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Review



Associations between common mental disorders and vaccination readiness against seasonal influenza and Covid-19 of chronically ill adult patients in primary care – a systematic review

Linda Sanftenberg ^{a,*}, Laura Kraeker ^a, Fabian Walter ^b, Ioanna Tsiligianni ^{c,d}, Izolde Bouloukaki ^c, Marco Roos ^b, Jochen Gensichen ^{a,e}

- ^a Institute of General Practice and Family Medicine, LMU University Hospital, LMU, Munich, Germany
- ^b General Practice, Faculty of Medicine, University of Augsburg, Augsburg, Germany
- ^c Clinic of Social and Family Medicine, Department of Social Medicine, Faculty of Medicine, University of Crete, Greece
- ^d Department of Primary Care and Population Health, Medical School, University of Nicosia, Cyprus
- ^e German Center of Mental Health, Augsburg, Munich, Germany

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ABSTRACT

Background: Chronically ill are advised to receive annual vaccinations against Covid-19 and seasonal influenza. Furthermore, chronically ill show an increased prevalence of comorbid common mental disorders (CMDs), like depression, anxiety, and somatoform disorders. With vaccination rates remaining insufficient among these vulnerable patients, prior research assumes an association between CMDs and vaccination readiness. As diagnoses, treatment and vaccination of those patients are performed mainly in general practice, the aim of this review is to describe associations between CMDs and vaccination readiness against seasonal Influenza and Covid-19 in chronically ill adult patients in primary care.

Methods: A systematic literature search was conducted in Medline, Embase, PsycINFO, the Cochrane Library and ERIC. Randomized controlled trials (RCTs), clustered RCTs and observational studies were considered. Two authors screened the studies and assessed the risk of bias independently (Cochrane Risk of Bias 2-Tool). We followed the PRISMA guideline. The study protocol was published in PROSPERO (CRD42024621413). The results were synthesized narratively.

Results: Of 9820 identified studies, seven observational studies met the inclusion criteria. Regarding Covid-19, three studies could show, that CMDs might lead to decreased vaccination readiness in adults. Regarding seasonal influenza, no significant association between vaccination readiness and CMDs occurred. In terms of vaccination rates, no significant association between vaccinations against Covid-19 and CMDs could be identified. Two studies identified a significant association between decreasing vaccination rates against seasonal influenza and CMDs.

Conclusion: CMDs tend to be associated with decreased vaccination readiness, however vaccination rates were not automatically affected as well. This could indicate a potential intention-behavior gap.

1. Introduction

Chronic diseases represent a major global health burden, accounting for approximately 74 % of all non-pandemic-related deaths, equivalent to 43 million lives lost in 2021 [1,2]. Individuals with pre-existing

cardiovascular, metabolic, or pulmonary conditions face heightened risks of complications and mortality from infections such as Covid-19 and seasonal influenza [3–5]. Consequently, seasonal vaccinations against Covid-19 and seasonal influenza e.g., in form of coadministrations are strongly recommended for these patients by

Abbreviation: CAD, coronary artery disease; CI, Confidence Interval; CMD, common mental disorder; COPD, chronic obstructive pulmonary disease; CRD, Centre for Reviews and Dissemination; OR, odds ratio; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; PROSPERO, International prospective register of systematic reviews; RCTs, Randomized controlled trials; TPB, Theory of Planned Behavior; WHO, World Health Organization.

E-mail address: linda.sanftenberg@med.uni-muenchen.de (L. Sanftenberg).

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^{*} Corresponding author.

different national as well as international health authorities [6,7]. Despite these clear guidelines, vaccination rates remain insufficient, even in countries with established and accessible healthcare systems [8,9].

