Patient Education and Counseling 127 (2024) 108355

Contents lists available at ScienceDirect

Patient Education and Counseling

journal homepage: www.journals.elsevier.com/patient-education-and-counseling

Research Paper

Depression and vaccination behavior in patients with chronic physical illness – A cross-sectional survey

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ARTICLE INFO

Keywords:
Vaccines
Vaccine hesitancy
Depression
Primary care
Chronic physical illness
COVID-19
Influenza

ABSTRACT

Objective: Chronically ill are vulnerable to vaccine preventable infections. Consequently, their vaccination behavior is highly relevant. Depressive comorbidities are frequent in these patients. Furthermore, these patients are mainly diagnosed, treated and vaccinated in primary care. Therefore, we aimed to investigate the associations between depression and vaccination behavior (COVID-19 and influenza) in adult chronically ill primary care patients.

Methods: In a cross-sectional survey, we examined depression (PHQ9), psychological antecedents of vaccinations (Confidence and Constraints), health care utilization, and vaccination status. Based on an effect model, descriptive statistics and mixed linear/logistic models were calculated. (German Clinical Trials Register, DRKS00030042).

Results: n = 795 patients were analyzed. Both psychological antecedents of vaccinations (Confidence and Constraints) mediated a negative association between depression and vaccination behavior, healthcare utilization mediated a positive association. The total effect of depression was negligible.

Conclusions: As the effects of vaccination readiness and healthcare utilization are opposing, different total effects depending on the study population are possible. Further studies are needed to investigate additional predictors of vaccination behavior.

Practice implications: We suggest tackling vaccine acceptance in chronically ill through increasing confidence using communication-based interventions, for which primary care is the suitable setting. Constraints might be reduced by reminder and recall systems.

1. Introduction

People with chronic physical illnesses are at increased risk for many vaccine-preventable infections including COVID-19 or influenza [1–3]. Nevertheless, vaccination rates often remain suboptimal and imply the need to understand vaccination behavior in this vulnerable group.

Vaccines against COVID-19 and influenza are both meant to prevent respiratory infections with single-strand RNA viruses, which frequently mutate and require regular vaccine adaptation and booster vaccination [4]. Both vaccines are indicated for the same population of patients with chronic physical illness and elderly frail people. In Germany, three doses of COVID-19 vaccines are recommended for basic immunization for every adult, additional booster vaccinations against COVID-19 and a seasonal influenza vaccination is recommended especially for persons above **60 years** of age and chronically ill patients [1]. Co-administration of COVID-19 and influenza vaccines is promoted in many European countries [5] and the US Food and Drug Association (FDA) proposed to synchronize COVID-19 and seasonal influenza vaccination by administering both annually [3].

Patients with chronic physical illnesses are frequently affected by comorbid depression [6]. This might be relevant to vaccination behavior since depression may negatively affect attitudes towards vaccination [7] and may have a negative effect on the use of preventive health measures in general [8]. On the other hand, patients with depression make more use of health care services and have more contacts with general practitioners [6], which might give more opportunities for encouragement

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https://doi.org/10.1016/j.pec.2024.108355
Received 20 September 2023; Received in revised form 6 May 2024; Accepted 15 June 2024
Available online 17 June 2024

for vaccination.

The association between depression and vaccination readiness or behavior remains inconclusive, with some studies reporting a negative association [9–12], and others reporting a positive [13,14] or no association [15–17]. Responsible for these varying results may be the diversity of the studied vaccines, target populations, applied methods to measure depression/anxiety symptoms, as well as different cultural and political backgrounds. There are no studies, which examine the association of mental health and vaccination behavior in German chronically ill patients. However, these insights are of utmost importance to elaborate target-group specific interventions and improve clinical guidelines for chronically ill in primary care in a next step. Primary care is a suitable setting as general practices play a key role in treating [18] and vaccinating [19] chronically ill patients.

We examined the association between depression and vaccination readiness, and concluded that depression was significantly associated with two dimensions of vaccination readiness against COVID-19: Confidence ($p = 0.010$) and Constraints ($p = 0.041$) [7]. Consequently, both psychological antecedents **affected** the intention to get vaccinated in chronically ill suffering from symptoms of depression. However, as an intention-behavior gap had been observed in terms of other vaccinations or target groups [20,21], **we sought to evaluate both** levels of vaccine acceptance: the intention to get vaccinated (vaccination readiness) as well as the actual vaccination behavior.

