

Citation: Ahadinezhad B, Maleki A, Akhondi A, Kazemi M, Yousefy S, Rezaei F, et al. (2024) Are behavioral economics interventions effective in increasing colorectal cancer screening uptake: A systematic review of evidence and meta-analysis? PLoS ONE 19(2): e0290424. https://doi.org/ 10.1371/journal.pone.0290424

Editor: Ronald Chow, University of Toronto Temerty Faculty of Medicine, CANADA

Received: November 14, 2022

Accepted: August 8, 2023

Published: February 5, 2024

Peer Review History: PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pone.0290424

Copyright: © 2024 Ahadinezhad et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper and its <u>Supporting Information</u> files.

RESEARCH ARTICLE

Are behavioral economics interventions effective in increasing colorectal cancer screening uptake: A systematic review of evidence and meta-analysis?

Bahman Ahadinezhad¹, Aisa Maleki², Amirali Akhondi², Mohammadjavad Kazemi², Sama Yousefy², Fatemeh Rezaei², Omid Khosravizadeh¹*

1 Social Determinants of Health Research Center, Research Institute for Prevention of Non-Communicable Diseases, Qazvin University of Medical Sciences, Qazvin, Iran, 2 Student Research Committee, Qazvin University of Medical Sciences, Qazvin, Iran

* Omid.khosravizadeh@gmail.com

Abstract

Various interventions have been investigated to improve the uptake of colorectal cancer screening. In this paper, the authors have attempted to provide a pooled estimate of the effect size of the BE interventions running a systematic review based meta-analysis. In this study, all the published literatures between 2000 and 2022 have been reviewed. Searches were performed in PubMed, Scopus and Cochrane databases. The main outcome was the demanding the one of the colorectal cancer screening tests. The guality assessment was done by two people so that each person evaluated the studies separately and independently based on the individual participant data the modified Jadad scale. Pooled effect size (odds ratio) was estimated using random effects model at 95% confidence interval. Galbraith, Forrest and Funnel plots were used in data analysis. Publication bias was also investigated through Egger's test. All the analysis was done in STATA 15. From the initial 1966 records, 38 were included in the final analysis in which 72612 cases and 71493 controls have been studied. About 72% have been conducted in the USA. The heterogeneity of the studies was high based on the variation in OR $(I^2 = 94.6\%, heterogeneity X^2 = 670.01 (d.f. = 36), p < 0.01)$. The random effect pooled odds ratio (POR) of behavioral economics (BE) interventions was calculated as 1.26 (95% CI: 1.26 to 1.43). The bias coefficient is noteworthy (3.15) and statistically significant (p< 0.01). According to the results of this meta-analysis, health policy and decision makers can improve the efficiency and cost effectiveness of policies to control this type of cancer by using various behavioral economics interventions. It's noteworthy that due to the impossibility of categorizing behavioral economics interventions; we could not perform by group analysis.

Introduction

Colorectal cancer is the third leading cause of death in the world, and it is expected in 2021, about 52,980 people in the United States will die from colon cancer [1]. In 2020, colorectal cancer accounted for 935,173 deaths [2]. In 2019, colorectal cancer was the second leading cause

Funding: The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

of disability-adjusted life years (DALYs) [3]. Between 1990 and 2019, worldwide, colorectal cancer cases more than doubled. So that cases have increased from 842098 to 2.17 million and deaths have increased from 518,126 to 1.09 million [4]. During this period, a significant increase in incidence is observed in adults under 50 years of age, especially in countries with high socio-demographic index [4].

Globally, behavioral factors were the main drivers of DALYs from colorectal cancer in 2019 [4]. Colorectal cancer is most commonly diagnosed in people aged 65 to 74 years, but it is estimated that 10.5 percent of new cases of colorectal cancer occur in people younger than 50 years [5]. According to the recommendations of the World Health Organization and the American Cancer Prevention Association, all people over the age of 50 are at risk of developing colorectal cancer and should accomplish various screening methods [6].

Screening can be effective in reducing the incidence and mortality rate of colorectal cancer [7]. The US Preventive Services Task Force has concluded with high confidence that colorectal cancer screening in adults aged 50 to 75 years has a significant net benefit [5]. Also, this group has concluded with moderate certainty that colorectal cancer screening in adults aged 45 to 49 years has a moderate benefit [5].

Numerous interventions such as advance notification letters, postal reminders and phone navigation calls have been employed to improve the uptake of CRC screening [8]. Through a scoping review, Leach et al. [9] investigated the impact of various interventions on colorectal cancer screening in the United States. They reviewed 13 projects promoting CRCS. The obtained results showed that in the intervention arms, performing colorectal cancer screening by any modality was 16% more than the control group. The result gained from the review of the evidence related to low-income and middle-income countries disclosed that the interventions had a positive effect on increasing the uptake of colorectal cancer screening [10]. Conclusion of another review confirmed the beneficial effect of removing financial obstacles in increasing colorectal cancer screenings [11].

Recently, BE based interventions have been implemented by researchers. Such interventions seek to utilize the heuristics employed by human in making judgments and decisions [12–14]. Designed interventions usually involve small changes and nudge people [15]. Different types of nudging tools can be used to improve the uptake of CRC screening [13]. Choice architecture, perceived social norms, default options, financial incentives, and other techniques can all be applied to influence screening behaviors [13]. Huf et al. [16], Becker et al. [17], Lieberman et al. [18], Green et al. [19], Nisa et al. [20], Slater et al. [21], Mehta et al. [22], Mehta et al. [23], Ritvo et al. [24], Kullgren et al. [25], Vanroosbroeck et al. [26] have confirmed the positive results of behavioral economic interventions. Studies using behavioral economics interventions to promote colorectal screening have reported heterogeneous results. In a rapid review, Taylor et al. [8] concluded that behavioral economics interventions have a mixed effect on increasing the uptake of colorectal cancer screening. To date, the robustness of empirical and confirmatory evidence regarding the effectiveness of BE interventions in promoting the use of CRC screening remains unclear. Therefore, in this paper, the authors have attempted to provide a pooled estimate of the effect size of the BE interventions running a systematic review based meta-analysis.

Materials and methods

Search strategy

This research was accomplished based on PRISMA guidelines. Searches were performed in PubMed, Scopus and Cochrane databases. The keywords used in the search are: Bowel cancer, Colorectal cancer, Faecal immunochemical test, Faecal occult blood test, Colonoscopy, Flexible Sigmoidoscopy, Colonography, Screen, Behavioral economics, Nudge, Incentive, Norms, Default, Salience, Priming, Commitment, Heuristics, bias, aversion, decision fatigue, regret, Order effect, Behavior, Participation, Adherence, Uptake, Utilization, Practices. Search strategies according to databases are presented in Table A in <u>S1 Appendix</u>.

Eligibility criteria

We included studies that met the following eligibility criteria: 1) had a randomized trial design, 2) investigated behavioral economics informed interventions, 3) were written in English, 4) were published during the period from 2000 to 2022, 5) used only human samples and 6) had the data needed to calculate the effect size. Studies that did not report odds ratio (OR) were still included in the analysis if OR could be calculated with 2×2 cross-tabulations. Qualitative studies, gray literature, articles have been published in non-English languages, results have been presented as posters and lectures, and informal reports; were excluded from the analysis.

Data extraction & literature quality assessment

Two members of the research team independently check extracted the data. Items that were not agreed upon by the two researchers were reviewed and extracted by a third evaluator. From the reviewed studies, information such as the name of the first author, year of publication, country of study, study design, type of intervention, outcome variable and sample size have been extracted. To perform meta-analysis, the total number of cases, the total number of controls, the number of successful cases, the number of unsuccessful cases, the number of successful controls, and the number of failed controls were extracted.