The low uptake rates raise concerns about vaccination readiness and highlight the urgent need to identify factors to increase behavior change in terms of vaccinations. The Theory of Planned Behavior (TPB) describes the willingness for behavior change by considering intention or readiness for action as core elements for actual behavior. According to this model, individuals are more likely to change their behavior if they believe in its positive consequences (attitudes), perceive social and familial pressure to engage in it (subject norms), and feel that they have control over its execution (perceived control). [10] With regard to the perception of vaccinations, vaccination readiness is the behavior theoretical prerequisite [11]. Vaccination readiness refers to the psychological and contextual factors that influence an individual's willingness to get vaccinated, while vaccine hesitancy involves the delay or refusal of vaccines despite their availability [12,13]. Individuals with chronic physical illnesses are significantly more likely to develop mental comorbidities such as depression or anxiety, with prevalence rates ranging from 26.8 % to 45.8 %, depending on the country [14]. In primary care settings, CMDs are particularly prevalent, with estimated prevalence rates between 16.5 and 38.0 % for depressive disorders, 13.5-21.7 % for anxiety disorders, and 11.3-25.0 % for somatoform disorders [15,16]. As many chronically ill show symptoms of CMDs, it can be assumed that CMDs might influence their vaccination readiness. Diagnosis and treatment of chronic illness, CMDs and delivery of vaccinations is provided mainly in primary care [17-19]. Existing research on the relationship between CMDs and vaccination readiness independent from any physical chronical illness show very diverse results. Some studies indicated, that CMDs were associated with decreased vaccination readiness, while others indicated an increase in vaccination readiness associated with CMDs [20-23]. In our survey among chronically ill primary care patients, we revealed that psychological antecedents of vaccination readiness against Covid-19 and seasonal influenza are comparable, with no significant differences. [24] Consequently, a systematic review of published observational studies for both vaccinations might improve the evidence for clinical implications, since counselling on both vaccinations will be offered synchronously in many cases.

Therefore, the aim of this review was to explore the association between CMDs and vaccination readiness among primary care patients with at least one chronic physical illness, thereby addressing a crucial intersection of physical and mental health in a vulnerable, high-risk population.

2. Material and methods

The review was conducted according to PRISMA Guidelines for systematic reviews [25] and the study protocol including the search strategy was published beforehand at PROSPERO (CRD 42024621413).

2.1. Literature search

A systematic literature search was conducted in five databases (Medline, Embase, Cochrane Library, PsycInfo and ERIC) in December 2024. We focused on adult patients and include all studies with involvement of any primary care provider (e.g., general practitioner) in a managing or treating role. We considered studies on vaccination readiness against Covid-19 and seasonal influenza, different types of chronical illness, as well as observational studies. CMDs could have been retrieved from medical records, self-reported or assessed via validated questionnaires. The setting was not included in our search strategy, but rather considered when screening, to keep the search as sensitive as possible (full search strategy provided in supplemental file 1). No filters or time limits were set. Criteria for inclusion or exclusion of the studies are provided (supplemental file 2). Additionally, we searched references

of other reviews and followed up on retrieved study protocols. Literature was managed and duplicates were removed via EndNote 20.2.1.

2.2. Literature screening

Titles and abstracts were screened independently by two investigators (LK, FW). Both investigators screened independently all included full text articles for eligibility and evaluated the reference lists for other possibly eligible studies. Any discrepancies were discussed with a third researcher (LS) and a consensus was reached.

2.3. Data extraction

Data was extracted by one reviewer (LK) using a standardized data extraction sheet created for this review. A second reviewer (LS) critically checked the first data extraction process. Any disagreement was resolved between both reviewers. Both reviewers were not blinded to any information concerning the paper. Data extraction considered the following data: basic descriptive study information (e.g., date of publication, aim of the study), methods (e.g., recruitment, screening tool), participants (e. g., sample size, age, co-morbidities), results (e.g., vaccination readiness, vaccination rates), and study design. Risk of Bias was assessed via the ROBINS-E-Tool [26]. All relevant information was extracted using the extraction sheets created for this review. The different studies were rated into three categories: low bias, high bias or unclear bias. Any unclear decision was reported and resolved in discussion.

2.4. Data analysis

We reported our results in form of a narrative synthesis. As the included studies differed strongly from each other in terms of different data sources and applied survey instruments, we decided against a meta-analysis. If psychometric properties of study participants have not been published in the included study, we asked the respective corresponding author for providing primary data and calculated the associations of categorized psychometric data with vaccination readiness using a chi-square test.