The associations between psychological antecedents and vaccination readiness could not be shown against seasonal influenza. As data collection was performed during ongoing pandemic waves of COVID-19 with varying hygiene measures, these results may be subject to a COVID-19 specific risk of bias [22]. Therefore, the present analysis combines the number of COVID-19 vaccinations received with the receipt of one dose of a seasonal influenza vaccination.

The aim of this study is to evaluate the association of Confidence and Constraints, as well as symptoms of depression with actual vaccination behavior against COVID-19 and seasonal influenza in German primary care patients with at least one chronic physical illness.

2. Materials and methods

2.1. Patients and procedure

Eligible patients were identified by 13 general practices in Bavaria, Germany. General practices with different characteristics were chosen (five individual practices, six group practices, and two medical care centers, from urban and rural regions). Electronic practice management systems were used to identify patients, who were at least 18 years or older, had been patients at the general practice for at least six months, and suffered from one or more of the following chronic physical illnesses: bronchial asthma, chronic obstructive pulmonary disease (COPD), diabetes type 1 or 2, coronary artery disease (CAD) or breast cancer. In the first step, a total of $n = 3.152$ patients meeting those criteria were contacted personally via postal mailings signed by their general practitioner and invited to answer a paper-based questionnaire by mail between August and October 2022, stamped return envelopes were provided. As an incentive, patients were informed about a charitable donation (UNICEF Children`s Fund) of three Euros per complete answered patient questionnaire. Postal mailings were only sent once, without a reminder. Questionnaires that were returned until December 1, 2022, were included in the study. In the second step starting in late December 2022, further patient-related data was obtained from the respective general practitioner for those patients who participated. General practitioners were incented with ten Euros per patient they provided data on.

2.2. Ethics

All procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the ethics committee of the Ludwig-Maximilians-University in Munich under case number 21–1232. All **patients** provided informed written consent for their participation and the utilization of their pseudonymized data.

2.3. Measurements

For sociodemographic characteristics, the patients were asked for their age, sex, and education (with or without German university entrance qualification (Abitur)). General practitioners (GPs) provided information on which and how many chronic illnesses patients suffered from and on the number of consultations with the respective general practitioner in the past 12 months.

Both patients and GPs were asked about the patients' vaccination status. Vaccinations in Germany are not monitored centrally and might be administered at various occasions and locations (e.g., in inpatient as well as outpatient care, in vaccination centers, in pharmacies, or as part of routine occupational health check-ups and many more). Consequently, general practitioners' records are not always up to date. In addition, vaccinations **are only** been recorded in a paper-based vaccination book, **which can get misplaced or not kept up to date**. Patients might also forget vaccinations, which they had received. [23] **Both sources of information can therefore be potentially incomplete** [24]. Consequently, in cases where patient and general practitioner provided different information on vaccination status, the higher value was used for the analysis.

For influenza, we collected data whether the patient had received a flu shot in the season 2022/23. For COVID-19, we obtained data on the total number of received vaccination doses, regardless of which specific vaccine was used.

To measure vaccination readiness, patients were asked for their level of agreement with statements regarding the 5Cs using a Likert scale from 1 (strongly disagree) to 7 (strongly agree). High scores for Confidence and low scores for Constraints have been shown to be associated with better intention to vaccinate and vaccination behavior [25]. "*Confidence* is defined as trust in (i) the effectiveness and safety of vaccines; (ii) the system that delivers them, including the reliability and competence of the health services and health professionals and (iii) the motivations of policy-makers who decide on the needed vaccines". The corresponding item is: "I am completely confident that vaccines are safe" [25]. "*Constraints* are relevant when physical availability, affordability and willingness-to-pay, geographical accessibility, ability to understand (language and health literacy) and appeal of immunization services affect uptake". The corresponding item is: "Everyday stress prevents me from getting vaccinated" [25].

Symptoms of depression were measured using the PHQ-9 score. This German validated self-administered questionnaire consists of nine items, each scoring one of the DSM-IV criteria for major depression resulting in a sum score ranging from 0 to 27 [26]. The items evaluate symptoms within the last two weeks with a Likert scale from 0 (not at all) to 4 (nearly every day). Sensitivity is reported to be 0.80 (95 % CI [0.71, 0.87]) and specificity to be 0.92 (95 % CI [0.88, 0.95]) with a cut-off of 10 or higher for detecting major depression [27].