The quality assessment was done by two people so that each person evaluated the studies separately and independently based on the individual participant data the modified Jadad scale (Table B in <u>S1 Appendix</u>).

Outcomes

The main outcome is the up taking the colorectal cancer screening tests. Studies have used proxies such as: uptake, utilization and intention-to-perform to investigate screening demand. Different types of screening tests are reported in Table 1.

Statistical analysis

First, the data related to the number of successes and failures in the case and control groups were extracted from the studies as an EXCEL file. The confidence interval of the estimates was considered to be 95%. All the analysis was completed in STATA 15. The pooled effect size has been calculated using fixed and random effects model estimation. In order to check the heterogeneity, we estimated the I² index. I² was introduced by Higgins and Thompson. This statistic calculates the variance ratio due to heterogeneity in the estimates of the studies [27]. As well as the drivers of heterogeneity have been identified through meta-regression. Meta-regression estimates the significance of each source of heterogeneity in the pooled effect size through regression analysis [28]. The presence of publication bias was checked graphically by funnel plot, by nonparametric trim-and-fill analysis and by egger test. By performing two analyses, we evaluated the sensitivity of the pooled effect size to the important parameters and the results of each study was assessed by using leave-one-out meta-analysis. The logic of selecting parameters for sensitivity analysis was the consensus of the authors.

Ref	Study	Year	Country	Design	Outcome	Intervention
[17]	Bakr et al	2020	USA	RCT	CRC screening uptake	Letter leveraging social psychology and behavioral economics principles
29]	Brenner et al	2016	USA	RCT	CRC screening uptake	Decision Aids
[30]	Clouston et al	2014	Canada	RCT	CRC screening uptake	Patient aid
[31]	Gabel et al	2020	Denmark	RCT	CRC screening uptake	Self-administered web-based decision aid
[19]	Green et al	2019	USA	RCT	CRC screening uptake	Mail and lottery
[25]	Kullgren et al	2014	USA	RCT	CRC screening uptake	Receipt 1 in 10 Chance
[25]	Kullgren et al	2014	USA	RCT	CRC screening uptake	Raffle for \$500
[32]	Lipkus et al	2005	USA	RCT	CRC screening uptake	Tailored risk factor information
[33]	Lo et al	2014	England	RCT	CRC screening uptake	Implementation intentions
[22]	Mehta et al	2018	USA	RCT	CRC screening uptake	Opt-out of screening
[23]	Mehta et al	2017	USA	RCT	CRC screening uptake	Active choice
[34]	Mehta et al	2019	USA	RCT	CRC screening uptake	Lottery incentive
[35]	Mehta et al	2019	USA	RCT	CRC screening uptake	Active choice
[36]	Mehta et al	2021	USA	RCT	CRC screening uptake	Loss framed incentive
[37]	Mehta et al	2020	USA	RCT	CRC screening uptake	Text + Lottery
[38]	Menon et al	2011	USA	RCT	CRC screening uptake	Tailored counseling
[<mark>39</mark>]	Miller et al	2018	USA	RCT	CRC screening uptake	decision aid
[<u>40]</u>	Miller et al	2011	USA	RCT	CRC screening uptake	web-based decision aid
[41]	Myers et al	2007	USA	RCT	CRC screening uptake	Tailored message
[42]	Myers et al	2013	USA	RCT	CRC screening uptake	Preference-based navigation
[43]	Myers et al	2014	USA	RCT	CRC screening uptake	Tailored Navigation Intervention
[44]	Neter et al	2014	Israel	RCT	CRC screening uptake	Implementation Intentions
[45]	O'Carroll et al	2015	USA	RCT	CRC screening uptake	Anticipated regret
[46]	Pignone et al	2011	USA	RCT	CRC screening uptake	Decision Aid
[47]	Schroy et al	2011	USA	RCT	CRC screening uptake	Decision aid + personalized risk assessment
[48]	Schwartz et al	2017	USA	RCT	CRC screening uptake	Nudge
[49]	Steckelberg et al	2011	Germany	RCT	CRC screening uptake	Evidence based information on risk
[50]	Stoffel et al	2019	Spain	RCT	CRC screening uptake	Social norms
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Social responsibility
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Anticipated regret
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Account effect
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Benefit of early detect.
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Scarcity
[51]	Stoffel et al	2021	Cyprus	RCT	CRC screening uptake	Social norms
[<u>52</u>]	Trevena et al	2008	Australia	RCT	CRC screening uptake	Decision aid
[53]	Vernon et al	2011	USA	RCT	CRC screening uptake	Tailored Interactive Computer-Delivered Intervention
[54]	Wardle et al	2003	UK	RCT	CRC screening uptake	Psych educational Intervention

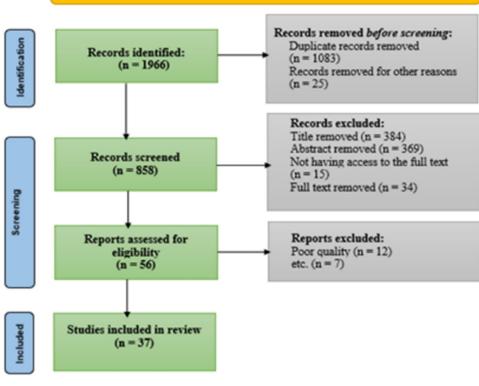
Table 1. Characteristics of studies included in the final analysis.

https://doi.org/10.1371/journal.pone.0290424.t001

Results

Fig 1 displays the PRISMA flowchart. In the initial search, 1966 articles were found. After the necessary screenings, 37 studies were included in the analysis.

37 studies were included in the final analysis, in which 72612 cases and 71493 controls have been studied. The <u>Table 1</u> shows the characteristics of the studies included in the analysis. All studies were randomized clinical trials. As seen in the table, in the reviewed studies, almost all common tests have been investigated as response variables and proxies for colorectal cancer screening demand. In addition, in the aforementioned studies, the effectiveness of various



Identification of studies via databases

Fig 1. PRISMA flowchart.

https://doi.org/10.1371/journal.pone.0290424.g001

types of BE informed interventions have been tested. Interestingly, based on our search, most of the studies were conducted after 2010.

Fig 2 shows the frequency distribution of reviewed studies in the world. The red areas show the countries with a high number of studies and the blue areas show the less studied countries, respectively. The areas seen in green are the countries from which we could not find a study. Based on the map, most of the studies found (about 72%) have been conducted in the USA. It is noteworthy that the percentage frequency of studies in other countries is the same (approximately 3%).

Assessment of heterogeneity size

The obtained information revealed that studies have considerable heterogeneity. So that value of I² index 94.9% was found (heterogeneity X² = 731.89, d.f. = 37, p <0.01). Meta regression results in Table 2 determine heterogeneity factors. Differences in follow-up time and quality scores have been the two main sources of heterogeneity between studies (p<0.05). The details of the quality assessment of studies based on The Modified Jadad Scale are shown in Table B in S1 Appendix. It is quite obvious that the effect of these two factors has become insignificant in the random effects model. Therefore, the estimates of the random effects model show us the final effect size.