Studies reporting multivariable linear regression analyses could be presented with standardized beta coefficients, 95 % confidence intervals, and p-value.

3. Results

After systematic literature search, n=9.820 studies have been identified. After removal of duplicates and screening of titles and abstracts, n=182 full texts have been assessed for eligibility. Finally, seven studies could have been included for data extraction.

The process of literature search is displayed in the figure below (Fig. 1).

All included studies have been published within the last five years, were cross-sectional observational studies and included patients suffering from depression and/or anxiety. There was no publication regarding somatoform disorders. Three studies have been conducted in the USA, two studies in Germany, one study in Greece and one study in Romania. Three studies identified an association of CMDs with a decreased vaccination readiness against Covid-19, two studies identified an association of CMDs with a decreased vaccination readiness against seasonal influenza. Associations between CMDs and vaccination rates have been published exclusively for seasonal influenza. One study revealed an association between CMDs and an increase in vaccination rates, another study revealed a decrease in vaccination rates, whereas a third study could not detect any association between CMDs and vaccination rates. Table 1 shows a brief summary of the key characteristics to each study included.

<Table 1: Characteristics of included studies>.

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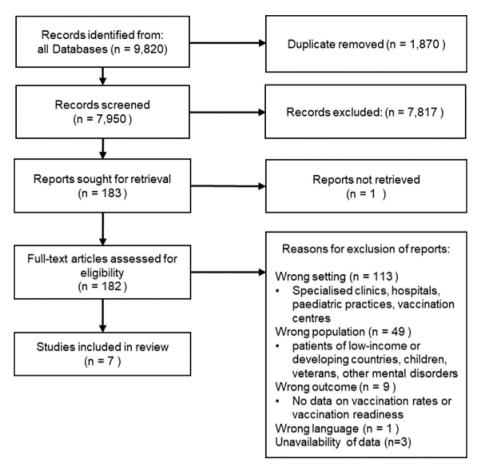


Fig. 1. PRISMA Flowchart of the identification process of the included studies.

3.1. Study population

Both publications by Sanftenberg et al. (2023) and Keppler et al. (2024) referred to the same study population, however different research questions and ways of data analysis have been applied. The study population showed a mean age of 67 years (range: 18–94 years), almost half of them identified themselves as female (47.4%). Most of the study participants had no academic qualification (58.6%) and lived in shared households (73.5%). As inclusion criteria was a medical diagnosis of chronical illness, 28.4% of the study participants were diagnosed with bronchial asthma, 12.8% with chronic obstructive pulmonary disease (COPD), and 41.9% with diabetes mellitus type 1 or type 2. Additionally, 26.9% of these study participants had coronary artery disease (CAD), while 2.9% were diagnosed with breast cancer.

Bazargan et al. (2020) focused on a population of older African-American adults (mean age: 74 years; range: 65–96) residing in South Los Angeles, USA. The sample was predominantly female (65 %) and 37 % of those patients were diagnosed with diabetes mellitus type 2, 30 % with heart related conditions, 27 % with COPD, while 15 % had already experienced a stroke. Additionally, 30 % of these study participants have been identified as disabled.

The study by Eyllon et al. (2022), reported on a predominantly white (89.7 %), female (62.5 %) and middle-aged sample (44, 2 % of participants were 40–64 years old). The majority of these study participants (69.8 %) reported an academic degree, and income levels were described as moderate to high (57.3 % reported an income of at least 75.000\$ per year). The most common conditions included hypertension (30.3 %), overweight/obesity (27.8 %), and respiratory disease (16.5 %). Cardiovascular disease affected 14.0 % of individuals, while diabetes (Type I or II) was present in 10.3 %. Other conditions included malignant cancer (7.6 %), chronic kidney disease (5.8 %), chronic liver

disease (4.9 %), and immunodeficiency (4.1 %).

In the study by Bouloukaki et al. (2024), participants with asthma (38 %) or COPD (62 %) were recruited, most of whom were older adults (58 % aged \geq 65 years). The sample was slightly male-dominant (54 %), and 36 % had completed only primary education. Additional comorbidities included hypertension (59 %), cardiovascular disease (28 %), type 2 diabetes (24 %), gastroesophageal reflux disease (20 %), inflammatory arthritis (10 %), and cancer (7 %).

