.7 %)	1702 (7.0 %)
general/family medicine	500 (2.0 %)	474 (2.0 %)
internal medicine	180 (0.7 %)	190 (0.8 %)
gastroenterology	172 (0.7 %)	217 (0.9 %)
urology	117 (0.5 %)	100 (0.4 %)
others	11 (<0.1 %)	19 (0.1 %)
total	2938 (11.6 %)	2702 (11.2 %)

declined (10.4 % vs 9.7 %; RR: 0.93 [0.88–0.99], $p = 0.016$) whereas the utilization of screening colonoscopy increased (2.9 % vs 3.5 %; RR: 1.21 [1.04–1.39], $p = 0.011$) in the cohort that received gender-specific invitation letters. This change in preference for screening colonoscopy was predominantly observed in the female population (2.7 % vs 3.3 %, RR: 1.23 [1.02–1.50]; $p = 0.034$), while only a trend toward a higher utilization rate was detected in the male population (3.2 % vs 3.8 %, RR: 1.17 [0.94–1.46], $p = 0.16$) (► **Table 4**). Next, we analyzed how gender-specific invitation letters affect selection of medical providers of CRC screening. While the contribution of general medicine practitioners did not change (2.0 % vs 2.0 %; R: 1.00 [0.88–1.13], 0.97), we observed that fewer gynecologists provided CRC screening (7.7 % vs 7.0 %; RR: 0.91 [0.85–0.97], $p = 0.006$). In contrast, the relative contribution of gastroenterologists to CRC screening increased (1.4 % vs 1.8 %; RR: 1.30 [1.06–1.60], $p = 0.011$).

Discussion

CRC screening is effective in reducing the incidence and mortality of CRC [1]. However, motivating the target population to utilize screening services is a major challenge for most national programs. In Germany, the utilization rate is low compared to other European countries [23]. Furthermore, a gender gap in the utilization of CRC screening can be observed, with a significantly lower rate in the male population [9, 11]. Both observations could be confirmed by our study: the semiannual utilization rate of fecal blood tests plus screening colonoscopy was approximately 11 %, and the rate was much lower in males than females. We then assessed the effect of gender-specific invitation letters on CRC screening and showed that utilization rate was not changed compared to the group that received standard invitation letters. However, the use of screening colonoscopies was significantly increased at the expense of a reduced utilization rate of gFOBT/FIT. Interestingly, this shift in the selection of screening methods was only statistically significant in the female population, while no changes were observed in the male population. It should be noted that most recipients of invitation letters were female (60.2 %),

► **Table 4** Relative changes of utilization rates for different screening methods.

screening method	gender	utilization rate group – standard invitation	utilization rate group – sex-specific invitation	RR (2015/2016 vs. 2013/2014), 95 % CI; p-value
all	all	11.6 %	11.2 %	0.97 (0.92–1.02); 0.19
	female	15.4 %	14.7 %	0.95 (0.90–1.01); 0.10
	male	5.8 %	5.9 %	1.02 (0.91–1.15); 0.75
gFOBT/FIT	all	10.2 %	9.5 %	0.93 (0.88–0.98); 0.015
	female	14.1 %	13.0 %	0.92 (0.87–0.98); 0.012
	male	4.3 %	4.1 %	0.96 (0.84–1.10); 0.596
screening colonoscopy (all 55 years old)	all	2.9 %	3.5 %	1.21 (1.04–1.39); 0.01
	female	2.7 %	3.3 %	1.23 (1.02–1.50); 0.034
	male	3.2 %	3.8 %	1.17 (0.94–1.46); 0.16

while the gender distribution of the general population of Bavaria for individuals between 50 and 55 years is nearly balanced [20]. This discrepancy is due to the fact that majority of individuals insured by BARMER Bavaria are female (approximately 58 %). For our analysis, we excluded individuals who had had a diagnostic colonoscopy before they became eligible for CRC screening. We found that this group was surprisingly large (5037 persons) and suggest that this observation should be considered as a potential bias in studies that assess the effect of CRC screening programs.