Assessment of publication bias

The results of the of publication bias assessment are presented graphically by funnel plot in Fig 3, by nonparametric trim-and-fill analysis in Table 3 and by egger test in Table 4

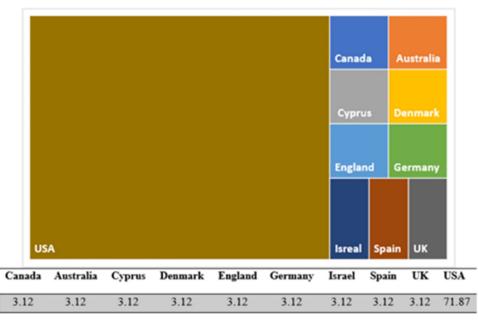


Fig 2. Frequency of reviewed studies in the world (%), Source: Study findings.

https://doi.org/10.1371/journal.pone.0290424.g002

respectively. In the funnel plot, the studies are almost asymmetrically distributed, and most of the studies are located at the top of the funnel (that is, studies with high precision). 3 studies are outside the 95% confidence interval. The plot obtained reveals the existence of the publication bias.

Based on plot b in Fig 3 the six studies (orange dots) trimmed and filled on the right side of the funnel plot can be attributed to the possible presence of publication bias. Also, based on the information in Table 3, it is clear that imputing studies (orange dots) on the right side of the funnel plot could lead to an increase in the pooled odds ratio from 1.27 (95% CI: 1.101 to 1.468) to 1.40 (95% CI: 1.209 to 1.624).

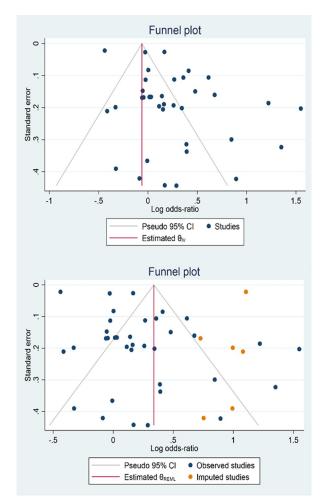
As well as Also, the results of the Egger test confirm the existence of publication bias. According to Table 4, it can be easily seen that the bias coefficient is noteworthy (3.48) and statistically significant (p < 0.01).

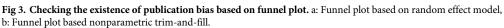
Considering the substantial size of the heterogeneity, the pooled odds ratio obtained from the random model is acceptable for us. It was estimated as 1.26 (95% CI: 1.11 to 1.43). The Fig 4 illustrations the forest plot by intervention. According to the results presented in the figure, the largest effect size was obtained on opting out intervention 3.86 (95% CI: 2.05 to 7.27), which was related to a single study by Mehta et al. (2018). While the lowest effect size was obtained for Anticipated regret intervention 0.76 (95% CI: 0.52 to 1.11).

Model	Variables	β	SE	[95% conf. interval]
Fixed Effect	Follow up period	-0.009	0.004	-0.018 to -0.001
	Quality Score	-0.206	0.013	-0.233 to -0.179
	Cons	1.051	0.075	0.897 to 1.203
Random Effect	Follow up period	-0.003	0.011	-0.027 to 0.021
	Quality Score	-0.030	0.065	-0.164 to 0.102
	Cons	0.429	0.398	-0.381 to 1.239

Table 2. Sources of heterogeneity based on meta-regression analysis.

https://doi.org/10.1371/journal.pone.0290424.t002





https://doi.org/10.1371/journal.pone.0290424.g003

Table 3.	Nonparametric trim-and-fill anal	vsis of	publication bias, imp	puting on the right and left.

Imputing Side	Studies	Log odds-ratio	[95% conf. interval]	
Imputing on the left	Observed	1.27	1.101 to 1.468	
	Observed + Imputed	1.27	1.101 to 1.468	
Imputing on the right	Observed	1.27	1.101 to 1.468	
	Observed + Imputed	1.40	1.209 to 1.624	

https://doi.org/10.1371/journal.pone.0290424.t003

Table 4. The results of the Egger test	(checking the existence of publication bias).
--	---

Std_Eff	β	SE	t	P > t	[95% CI]
Slope	0.82	0.08	10.00	0.000	0.656 to 0.991
Bias	3.48	1.06	3.27	0.002	1.324 to 5.652

Test of H0: no small study effects, p< 0.01

https://doi.org/10.1371/journal.pone.0290424.t004

Study Year	Outcome		OR (95% CI) (I-
Framing Stoffel et al 2021 Stoffel et al 2021 Mehta et al 2020 I-V Subtotal (I-square D+L Subtotal	Uptake eight weeks Uptake eight weeks Completed a colonoscopy d = 0.0%, p = 0.813)		1.03 (0.74, 1.43)0. 1.15 (0.83, 1.59)0. 1.33 (0.56, 3.18)0. 1.10 (0.89, 1.38)1. 1.10 (0.89, 1.38)
Active choice Mehta et al 2017 Mehta et al 2019 I-V Subtotal (I-square D+L Subtotal	Completed colonoscopy CRC screening completion d = 0.0%, p = 0.365)		0.92 (0.40, 2.09)0. 1.48 (0.80, 2.73)0. 1.24 (0.76, 2.04)0. 1.24 (0.76, 2.04)
	FOBT uptake Uptake eight weeks d = 81.5%, p = 0.020)		0.64 (0.62, 0.67)2 0.96 (0.69, 1.33)0 0.65 (0.62, 0.68)2 0.76 (0.52, 1.11)
Decision aid Breission aid Steckelberg et a2011 Miller et al 2018 Miller et al 2011 Clouston et al 2014 Trevena et al 2008 Pignone et al 2014 Gabel et al 2019 Schwartz et al 2019 Schwartz et al 2019 D-L Subtotal	Intent to screen Informed choice in CRC screening Rates of CRC screening CRC screening FOBT completion rates intention to screen reening Completion of a CRC screening test Informed choice CRCS Colorectal Cancer Uptake dorectal Ca		2.44 (1.07, 5.59)0. 0.98 (0.78, 1.22)1. 4.77 (3.16, 7.00)0. 1.48 (0.76, 2.87)0. 1.51 (1.28, 1.781). 0.72 (0.34, 1.55)0. 1.16 (0.78, 1.740). 1.12 (0.76, 1.64)0. 1.12 (0.76, 1.64)0. 1.43 (1.16, 1.76)1. 1.43 (1.6, 1.76)1. 1.44 (1.27, 1.55)5. 1.45 (1.10, 1.92)
Implementation intent Neter et al 2014 Hing Lo et al 2013 I-V Subtotal (I-square D+L Subtotal	ion Test adherence Screening uptake d = 96.3%, p = 0.000)	** *	1.18 (1.12, 1.24)19 0.97 (0.92, 1.02)18 1.07 (1.03, 1.11)35 1.07 (0.88, 1.30)
D+L Subtotal	Any CRC test FOBT completion within 30 FOBT completion within 31 FIT completion rate d = 51.7%, p = 0.082)		1.17 (0.81, 1.70)0 1.30 (0.89, 1.89)0 1.41 (0.95, 2.09)0 0.66 (0.44, 1.00)0 0.99 (0.48, 2.03)0 1.10 (0.91, 1.33)1 1.09 (0.82, 1.43)
Navigation Myers et al 2013 Myers et al 2014 I-V Subtotal (I-square D+L Subtotal	Screening adherence CRC screening adherence d = 79.8%, p = 0.026)		3.39 (2.36, 4.88)0. 1.96 (1.43, 2.69)0. 2.48 (1.95, 3.15)0. 2.56 (1.50, 4.37)
Opting out Mehta et al 2018 I-V Subtotal (I-square D+L Subtotal			3.86 (2.05, 7.27)0. 3.86 (2.05, 7.27)0. 3.86 (2.05, 7.27)
	ail Colorectal Screening intention d = .%, p = .)	*	1.85 (1.50, 2.27)1. 1.85 (1.50, 2.27)1. 1.85 (1.50, 2.27)
Scarcity effect Bakr et al 2020 Stoffel et al 2021 I-V Subtotal (I-square D+L Subtotal	Participation in CRC screening Uptake eight weeks d = 61.3%, p = 0.108)		1.30 (1.05, 1.62)1. 0.94 (0.68, 1.31)0. 1.18 (0.98, 1.42)1. 1.14 (0.83, 1.56)
Social norms Stoffel et al 2019 Stoffel et al 2021 I-V Subtotal (I-square D+L Subtotal	CRC screening uptake Uptake eight weeks d = 0.0%, p = 0.950)		1.00 (0.85, 1.18)1. 1.01 (0.73, 1.41)0. 1.00 (0.87, 1.16)2. 1.00 (0.87, 1.16)
Social responsibility Stoffel et al 2021 I-V Subtotal (I-square D+L Subtotal			1.02 (0.74, 1.41)0. 1.02 (0.74, 1.41)0. 1.02 (0.74, 1.41)
D+L Subiolai	Number of cancer preventive behaviors FOBT screening rates Increase screening use Any CRCS Any Screening test d = 77.8%, p = 0.001)		1.18 (1.12, 1.24)18 0.72 (0.49, 1.06)0. 1.61 (1.20, 2.16)0. 0.95 (0.71, 1.26)0. 2.33 (1.30, 4.18)0. 1.18 (1.12, 1.24)2(1.19 (0.93, 1.54)
Heterogeneity betwee I-V Overall (I-squared D+L Overall	n groups: p = 0.000 = 94.9%, p = 0.000)	0	0.98 (0.96, 1.00)10 1.26 (1.12, 1.43)
	.137	1 I 1 7.2	-