In the study by Ionescu et al. (2021) women (65.7 %) were slightly stronger represented, with the majority aged 35–64 years. Most lived with a partner (70.7 %), and 75.7 % were in stable relationships. The majority had completed secondary education (54 %). Around 53.4 % presented with prior physical conditions such as cardiovascular diseases (34.1 %), rheumatic or musculoskeletal conditions (12.5 %) or metabolic disorders (11.8 %).

Lawrence et al. (2020) examined a cohort of older adults (mean age: 70.8 ± 4.4 years), 59.1% of whom were female and 56.7% white. Over half of participants were unmarried (54.8 %). An adapted Charlson-Romano Comorbidity Index was used used a an adapted Charlson-Romano Comorbidity Index to assess chronic physical conditions of the patient including diagnoses like diabetes, cancer, cardiovascular diseases, dementia, chronic pulmonary disease, liver disease, hemi or paraplegia, renal disease, cancer and HIV or AIDS.

3.2. Common mental disorders (CMDs)

The included studies have used different data sources as well as different assessment tools. In addition to validated questionnaires, medical records or self-reported diagnoses have been considered as data sources. Sanftenberg et al. (2023) and Keppler et al. (2024) used the validated Patient Health Questionnaire-9 (PHQ-9) to assess symptoms of

Table 1
Characteristics of included studies.

Vaccination readiness	Author year country	Study design	Setting	Sample size	Participants	Common mental disorders	Data source	Type of Vaccine	Association of CMDs
	Sanftenberg et al. (2023) Germany [24]	cross- sectional study	General practices (n = 13)	n = 795	Aged ≥18 years at least one chronic physical illness: bronchial asthma, Chronic obstructive pulmonary disease (COPD), diabetes mellitus type 1 or 2, coronary artery disease (CAD), or breast cancer	Depression (PHQ-9) Anxiety (OASIS)	Original study data	Covid- 19/ Influenza	Decreased vaccination readiness
					visited their general practice within the last six months				
	Bouloukaki et al. (2024) Greece [27]	cross- sectional study	Primary Health Care Centre (n = 6)	n = 264	Aged ≥18 years and Diagnosis of asthma or COPD	Self-reported diagnosis: Depression (n = 34) Anxiety disorder (n = 16)	Additional analysis of raw data	Covid-19	Decreased vaccination readiness
						Anxiety (GAD-7- Score)			
	Eyllon et al. (2021) USA [28]	cross- sectional study	Multi-specialty group medical practice with focus on Primary Care (n = 1)	n = 14,365	Aged ≥18 years	Medical records according to ICD-10: Generalized Anxiety Disorder (n = 785) Major Depressive Disorder (n = 1656) Other anxiety disorders (n = 2519)	Original study data	Influenza	Decreased vaccination readiness
	Ionescu et al. (2021) Romania [29]	cross- sectional study	General practitioner $(n=1)$	n = 440	Aged ≥18 years	Self-reported diagnosis: Depression (n = 21) Anxiety(n = 3) + Anxiety (SAS-	Additional analysis of raw data	Covid-19	Decreased vaccination readiness
						Score)			
	Bazargan et al. (2020) USA [30]	cross- sectional study	University Department of Family medicine $(n=1)$	n = 620	Aged ≥65 years resided in Service Planning Area 6 in South Los Angeles, identified as African American or Black, diagnosed and/or managing a cardiometabolic disease, and possess the ability to complete a full interview in English. Aged ≥18 years	Depression (GDS) (no numbers available)	Original study data	Influenza	Decreased vaccination rates
Vaccination rates	Keppeler et al. (2024) Germany [31]	cross- sectional study	General Practices (n = 13)	n = 795	at least one chronic physical illness: bronchial asthma, COPD, diabetes type 1 or 2, CAD, or breast cancer visited their general practice	Depression (PHQ-9) Minimal to severe $(n = 722)$	Original study data	Influenza	No significant association
	Lawrence et al. (2020) USA [32]	cross- sectional study	Primary Care Patient Data registry Information either from Family Medicine or Primary Care clinic visits	n = 4102	within the last six months Aged 65–80 years	Medical records: two diagnoses according to ICD-9-CM in a one-year period Depression: $n = 204$ Anxiety: $n = 114$ Either: $n = 274$	Original study data	Influenza	Increased vaccination rates