2.4. Data analysis

Descriptive statistics were calculated via means and standard deviations, respectively frequencies and percentages. We dichotomized the COVID-19 vaccination status into two categories (0 = 0–3 doses; 1 = 4 doses or more). At the time of data analysis, less than three doses of COVID-19 were considered to provide insufficient protection and were linked to restrictions (e.g., in terms of access to public events). At least four doses of COVID-19 were recommended for sufficient immune

protection in the study population [1].

Furthermore, a binary variable was calculated that combined the vaccination status of COVID-19 and influenza. It indicated whether a patient had received any vaccines in addition to the first three doses against COVID-19 (0 = vaccinated three times or less against COVID-19, no flu shot in season 2022/23, 1 = four or more vaccinations against COVID-19 AND/OR flu shot in 2022/23).

Fig. 1 summarizes these hypothesized associations in an effect model with the respective assumed directions of effects. For analysis, models for each path were calculated. Since data was clustered in 13 different general practices with potential effects on vaccination behavior, general mixed models were used to account for these effects. With linear outcome variables (e.g., Confidence, Constraints, Number of Consultations) linear mixed models were calculated. For paths with vaccination behavior as the outcome, mixed logistic models were calculated.

All models were controlled for the following same combination of variables (patient-related factors): age, sex, education, and number of diagnoses. Note: we also calculated the models with a three-level variable for vaccination behavior, which resulted in very similar results. Consequently, p-values were doubled due to Bonferroni correction. Ultimately, we used the above-described binary variable (2.3) since it allowed us to calculate total effects.

The results are expressed as unstandardized β-coefficients respectively logits, standard errors, degrees of freedom, t respectively z values, and p-values.

A statistical significance was based on a p-value of 0.05. All analyses were carried out in SPSS 28 and R Version 4.2.2.

3. Results

3.1. Descriptive characteristics

The response rate was n = 864 (26.4 %), of which n = 69 had to be excluded **due to missing data, resulting in a total sample size of n = 795**. The sociodemographic baseline characteristics of the **patients** are shown in Table 1. The mean age of the patients was 66.78 years (18–94 years). The broad range was affected by outliers, as the age group between 60–80 years old represented two thirds of the study population (60.6 %). **Men and women were equally represented**, with 52.5 % male and 47.4 % female patients. Most patients had lower education (without German Abitur, 58.7 %). The most prevalent chronic physical illness was diabetes type 1 or 2 (41.9 %), followed by bronchial asthma (28.4 %) and coronary artery disease (26.9 %). **More than one chronic physical disease was mentioned by 23.1 % of the evaluated patients.**

The mean of number of consultations with the respective general practitioners in the last 12 months was 9.44 (1–46 consultations; median 8, IQR: 8). Again, this broad range was affected by outliers. A consultation every five weeks per patient on average suggests a well integration of our study population into primary care.

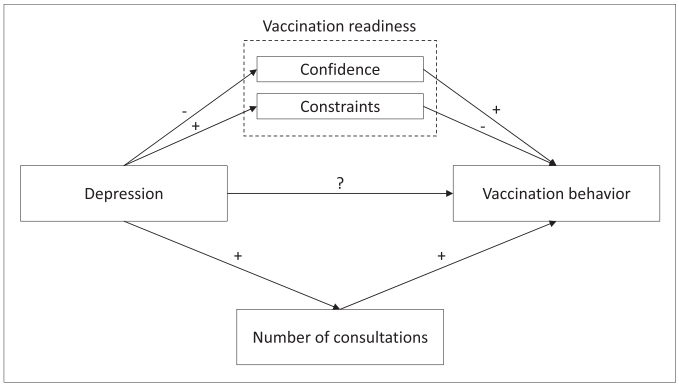

Fig. 1. Hypothesized associations between depression and vaccination behavior with the assumed direction of the association.> .

Table 1
Baseline characteristics of the **patients** (n = 795).