Fig 4. Results of fixed and random effects meta-analysis by intervention.

https://doi.org/10.1371/journal.pone.0290424.g004

Sensitivity analysis

The results of sensitivity analysis are presented in Tables 5 and 6. Based on the results of Table 5, the size and significance of the pooled odds ratio has been not sensitive to poor study quality. While after excluding studies that had a follow-up period of less than 3 months and 6 months, the pooled odds ratio had been increased from 1.27 (95% CI: 1.07 to 1.50) to 1.37 (95% CI: 1.16 to 1.61) and 1.35 (95% CI: 1.07 to 1.70), respectively.

Table 6 shows the results of the Leave-one-out meta-analysis. This analysis shows that excluding individual studies causes the pooled odds ratio to fluctuate between 1.22 (95% CI: 1.07 to 1.37) and 1.29 (95% CI: 1.12 to 1.49). That is, by removing and adding each study, the odds ratio changes, but it is still significant.

Sensitivity analysis criteria	Omitted studies	POR	95% CI
Quality score < 5	Wardle et al. (2003), Lipkus et al. (2005) Miller et al. (2011), Pignone et al. (2011) Vernon et al. (2011), Myers et al. (2013) Neter et al. (2014), Clouston et al. (2014) Gabel et al. (2020), Stoffel et al. (2019) Mehta et al. (2019)	1.27	(1.07 to 1.50)
Follow up < 3	Kullgren et al. (2014), Kullgren et al. (2014) Trevena et al. (2008), Stoffel et al. (2019) Stoffel et al. (2021), Stoffel et al. (2021) Stoffel et al. (2021), Stoffel et al. (2021) Stoffel et al. (2021), Stoffel et al. (2021)	1.37	(1.16 to 1.61)
Follow up < 6	Kullgren et al. (2014), Kullgren et al. (2014) Trevena et al. (2008), Stoffel et al. (2019) Stoffel et al. (2021), Stoffel et al. (2021) Stoffel et al. (2021), Stoffel et al. (2021) Stoffel et al. (2021), Stoffel et al. (2021) Gabel et al. (2020), Lo et al. (2014) Mehta et al. (2020), Mehta et al. (2018) Mehta et al. (2017), Mehta et al. (2020) Miller et al. (2011), Wardle et al. (2003) Mehta et al. (2019)	1.35	(1.07 to 1.70)

Table 5. Results of sensitivity analysis.

https://doi.org/10.1371/journal.pone.0290424.t005

Discussion

This study sought to answer this question: Are BE informed interventions effective in increasing demand for colorectal cancer screening? To answer this question, we estimated the pooled effect size of randomized clinical trial studies through a systematic review of published evidence during the period 2000 to 2022. The meta-analysis run in this study covered 144105

Omitted study	OR	95% CI	Omitted study	OR	95% CI
Study 1	1.27	1.09 to 1.47	Study 20	1.25	1.08 to 1.44
Study 2	1.25	1.09 to 1.44	Study 21	1.25	1.09 to 1.46
Study 3	1.27	1.09 to 1.46	Study 22	1.27	1.10 to 1.47
Study 4	1.27	1.09 to 1.47	Study 23	1.29	1.12 to 1.49
Study 5	1.27	1.10 to 1.47	Study 24	1.27	1.10 to 1.47
Study 6	1.27	1.09 to 1.47	Study 25	1.27	1.10 to 1.47
Study 7	1.27	1.09 to 1.47	Study 26	1.27	1.10 to 1.47
Study 8	1.29	1.11 to 1.49	Study 27	1.28	1.10 to 1.49
Study 9	1.28	1.10 to 1.49	Study 28	1.28	1.10 to 1.49
Study 10	1.28	1.10 to 1.47	Study 29	1.27	1.10 to 1.47
Study 11	1.27	1.09 to 1.46	Study 30	1.28	1.10 to 1.49
Study 12	1.24	1.08 to 1.41	Study 31	1.28	1.10 to 1.49
Study 13	1.29	1.12 to 1.49	Study 32	1.28	1.10 to 1.49
Study 14	1.28	1.10 to 1.47	Study 33	1.28	1.10 to 1.49
Study 15	1.27	1.09 to 1.47	Study 34	1.28	1.10 to 1.49
Study 16	1.25	1.08 to 1.44	Study 35	1.28	1.11 to 1.49
Study 17	1.22	1.07 to 1.37	Study 36	1.28	1.10 to 1.49
Study 18	1.27	1.09 to 1.46	Study 37	1.25	1.08 to 1.44
Study 19	1.23	1.07 to 1.40			

Table 6. Leave-one-out meta-analysis.