To optimize the acceptance of CRC screening, interventions at multiple levels of care have been proposed, which aim at overcoming deficits in awareness and financial or structural barriers to utilization [24]. Effective methods include, among others, sending advance notification letters [14, 25] or reminder letters [26, 27]. Furthermore, involvement of general practitioners or other trusted care providers in advocating CRC screening has a strong impact on utilization rates [28, 29]. The latter provides a potential explanation for the gender gap observed among participants of the German CRC screening program, particularly regarding the use of gFOBT/FIT. As our and previous studies demonstrate, screening by gFOBT/FIT is most frequently provided by gynecologists in Germany [12, 17]. Many women are in regular contact with their gynecologist for routine check-ups or screening for gynecological cancers, which will more likely result in a trustful relationship and higher acceptance of the physician's recommendations regarding cancer screening. This assumption is supported by a German survey demonstrating that frequency of physician contacts is a significant predictor for gFOBT use [30]. Compared to gFOBT/FIT, the acceptance of screening colonoscopy is even lower in Germany compared to other European countries [11, 17]. Given the invasiveness of the procedure and the discomfort during bowel preparation, patient education on the advantage of colonoscopy for cancer prevention is particularly important. In our study, we show that optimizing invitation letters and leaflets in a gender-specific manner can improve the acceptance of screening colonoscopy, predominantly in the female population. In fact, improving the design of information leaflets (e. g., by including illustrations of procedures) was shown to enhance the under-

standing of the screening method [31]. Thus, gender-specific invitation letters and leaflets might positively affect the understanding of the utility of screening colonoscopy and thereby increase its acceptance. This observation is important for CRC prevention, as the utilization rates of screening colonoscopy have been gradually declining since the introduction of the German CRC screening program in 2008 [32]. However, the absolute increase of screening colonoscopy use resulting from gender-specific invitation letters is very low (from 2.9 to 3.5 % among individuals ≥ 55 years). Furthermore, a parallel minor decrease of gFOBT/FIT use was observed (from 10.2 to 9.5 %). Therefore, our data suggests that individuals who would decide for gFOBT/FIT opted for screening colonoscopy instead after introduction of gender-specific invitation letters. Since colonoscopy is currently the most sensitive and specific method to detect premalignant lesions [33], this shift in preference of screening method might enhance the overall quality of CRC screening. A major goal of the gender-specific invitation procedure was to improve the acceptance of CRC screening in the male population. Our data clearly shows that this aim was not achieved. The use of neither gFOBT/FIT nor screening colonoscopy was increased in the male population. Therefore, additional measures are needed to improve the acceptance of CRC screening, such as the use of reminder letters [27]. In another approach, Hoffmeister et al. showed that adding gFOBTs directly to invitation letters resulted in higher utilization rates compared to sending invitation letters only. Hence, combining invitation letters with FITs, as already implemented by the Dutch CRC screening program, could also similarly enhance utilization of CRC screening in Germany. However, the broad application of such validated approaches is often limited by their relative costs [34].

Our study has several limitations. First, the study design is observational, and no randomization of the study population was performed. Instead, we analyzed utilization rates 2 years before and after the introduction of gender-specific invitation letters. Since the participation rate of CRC screening was observed to fluctuate annually [12], our findings could be biased in this respect. Secondly, many caveats are inherent to the gender-

specific design of health information. The main challenge is the perception of gender-specificity, which can vary strongly between different age groups and is influenced by the social, religious, and cultural background of the target population [35]. Whether the invitation letters used in this study are truly perceived as gender-specific by the target population has not been investigated and is an important, open question.

In summary, our study demonstrates that gender-specific design of invitation letters can potentially improve the acceptance of specific CRC screening services, such as colonoscopy. However, randomized studies as well as further improvement of the gender-specific design will be needed to fully assess their utility for CRC screening.

Author contributions

T.Z. and M.E. wrote the manuscript. T.G., C.S., and S.B. conceived the study and performed data collection. T.Z. and T.H. performed data analysis. M.P.E. and J.R. supervised the project.

Conflict of Interest

The authors declare that they have no conflict of interest.

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