Variable	Categories	Values
Age, M (SD)	-	66.78 (14,02)
Biological sex, n (%)	Male	417 (52.5 %)
	Female	377 (47.4 %)
	Diverse	1 (0.1 %)
Education, n (%)	Lower level of education (without Abitur)	467 (58.7 %)
	Higher level of education (with Abitur)	274 (34.5 %)
	Missing data	54 (6.8 %)
Diagnoses, n (%)	Bronchial asthma	226 (28.4 %)
	COPD	102 (12.8 %)
	Diabetes type 1 or 2	333 (41.9 %)
	CAD	214 (26.9 %)
	Breast cancer	23 (2.9 %)
Number of diagnoses, n (%)	1	501 (63.0 %)
	2	159 (20.0 %)
	3	25 (3.1 %)
	4	1 (0.1 %)
	Missing data	109 (13.7 %)
Number of consultations, M (SD)	-	9.44 (6.89)
	Missing data, n (%)	214 (26.92 %)
COVID-19 vaccinations, n (%)	0	13 (1.6 %)
	1	3 (0.4 %)
	2	28 (3.5 %)
	3	345 (43.3 %)
	4	360 (45.3 %)
	5	46 (5.8 %)
Flu shot in 2022/23, n (%)	No	355 (44.7 %)
	Yes	440 (55.3 %)
Vaccination status (combined), n (%)	Not more than three COVID-19 vaccinations, no flu shot in 2022/23	243 (30.6 %)
	Four or more COVID-19 vaccinations AND/OR flu shot in 2022/23	552 (69.4 %)
PHQ-9 sum score, M (SD)	-	5.99 (4.57)
Level of depression severity (PHQ9), n (%)	No depression symptoms (0)	53 (6.7 %)
	Minimal depression symptoms (1–4)	289 (36.4 %)
	Mild depression symptoms (5–9)	287 (36.1 %)
	Moderate depression symptoms (10–14)	105 (13.2 %)
	Moderate to severe depression symptoms (15–19)	28 (3.5 %)
	Severe depression symptoms (20–27)	13 (1.6 %)
	Missing data, n (%)	20 (2,5 %)

The COVID-19 vaccination rate was relatively high with only 44 patients (5.5 %) being vaccinated two times or less. Only 13 patients (1.6 %) were not vaccinated at all. On the other hand, just slightly over half of the patients (55.3 %) had received a flu shot in season 2022/23. When looking at the combined vaccination status, 30.6 % had received three or fewer COVID-19 vaccines and no flu shot in season 2022/23 %, and 69.4 % had received four or more COVID-19 vaccines AND/OR a flu shot in 2022/23.

Regarding depression, the mean of the PHQ-9 sum score was 5.99

(SD 4.57). Minimal or mild symptoms of depression were measured in 576 patients (72.5 %). Clinically relevant symptoms of a major depression (PHQ-9 ≥10) occurred in 146 patients (18.3 %).

When considering Confidence and Constraints as psychological antecedents of vaccination (scale: 1 – 7), we measured high values for Confidence in the context of COVID-19 (M = 5.67, SD = 1.38) and in the context of influenza (M = 5.65, SD = 1.41). The overall mean of both Confidence values combined is 5.66 (SD = 1.23). Values for Constraints were low concerning COVID-19 (M = 1.37, SD = 1.00) as well as concerning influenza (M = 1.62, SD = 1.15). The overall mean of both values for Constraints is 1.50 (SD = 0.91).

3.2. Mixed Models

Complete data for every model is provided in the Appendix (supplementary tables A1 – A8). The main results are displayed in Fig. 2. First, all associations show the predicted direction. Depression is negatively associated with Confidence (β = −0.046, p = <0.001, 95 % CI [−0.066, −0.026], n = 692) and positively associated with Constraints (β = 0.019, p = 0.006, 95 % CI [0.004, 0.034], n = 689). Depression also is associated with more contacts with general practitioners (β = 0.241, p = < 0.001, 95 % CI [0.137, 0.346], n = 520). No direct association between depression and vaccination behavior was detected (β = 0.007, p = > 0.999, 95 % CI [−0.052, 0.067], n = 514). As expected, higher Confidence (β = 0.863, p = < 0.001, 95 % CI [0.678, 1.061], 692) and lower Constraints (β = −0.599, p = < 0.001, 95 % CI [−0.818, −0.388], n = 689) associated with better vaccination behavior. A higher number of consultations also showed a positive yet not significant association with vaccination behavior (β = 0.044, p = 0.055, 95 % CI [0.002, 0.091], n = 520).

The combined effect of depression mediated via Confidence on vaccination behavior is negative (logit = −0.006, p = < 0.001, 95 % CI [−0.009, 0.000], n = 692) as well as the combined effect mediated via Constraints (logit = −0.002, p = 0.005, 95 % CI [−0.002, −0.004], n = 689). The combined effect of depression mediated via the number of consultations is positive and significant (logit = 0.002, p = 0.026, 95 % CI [−0.000, 0.000], n = 520).