https://doi.org/10.1371/journal.pone.0290424.t006

participants (72612 cases and 71493 controls). Our estimate of the pooled effect size for all behavioral economics interventions revealed that these interventions have an increasing effect on screening demand. However, the effect size was different based on the type of intervention. In line with our results, Taylor et al. [8] through systematic reviewing the evidence, concluded that the effect of BE intervention on stimulating the demand for screening is significant and that these types of intervention have the potential to improve participation in screening. It is worth mentioning that our study differs from Taylor et al's study in several aspects. First, our search covers a wider range of databases. Second, unlike their study, in addition to the systematic review, we also have estimated the pooled effect size of the interventions. Cadario and Chandon [55] through meta-analyzing of evidence concluded that nudge interventions are more effective in reducing unhealthy eating. By reviewing and meta-analyzing more than 200 studies, Mertens et al. [56] determined choice architecture interventions improve behavior to a small to moderate extent. In another meta-analysis, Beshears and Kosowksy [57] found that choice architecture interventions had a moderate effect. Jachimowicz et al. [58] also reported a moderate effect size for choice defaults. Using a systematic review, Blaga et al. [59] exhibited there is mixed evidence about the effectiveness of behavioral economics interventions in controlling the risk factors of these types of diseases. The results of a systematic review by Valérie and colleagues [60] confirmed the effectiveness of nudging in selecting fruits and vegetables. In a scoping review of the use of behavioral economics interventions in pharmaceutical policy making, the researchers concluded that the effectiveness of the interventions was generally positive, but it depended on the context [61]. Our by group meta-analysis also clarified interesting results. Largest effect size was obtained on opting out interventions. There is a wealth of evidence on the effectiveness of opt out strategies in various behavioral domains. For example, Henriquez-Camacho et al. [62] by systematically reviewing and meta-analyzing 28 articles on the HIV screening uptake, concluded that opt-out strategy was superior to the opt-in, and the refusal rate was lower in the opt-out group. The results of a study indicated that opt-out mailed FIT kit outreach could considerably improve colorectal cancer screening rates in poor population [16]. Asgary et al. [63] also showed opt-out navigation improves breast cancer screening and can reduce multilevel barriers to screening among women with housing problems. A study in Canada found that with the introduction of the opt-out method, HIV testing rates increased [64]. Richter et al. [65] revealed the opt-out strategy folded treatment involvement and increased quit efforts. A study exhibited that opt-out protocol resulted in harmless discontinuation of antibiotics in patients with suspected sepsis [66]. The opt-out strategy takes advantage of the status quo bias. Opting out of a default option has a cognitive cost for people. Based on our estimates, navigation has the second highest effect size. Navigation is an evidencebased intervention that can significantly improve demand for preventive health services [67]. In fact, patients are guided through navigators. Patient navigators can be qualified personnel who help patients overcome changeable barriers to care and attain their care goals [68]. Patient navigation is used in diseases such as cancer screening [69], diabetes [70] and smoking cessation[71, 72]. Navigation intervention can be in the form of educating disease knowledge, education on health system, removing barriers to the medical care, coverage insurance, relaxing other financial barriers, coordinating care, refer to community centers and provide emotional support [68]. By reviewing 67 articles about chronic diseases, Mcbrien et al. [68] concluded that navigation programs improve care for patients. Ritvo et al. [24] showed that the intervention group (navigated) demanded colorectal screening significantly more than the control group. Another part of our findings revealed that leveraging social norms had no effect on stimulating demand for colorectal screening. Social norms indicate acceptable standards of behavior in a society. Since health behaviors are the result of the simultaneous effect of several factors. Therefore, it is possible that the mere leveraging of social norms has a stimulating

effect on behavior such as screening. Unfortunately, we could not find systematic and sufficient evidence about the effect of using social norms in screening. In a cross-sectional study among German men, Sieverding et al. [73] concluded that social norms play an important role in the demand for cancer screening. The results of a study showed that people receiving messages containing social norms performed well in the field of self-monitoring [74]. Notably, we found very little evidence of ineffectiveness of behavioral economics interventions. The results of a field experiment by Bronchetti et al. [75], disclosed that saving behavior did not change among treatment arm (opting out). There is still much debate among researchers and policymakers about the effectiveness of behavioral economics interventions. Some nudges used to change behavior may not be as effective as intended. Nudges that have a large short-term effect may not be very effective in the long term and must be repeated to have a lasting effect. Nudges that effectively change one targeted behavior may simultaneously affect other behaviors. Also, on larger scales, nudges may have tiny effect on planned outcomes. For example, Beshears et al. [76] found that the effectiveness of implementing automatic enrollment on the amount of retirement savings in the first four years of employment was significant but little. Nudges can also have adverse consequences. For example, violation of independence, doubts about positive welfare effects, long-term adverse effects and distortion of democracy and deliberation [77]. The effect size of BE interventions has been reported differently in studies. The range of effect sizes was wide from 0.64 to 3.86. So that, the largest effect size (3.86, 95% CI: 2.05 to 7.23) was reported by Mehta et al. [22]. This study examined the effect of opt-out versus opt-in messaging on fecal immunochemical test (FIT) completion. The authors concluded that optout messaging methods can improvement participation in population health outreach works. Owing to the short-term follow-up and the non-comprehensive nature of the studied subjects, the researchers could not perform a downstream diagnostic evaluation of the positive results, so caution should be exercised in generalizing their results in the long term and to other populations. The lowest effect size belonged to the study of O'Carroll et al. [45]. The researchers aimed to measure the effect of a regret evasion intervention on increasing the uptake of colorectal cancer screening. They found the role of regret evasion effective in increasing FOBT uptake. The effect size of this study should also be interpreted with caution. Because in the sample size used, there was little data related to ethnicity. To some extent, this discrepancy could be due to heterogeneity between studies. This heterogeneity can be caused by the variety of interventions and the variety of screening measures. The pooled odds ratio in our study has been estimated more than one and was statistically significant. It means behavioral economics-based interventions are effective in encouraging the demand for colorectal cancer screening. In another review, the authors found compelling evidence that nudges are effective in promoting adherence to guidelines [78]. Möllenkamp and colleague [79] review showed that nudges can improve chronic disease self-management. Summary evidence from a meta-analysis review has revealed that if the information presented about preventive behaviors emphases on the benefits of these actions rather than the losses, people are more likely to perform preventive behaviors [80]. The message frame promoting cancer screening can influence the screening decision [81]. For example, underserved women answered more positively to tailored letter than to a general letter encouraging breast cancer screening. The results of a study by Liang et al. [82] disclosed that nudging (an approach based on behavioral economics) improved the number of appointments scheduled for Medicare health visits and Pap smear test. The authors further conclude that framing and modifying the language of e-messaging can have a significant and long-term impact on patient engagement and access to care [82]. The results of a randomized clinical trial on chronic kidney disease screening in Japan showed that behavioral economics interventions had an improvement effect [83]. Quinn et al. [84] also concluded in their study that the choice architecture based on behavioral economics can

improve the choice of healthy foods by students. In one study, the authors concluded that compared to standard profit-based incentives, offering lottery incentives and losses framed incentives did not lead to a significant increase in HIV testing. However, when low-cost incentives are offered to promote HIV testing, designing lottery prizes may be a better approach than profit-based incentives [85]. Nudges can also have adverse consequences. For example, violation of independence, doubts about positive welfare effects, long-term adverse effects and distortion of democracy and deliberation [77]. The presence of evidence about the minor effects of nudges does not diminish the role of psychological factors in changing behavior. Also, the existence of observations indicating the mild effects of nudges does not mean that behavioral economics techniques such as choice architecture are not useful for policy makers. Behavioral economics is a relatively new area of economics, it does not (and should not) completely replace conventional economics. Rather, it can be considered a complement to neoclassical economics.

Conclusion

Our meta-analysis revealed that BE interventions are effective in increasing demand for and uptake of colorectal cancer screening. Based on the average cost, BE interventions can be very valuable tools for behavior change [86]. Therefore, health policy and decision makers can improve the efficiency and cost effectiveness of policies to control this type of cancer by using various behavioral economics interventions.

Limitations

Some limitations can be considered for our study: First, we only analyzed interventions that were directly or indirectly related to behavioral economics. Therefore, some studies that were not in the scope of our keywords may not have been included in the analysis. Second, it was not possible for us to access some specialized databases. Third, we did not include gray evidence and published in non-English languages. Therefore, we suggest that readers generalize our results with caution. Future studies could obtain more accurate estimates of effect size by including a wider range of keywords, searching more comprehensive databases, and examining gray and published literature in other languages.

Supporting information

S1 Checklist. PRISMA 2020 for abstracts checklist. (DOCX)

S2 Checklist. PRISMA 2020 checklist. (DOCX)

S1 Appendix. (DOCX)

Author Contributions

Conceptualization: Bahman Ahadinezhad, Aisa Maleki, Amirali Akhondi. Data curation: Bahman Ahadinezhad, Aisa Maleki, Amirali Akhondi. Formal analysis: Bahman Ahadinezhad, Aisa Maleki, Amirali Akhondi. Investigation: Aisa Maleki, Sama Yousefy, Fatemeh Rezaei. Methodology: Omid Khosravizadeh.

- Writing original draft: Mohammadjavad Kazemi, Sama Yousefy, Fatemeh Rezaei, Omid Khosravizadeh.
- Writing review & editing: Bahman Ahadinezhad, Aisa Maleki, Amirali Akhondi, Mohammadjavad Kazemi, Omid Khosravizadeh.

References

- 1. <References>. Siegel R.L., et al., Cancer statistics, 2021. Ca Cancer J Clin, 2021. 71(1): p. 7–33. https://doi.org/10.3322/caac.21654 PMID: 33433946
- 2. Ferlay, J., M. Laversanne, and M. Ervik, Global Cancer Observatory: Cancer Tomorrow. Lyon, France: International Agency for Research on Cancer [cited 2021 Feb 25]. 2020.
- Vos T., et al., Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet, 2020. 396(10258): p. 1204–1222. https://doi.org/10.1016/S0140-6736(20)30925-9 PMID: 33069326
- Sharma R., et al., Global, regional, and national burden of colorectal cancer and its risk factors, 1990– 2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Gastroenterology & Hepatology, 2022. https://doi.org/10.1016/S2468-1253(22)00044-9 PMID: 35397795
- Davidson K.W., et al., Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. Jama, 2021. 325(19): p. 1965–1977. https://doi.org/10.1001/jama.2021.6238 PMID: 34003218
- 6. https://www.cancer.org/cancer/colon-rectal, C.C.G.H.O.t.H.S.T.I.A.f., 2020.
- Shaukat A. and Lehenbauer K.P., Screening for Colorectal Neoplasia. N Engl J Med, 2017. 376(16): p. 1599. https://doi.org/10.1056/NEJMc1702535 PMID: 28423295
- Taylor L.C., et al., Effectiveness of behavioural economics-based interventions to improve colorectal cancer screening participation: A rapid systematic review of randomised controlled trials. Preventive Medicine Reports, 2022. 26. https://doi.org/10.1016/j.pmedr.2022.101747 PMID: 35284211
- Leach K.M., et al., Promoting colorectal cancer screening: A scoping review of screening interventions and resources. Preventive medicine, 2021. 147: p. 106517. <u>https://doi.org/10.1016/j.ypmed.2021</u>. 106517 PMID: 33711351
- Schliemann D., et al., The implementation of colorectal cancer screening interventions in low-and middle-income countries: a scoping review. Bmc Cancer, 2021. 21: p. 1–16.
- 11. Senore C., et al., Optimising colorectal cancer screening acceptance: a review. Gut, 2015. 64(7): p. 1158–1177. https://doi.org/10.1136/gutjnl-2014-308081 PMID: 26059765
- 12. Dolan P., et al., Influencing behaviour: The mindspace way. Journal of economic psychology, 2012. 33 (1): p. 264–277.
- **13.** Purnell J.Q., et al., Peer reviewed: Behavioral economics:"nudging" underserved populations to be screened for cancer. Preventing Chronic Disease, 2015. 12.
- 14. The rise of behavioural economics. Nat Hum Behav, 2017. 1(11): p. 767.
- **15.** Thaler R.H. and Sunstein C.R., Nudge: Improving decisions about health, wealth, and happiness. 2009: Penguin.
- Huf S.W., et al., Text messaging and opt-out mailed outreach in colorectal cancer screening: a randomized clinical trial. Journal of General Internal Medicine, 2021. 36: p. 1958–1964. <u>https://doi.org/10. 1007/s11606-020-06415-8 PMID: 33511567</u>
- Bakr O., et al., Application of behavioral economics principles improves participation in mailed outreach for colorectal cancer screening. Clinical and translational gastroenterology, 2020. 11(1). <u>https://doi.org/ 10.14309/ctg.00000000000115</u> PMID: 31972609
- Lieberman A., et al., Financial Incentives to Promote Colorectal Cancer Screening: A Longitudinal Randomized Control TrialFinancial Incentives to Promote Colorectal Cancer Screening. Cancer Epidemiology, Biomarkers & Prevention, 2019. 28(11): p. 1902–1908.
- Green B.B., et al., Financial incentives to increase colorectal cancer screening uptake and decrease disparities: a randomized clinical trial. JAMA network open, 2019. 2(7): p. e196570–e196570. https:// doi.org/10.1001/jamanetworkopen.2019.6570 PMID: 31276178
- Nisa C.F., Bélanger J.J., and Schumpe B.M., Parts greater than their sum: randomized controlled trial testing partitioned incentives to increase cancer screening. Annals of the New York Academy of Sciences, 2019. 1449(1): p. 46–55. https://doi.org/10.1111/nyas.14115 PMID: 31111509