The total effect of depression on vaccination behavior is negative and not significant (logit = −0.033, p = 0.225, 95 % CI [−0.074, 0.008], n = 695).

It should be mentioned that the individual paths are not directly comparable in their effect size or multipliable since the model is a combination of linear and logistic models with unstandardized β-coefficients or logits as effect estimates.

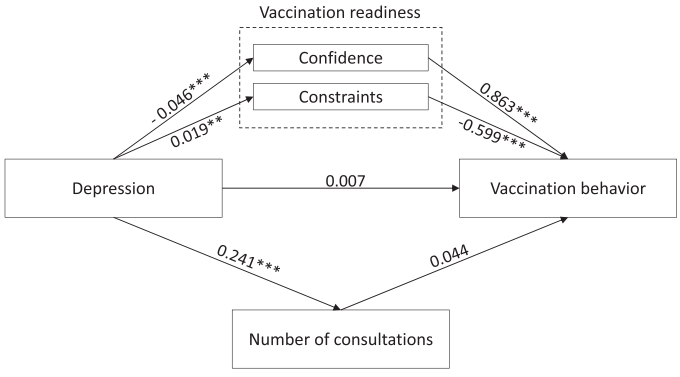

Fig. 2. Effect model with unstandardized effect sizes, n = 514 - 695, *: p < 0.05, **: p < 0.01, ***: p < 0.001 > .

4. Discussion and conclusion

4.1. Discussion

4.1.1. Summary of findings

This study investigated the associations between depression and vaccination behavior against influenza and COVID-19 in primary care patients in Germany with chronic physical illness. Our results show that (1) depression is negatively associated with vaccination behavior mediated via decreased vaccination readiness, (2) depression is positively associated with vaccination behavior via an increased number of consultations with general practitioners, (3) depression wasn't significantly associated with vaccination behavior, and (4) the effect of depression on vaccination behavior is negligible and not significant.

4.1.2. Comparison to literature

4.1.2.1. Mediating role of confidence and constraints between depression and vaccination behavior. A previous analysis has identified significant associations between symptoms of depression and vaccination readiness (intention to get vaccinated) [7]. The current analysis revealed a so called "intention-behavior gap", as these associations were not significant for the actual vaccination behavior in the same study population [28]. An inverse relation between mental disorders and both general and individual trust is well documented in the literature [29] as well as the positive association between depression and both lower self-control [30] and self-efficacy [31] which lead to higher perceived constraints [32]. The associations between Confidence respectively Constraints and actual vaccination behavior were estimated in accordance with the literature as more Confidence and fewer Constraints are related to positive vaccination behavior [25].

4.1.2.2. Mediating role of number of consultations between depression and vaccination behavior. **The evaluated patients** who suffer from depression had significantly more contacts with their general practitioner which is consistent with literature [6]. Comparable to a Spanish sample of n = 1038 hospitalized elderly people where three or more general practitioner visits were associated with receiving the influenza vaccine, our analyzed sample showed an increased rate of influenza vaccinations in patients with regular contacts to their general practitioners [33]. Lawrence et al. (2020) also concluded that an high healthcare utilization is associated with receiving the influenza vaccine in an US sample of 4102 elderly primary care patients [14]. However, the effect size between the number of consultations and vaccination behavior is relatively weak and not significant in our analyzed **patients**. We propose as a possible explanation that consultations with a recorded diagnosis of psychological problems tend to take more time during consultation hours [34] when time pressure is already a challenging in primary care [35]. Dedicating even more time to these patients for non-acute procedures like vaccinations might sometimes just not be possible or practicable.

4.1.2.3. Effect of depression on vaccination behavior. Besides the associations mediated by vaccination readiness and the number of consultations, depression did not directly affect vaccination behavior significantly. This might indicate that the association depression has on vaccination behavior is mainly mediated via both factors.

The total effect of depression on vaccination behavior describes the sum of all single effects. Due to inverse effects of depression and healthcare utilization on vaccination readiness, the total effect of depression on vaccination behavior is assumed to be negligible.

Lawrence et al. (2020) studied a sample of n = 4102 older US primary care patients and identified a positive association between mental health diagnoses (mainly depression and anxiety) and influenza vaccinations in patients with physical comorbidities [14]. On the other hand,

Sekizawa et al. (2020) and Eyllon et al. (2022) both showed negative associations between vaccination willingness and vaccination behavior in terms of COVID-19 in a Japanese general public sample (n = 11,846) respectively a US general public primary care sample (n = 14,365) [11, 12]. Further studies are needed to fully understand the relationships between patient-related influences and health care service-related factors and vaccination behavior.

4.2. Conclusion

This study investigated the effects between depression and vaccination behavior in German primary care patients with chronic physical illness. The effects between depression and vaccination behavior are mainly mediated through vaccination readiness and healthcare utilization. These effects are opposing, probably leading to different total effects depending on the studied population. Further studies are needed to investigate additional predicators of vaccination behavior.

4.3. Practice implications

Interventions tackling the acceptance of vaccinations should primarily focus on Confidence as its mediating effect seems to be strong [36]. In this context, communication-based short interventions might be appropriate. Improving physicians' communication skills has already been shown to enhance patients' adherence by among other things building rapport and trust [37]. Evidence-based information for patients increases their knowledge about vaccination, leads to an improved risk assessment and results in an actual increase in vaccination rates. This does not apply to patient information that is not evidence-based. In order to overcome the observed intention-behavior gap, it is therefore necessary to inform patients completely, transparently and correctly about risks and benefits of vaccination. [20].

Specifically, shared decision-making approaches have proven useful to convey educational information about vaccines, how they work, and the diseases they prevent since the incorporated bidirectional doctor-patient communication can address patients' concerns about vaccines and hence increase trust in the safety and effectiveness of vaccines [38, 39]. Primary care is a very suitable setting for increasing Confidence as general practitioners often have long-term relationships with their patients, which is in turn associated with higher trust [40]. In addition, they have very frequent contact with patients with physical illness, especially when psychological comorbidities are present. This highlights primary care's key role in health communication and vaccination. High Constraints may be met with reminder and recall systems vaccinations [32] which has already been proven to increase vaccine receipt in patients with chronic physical illness [41].

4.4. Strengths and Limitations

This study presents important results concerning a potential intention-behavior gap in terms of vaccine acceptance among a very hard-to-reach and therefore rarely studied target group. Considering the method of patient recruitment (postal invitation), as well as the target group (chronically ill patients with and without psychological comorbidities), the response rate achieved is above average [42,43]. Furthermore, the setting of primary care in Germany is not an established research environment, as there is a lack of infrastructure and experience among the general practice teams and their patients [44,45]. However, it has to be acknowledged, that our results may not reflect the larger population due to a low response rate.

Selection bias has to be considered since vaccines were the apparent topic of the study, and thus more patients with generally positive attitudes toward vaccination might have participated. Response bias might be relevant for self-reported data, particularly referring to symptoms of depression and vaccination readiness. Moreover, participating patients were likely to be well integrated into primary care and take care of their health due to their chronic physical illness. However, symptoms of depression and associated lack of self-management might have prevented some patients from engaging in the study comprising the representativeness of the study sample. Regarding the data, past COVID-19 infections could influence the number of received vaccinations and were not surveyed in the study. Additional comorbidities were not considered.

It also has to be stated that the missing values concerning healthcare utilization (n = 214) are mainly related to one individual practice (190 of the 214 missing values) which might have caused distortion to our results. Missing data in this practice (medical care center) can be explained due to the fact, that patient information was not provided by the treating general practitioner in this facility, but by the central coordination office. Data about the use of the health system were not available. Other items are not systematically affected by this circumstance. To examine the proportion of variance that is attributable to respective general practices, an intra-cluster correlation would be necessary.

Funding

This work was supported by the Friedrich-Baur-Stiftung, Germany (grant number/ ID: 18/12).

CRediT authorship contribution statement

Jochen Gensichen: Writing – review & editing, Supervision. **Marco Roos:** Writing – review & editing, Supervision. **Tobias Dreischulte:** Writing – review & editing, Supervision. **Nadine Heithorst:** Writing – review & editing, Supervision, Conceptualization. **Philipp Sckopke:** Writing – review & editing, Software, Methodology, Formal analysis, Conceptualization. **Linda Sanftenberg:** Writing – review & editing, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Simon Keppeler:** Writing – original draft, Visualization, Investigation, Formal analysis, Data curation.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

The authors would like to thank all patients taking part in this research. We especially would like to thank the general practitioners and their teams for providing this study's sample.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.pec.2024.108355.

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