- Slater J.S., et al., The Efficacy of Direct Mail, Patient Navigation, and Incentives for Increasing Mammography and Colonoscopy in the Medicaid Population: A Randomized Controlled TrialRCT to Increase Cancer Screening among Medicaid Clients. Cancer Epidemiology, Biomarkers & Prevention, 2018. 27(9): p. 1047–1056.
- Mehta S.J., et al., A Randomized Controlled Trial of Opt-in Versus Opt-Out Colorectal Cancer Screening Outreach. The American Journal of Gastroenterology, 2018. 113(12): p. 1848. https://doi.org/10.1038/s41395-018-0151-3 PMID: 29925915
- 23. Mehta S.J., et al., Active Choice and Financial Incentives to Increase Rates of Screening Colonoscopy-A Randomized Controlled Trial. Gastroenterology, 2017. 153(5): p. 1227–1229.e2. <u>https://doi.org/10.1053/j.gastro.2017.07.015</u> PMID: 28734830
- Ritvo P.G., et al., Personal Navigation Increases Colorectal Cancer Screening UptakePersonal Navigation in Colorectal Cancer Screening. Cancer Epidemiology, Biomarkers & Prevention, 2015. 24(3): p. 506–511.
- Kullgren J.T., et al., Financial incentives for completion of fecal occult blood tests among veterans: a 2stage, pragmatic, cluster, randomized, controlled trial. Annals of internal medicine, 2014. 161(10_Supplement): p. S35–S43. https://doi.org/10.7326/M13-3015 PMID: 25402401
- Van Roosbroeck S., Hoeck S., and Van Hal G., Population-based screening for colorectal cancer using an immunochemical faecal occult blood test: a comparison of two invitation strategies. Cancer epidemiology, 2012. 36(5): p. e317–e324. https://doi.org/10.1016/j.canep.2012.04.003 PMID: 22560885
- von Hippel P.T., The heterogeneity statistic I2 can be biased in small meta-analyses. BMC medical research methodology, 2015. 15(1): p. 1–8. <u>https://doi.org/10.1186/s12874-015-0024-z</u> PMID: 25880989
- Thompson S.G. and Higgins J.P., How should meta-regression analyses be undertaken and interpreted? Statistics in medicine, 2002. 21(11): p. 1559–1573. https://doi.org/10.1002/sim.1187 PMID: 12111920
- Brenner A.T., et al., Colorectal cancer screening in vulnerable patients: promoting informed and shared decisions. American journal of preventive medicine, 2016. 51(4): p. 454–462. <u>https://doi.org/10.1016/j.</u> amepre.2016.03.025 PMID: 27242081
- 30. Clouston K., et al., Does access to a colorectal cancer screening website and/or a nurse-managed telephone help line provided to patients by their family physician increase fecal occult blood test uptake?: results from a pragmatic cluster randomized controlled trial. BMC cancer, 2014. 14(1): p. 1–11. <u>https://doi.org/10.1186/1471-2407-14-263 PMID: 24739235</u>
- Gabel P., et al., The LEAD trial—The effectiveness of a decision aid on decision making among citizens with lower educational attainment who have not participated in FIT-based colorectal cancer screening in Denmark: A randomised controlled trial. Patient Education and Counseling, 2020. 103(2): p. 359– 368. https://doi.org/10.1016/j.pec.2019.08.029 PMID: 31451360
- Lipkus I.M., et al., Increasing colorectal cancer screening among individuals in the carpentry trade: test of risk communication interventions. Preventive medicine, 2005. 40(5): p. 489–501. https://doi.org/10. 1016/j.ypmed.2004.09.019 PMID: 15749130
- **33.** Lo S.H., et al., Preformulated implementation intentions to promote colorectal cancer screening: a cluster-randomized trial. Health Psychology, 2014. 33(9): p. 998. https://doi.org/10.1037/a0033507 PMID: 24245844
- Mehta S.J., et al., Effect of Financial Incentives on Patient Use of Mailed Colorectal Cancer Screening Tests: A Randomized Clinical Trial. JAMA Netw Open, 2019. 2(3): p. e191156. <u>https://doi.org/10.1001/jamanetworkopen.2019.1156</u> PMID: 30901053
- Mehta S.J., et al., Effect of Sequential or Active Choice for Colorectal Cancer Screening Outreach: A Randomized Clinical Trial. JAMA Netw Open, 2019. 2(8): p. e1910305. https://doi.org/10.1001/ jamanetworkopen.2019.10305 PMID: 31469393
- Mehta S.J., et al., Effect of Behavioral Economic Incentives for Colorectal Cancer Screening in a Randomized Trial. Clin Gastroenterol Hepatol, 2021. 19(8): p. 1635–1641.e1. <u>https://doi.org/10.1016/j.cgh.</u> 2020.06.047 PMID: 32623005
- Mehta S.J., et al., Text messaging and lottery incentive to improve colorectal cancer screening outreach at a community health center: A randomized controlled trial. Prev Med Rep, 2020. 19: p. 101114. https://doi.org/10.1016/j.pmedr.2020.101114 PMID: 32477853
- Menon U., et al., A randomized trial comparing the effect of two phone-based interventions on colorectal cancer screening adherence. Annals of Behavioral Medicine, 2011. 42(3): p. 294–303. https://doi.org/ 10.1007/s12160-011-9291-z PMID: 21826576
- Miller D.P. Jr, et al., Effect of a digital health intervention on receipt of colorectal cancer screening in vulnerable patients: a randomized controlled trial. Annals of internal medicine, 2018. 168(8): p. 550–557. https://doi.org/10.7326/M17-2315 PMID: 29532054

- 40. Miller D.P. Jr, et al., Effectiveness of a web-based colorectal cancer screening patient decision aid: a randomized controlled trial in a mixed-literacy population. American journal of preventive medicine, 2011. 40(6): p. 608–615. https://doi.org/10.1016/j.amepre.2011.02.019 PMID: 21565651
- Myers R.E., et al., A randomized controlled trial of the impact of targeted and tailored interventions on colorectal cancer screening. Cancer, 2007. 110(9): p. 2083–2091. <u>https://doi.org/10.1002/cncr.23022</u> PMID: 17893869
- 42. Myers R.E., et al., A randomized controlled trial of a tailored navigation and a standard intervention in colorectal cancer screening. Cancer epidemiology, biomarkers & prevention, 2013. 22(1): p. 109–117. https://doi.org/10.1158/1055-9965.EPI-12-0701 PMID: 23118143
- Myers R.E., et al., Increasing colon cancer screening in primary care among African Americans. Journal of the National Cancer Institute, 2014. 106(12): p. dju344. https://doi.org/10.1093/jnci/dju344 PMID: 25481829
- **44.** Neter E., et al., From the bench to public health: population-level implementation intentions in colorectal cancer screening. American journal of preventive medicine, 2014. 46(3): p. 273–280. https://doi.org/10.1016/j.amepre.2013.11.008 PMID: 24512866
- 45. O'Carroll R.E., et al., Anticipated regret to increase uptake of colorectal cancer screening (ARTICS): a randomised controlled trial. Social Science & Medicine, 2015. 142: p. 118–127. <u>https://doi.org/10.1016/j.socscimed.2015.07.026</u> PMID: 26301484
- 46. Pignone M., et al., Effectiveness of a patient and practice-level colorectal cancer screening intervention in health plan members: the CHOICE trial. Cancer, 2011. 117(15): p. 3352–3362. <u>https://doi.org/10. 1002/cncr.25924</u> PMID: 21319147
- Schroy P.C. III, et al., The impact of a novel computer-based decision aid on shared decision making for colorectal cancer screening: a randomized trial. Medical Decision Making, 2011. 31(1): p. 93–107. https://doi.org/10.1177/0272989X10369007 PMID: 20484090
- Schwartz P.H., et al., Providing quantitative information and a nudge to undergo stool testing in a colorectal cancer screening decision aid: a randomized clinical trial. Medical Decision Making, 2017. 37(6): p. 688–702. https://doi.org/10.1177/0272989X17698678 PMID: 28398836
- Steckelberg A., et al., Effect of evidence based risk information on "informed choice" in colorectal cancer screening: randomised controlled trial. Bmj, 2011. 342. https://doi.org/10.1136/bmj.d3193 PMID: 21636633
- 50. Stoffel S., et al., Testing behavioral interventions to optimize participation in a population-based colorectal cancer screening program in Catalonia, Spain. Preventive Medicine, 2019. 119: p. 58–62. <u>https://</u> doi.org/10.1016/j.ypmed.2018.12.013 PMID: 30594532
- Stoffel S., et al., Testing messages from behavioral economics to improve participation in a populationbased colorectal cancer screening program in Cyprus: Results from two randomized controlled trials. Preventive medicine reports, 2021. 24: p. 101499. <u>https://doi.org/10.1016/j.pmedr.2021.101499</u> PMID: 34430189
- Trevena L.J., Irwig L., and Barratt A., Randomized trial of a self-administered decision aid for colorectal cancer screening. Journal of medical screening, 2008. 15(2): p. 76–82. <u>https://doi.org/10.1258/jms.</u> 2008.007110 PMID: 18573775
- Vernon S.W., et al., A randomized controlled trial of a tailored interactive computer-delivered intervention to promote colorectal cancer screening: sometimes more is just the same. Annals of Behavioral Medicine, 2011. 41(3): p. 284–299. https://doi.org/10.1007/s12160-010-9258-5 PMID: 21271365
- 54. Wardle J., et al., Increasing attendance at colorectal cancer screening: testing the efficacy of a mailed, psychoeducational intervention in a community sample of older adults. Health Psychology, 2003. 22 (1): p. 99. https://doi.org/10.1037//0278-6133.22.1.99 PMID: 12558207
- Cadario R. and Chandon P., Which healthy eating nudges work best? A meta-analysis of field experiments. Marketing Science, 2020. 39(3): p. 465–486.
- Mertens S., et al., The effectiveness of nudging: A meta-analysis of choice architecture interventions across behavioral domains. Proceedings of the National Academy of Sciences, 2022. 119(1): p. e2107346118.
- Beshears J. and Kosowsky H., Nudging: Progress to date and future directions. Organizational behavior and human decision processes, 2020. 161: p. 3–19. <u>https://doi.org/10.1016/j.obhdp.2020.09.001</u> PMID: 33716395
- Jachimowicz J.M., et al., When and why defaults influence decisions: A meta-analysis of default effects. Behavioural Public Policy, 2019. 3(2): p. 159–186.
- Blaga O.M., Vasilescu L., and Chereches R.M., Use and effectiveness of behavioural economics in interventions for lifestyle risk factors of non-communicable diseases: a systematic review with policy implications. Perspectives in public health, 2018. 138(2): p. 100–110. <u>https://doi.org/10.1177/</u> 1757913917720233 PMID: 28715989

- Broers V.J., et al., A systematic review and meta-analysis of the effectiveness of nudging to increase fruit and vegetable choice. The European Journal of Public Health, 2017. 27(5): p. 912–920. https://doi. org/10.1093/eurpub/ckx085 PMID: 28655176
- Vandenplas Y., et al., Applications of Behavioral Economics to Pharmaceutical Policymaking: A Scoping Review with Implications for Best-Value Biological Medicines. Applied health economics and health policy, 2022: p. 1–15. https://doi.org/10.1007/s40258-022-00751-y PMID: 35972683
- Henriquez-Camacho C., et al., Opt-out screening strategy for HIV infection among patients attending emergency departments: systematic review and meta-analysis. Hiv medicine, 2017. 18(6): p. 419–429. https://doi.org/10.1111/hiv.12474 PMID: 28000338
- Asgary R., Naderi R., and Wisnivesky J., Opt-out patient navigation to improve breast and cervical cancer screening among homeless women. Journal of Women's Health, 2017. 26(9): p. 999–1003. https://doi.org/10.1089/jwh.2016.6066 PMID: 28103125
- Long R., et al., A 10-year population based study of 'opt-out'HIV testing of tuberculosis patients in Alberta, Canada: National implications. PLoS One, 2014. 9(6): p. e98993. <u>https://doi.org/10.1371/journal.pone.0098993 PMID: 24911262</u>
- 65. Richter K.P., et al., The Effects of Opt-out vs Opt-in Tobacco Treatment on Engagement, Cessation, and Costs: A Randomized Clinical Trial. JAMA Internal Medicine, 2023. 183(4): p. 331–339. https://doi.org/10.1001/jamainternmed.2022.7170 PMID: 36848129
- Moehring R.W., et al., Evaluation of an Opt-Out Protocol for Antibiotic De-Escalation in Patients With Suspected Sepsis: A Multicenter, Randomized, Controlled Trial. Clinical Infectious Diseases, 2023. 76 (3): p. 433–442. https://doi.org/10.1093/cid/ciac787 PMID: 36167851
- Coronado G.D., et al., Characteristics of patient navigation programs in the Cancer Moonshot ACCSIS colorectal cancer screening initiative. JNCI: Journal of the National Cancer Institute, 2023: p. djad032. https://doi.org/10.1093/jnci/djad032 PMID: 36810931
- McBrien K.A., et al., Patient navigators for people with chronic disease: a systematic review. PloS one, 2018. 13(2): p. e0191980. https://doi.org/10.1371/journal.pone.0191980 PMID: 29462179
- 69. Enard K., et al., Patient navigation to increase colorectal cancer screening among Latino Medicare enrollees: a randomized controlled trial. Cancer Causes & Control, 2015. 26: p. 1351–1359. <u>https://doi.org/10.1007/s10552-015-0620-6 PMID: 26109462</u>
- 70. Thom D.H., et al., Impact of peer health coaching on glycemic control in low-income patients with diabetes: a randomized controlled trial. The Annals of Family Medicine, 2013. 11(2): p. 137–144. <u>https://doi.org/10.1370/afm.1443</u> PMID: 23508600
- Lasser K.E., et al., Patient navigation to promote smoking cessation among low-income primary care patients: a pilot randomized controlled trial. Journal of ethnicity in substance abuse, 2013. 12(4): p. 374–390. https://doi.org/10.1080/15332640.2013.819311 PMID: 24215228
- 72. Quintiliani L.M., et al., Patient navigation and financial incentives to promote smoking cessation in an underserved primary care population: A randomized controlled trial protocol. Contemporary Clinical Trials, 2015. 45: p. 449–457. https://doi.org/10.1016/j.cct.2015.09.005 PMID: 26362691
- **73.** Sieverding M., Matterne U., and Ciccarello L., What role do social norms play in the context of men's cancer screening intention and behavior? Application of an extended theory of planned behavior. Health psychology, 2010. 29(1): p. 72. https://doi.org/10.1037/a0016941 PMID: 20063938
- 74. Liu C.-W., et al. Leveraging Social Norms and Implementation Intentions for Better Health. in Smart Health: International Conference, ICSH 2017, Hong Kong, China, June 26–27, 2017, Proceedings. 2017. Springer.
- 75. Bronchetti E.T., et al., When a nudge isn't enough: Defaults and saving among low-income tax filers. National Tax Journal, 2013. 66(3): p. 609–634.
- 76. Beshears J., et al., Borrowing to save? The impact of automatic enrollment on debt. The Journal of Finance, 2022. 77(1): p. 403–447.
- 77. Kuyer P. and Gordijn B., Nudge in perspective: A systematic literature review on the ethical issues with nudging. Rationality and Society, 2023. 35(2): p. 191–230.
- **78.** Nwafor O., et al., Effectiveness of nudges as a tool to promote adherence to guidelines in healthcare and their organizational implications: a systematic review. Social Science & Medicine, 2021. 286: p. 114321. https://doi.org/10.1016/j.socscimed.2021.114321 PMID: 34438185
- 79. Möllenkamp M., Zeppernick M., and Schreyögg J., The effectiveness of nudges in improving the selfmanagement of patients with chronic diseases: a systematic literature review. Health Policy, 2019. 123 (12): p. 1199–1209. https://doi.org/10.1016/j.healthpol.2019.09.008 PMID: 31676042
- Gallagher K.M. and Updegraff J.A., Health message framing effects on attitudes, intentions, and behavior: a meta-analytic review. Annals of behavioral medicine, 2012. 43(1): p. 101–116. <u>https://doi.org/10. 1007/s12160-011-9308-7</u> PMID: 21993844

- Skinner C.S., Strecher V.J., and Hospers H., Physicians' recommendations for mammography: do tailored messages make a difference? American Journal of Public Health, 1994. 84(1): p. 43–49. <u>https:// doi.org/10.2105/ajph.84.1.43 PMID: 8279610</u>
- Liang S.-Y., et al., Effects of Behavioral Economics–Based Messaging on Appointment Scheduling Through Patient Portals and Appointment Completion: Observational Study. JMIR Human Factors, 2022. 9(1): p. e34090. https://doi.org/10.2196/34090 PMID: 35353051
- Fukuma S., et al., Effect of nudge-based intervention on adherence to physician visit recommendations and early health outcomes among individuals identified with chronic kidney disease in screens. Journal of the American Society of Nephrology, 2022. 33(1): p. 175–185. <u>https://doi.org/10.1681/ASN.</u> 2021050664 PMID: 34903568
- Quinn E.L., et al., Peer reviewed: effects of a behavioral economics intervention on food choice and food consumption in middle-school and high-school cafeterias. Preventing chronic disease, 2018. 15.
- Andrawis A., et al., Applying Behavioural Insights to HIV Prevention and Management: a Scoping Review. Current HIV/AIDS Reports, 2022: p. 1–17.
- 86. Benartzi S., et al., Should governments invest more in nudging? Psychological science, 2017. 28(8): p. 1041–1055. https://doi.org/10.1177/0956797617702501 PMID: 28581899