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depression and the validated Overall Anxiety Severity and Impairment Scale (OASIS) score for symptoms of anxiety. In the publication of Bouloukaki et al. (2024) the participants self-reported prior medical diagnosis of depression and anxiety disorder; additionally, the validated Generalized Anxiety Disorder Scale -7 (GAD-7) was answered. Bazargan et al. (2020) utilized the validated Geriatric-Depression-Scale (GDS) to quantify the patients' symptoms of depression. Eyllon et al. (2022) identified both psychiatric and physical from patients' medical records and categorized them according to the ICD-10 classification system and included among other diagnoses major depression disorders, generalized anxiety disorders and other anxiety disorders. Ionescu et al. (2021) determined the patients' mental health using the Zung Self-Rating Anxiety Scale (SAS) and self-reported mental diagnosis from the patients. Lawrence et al. (2020) assessed mental comorbidities of the patients through their medical records. At least two ICD-9-CM codes needed to be present in the span of one year indicating depression or anxiety.

3.3. Vaccination readiness and vaccination behavior

In terms of vaccination readiness and vaccination behavior, different data sources and assessment instruments had been applied as well. In addition to already validated instruments, medical records and selfreported outcomes, specifically developed questionnaires for the respective study had been used. Vaccination readiness had been assessed with the German version of the validated 5C model in the analysis of Sanftenberg et al. (2023). Bouloukaki et al. (2024) implemented a selfdeveloped 20-item questionnaire in which patients could agree or disagree with statements in favor or against the intention to get vaccinated. Eyllon et al. (2022) utilized a 5-level Likert-Scale to assess participants' intent to receive a Covid-19 vaccine. Vaccination behavior was measured by asking participants whether they had ever received an influenza vaccine in Bazargan et al. (2020). Lawrence et al. (2020) used the medical records to determine whether a patient has received an influenza vaccination in the timespan between July 2014 and June 2016. Keppler et al. (2024) asked for the self-reported influenza vaccination uptake during the 2023/24 season and the total number of Covid-19 vaccinations already received since implementation in the German primary health care system. In the study of Ionescu et al. (2021) patients were asked if they were vaccinated against Covid-19 and if not, they were asked whether they wanted to get vaccinated.

3.4. Associations between CMDs and vaccination readiness

The identified relation between CMDs and vaccination readiness varies across the identified studies with differing conclusions on its impact. Sanftenberg et al. (2023) observed that depression was associated with decreased confidence in Covid-19 vaccine safety and efficacy, as well as the confidence ($\beta=-0.04,~95~\%$ CI $[-0.07,~-0.01],~p\leq0.010$) in the healthcare system. Furthermore, symptoms of depression increased the subjective perception of constraints (PHQ9, $\beta=0.02,~95~\%$ CI [0.001;~0.04],~p=0.041) in adult chronically ill patients. Symptoms of a generalized anxiety disorder seemed not to be associated with vaccination readiness. The publication by Bouloukaki et al. (2024) on vaccination readiness identified an association between a self-reported diagnosis of depression and decreased vaccination readiness against Covid-19(OR: 3.196 (95 % CI: [1.223–8.352] p=0.018).

After comparing the provided primary data of the survey performed by Bouloukaki et al. (2024) on self-reported symptoms of a generalized anxiety disorder (Generalized Anxiety Disorder 7-item scale; GAD-7) with vaccination readiness, we could identify a significant association between higher levels (GAD-7 Score \geq 10) of self-reported symptoms of a generalized anxiety disorder with a decreased vaccination readiness against Covid-19 (p=0.502; n=202).

The comparison of the provided primary data of the survey performed by Ionescu et al. (2021) on self-reported symptoms of a

generalized anxiety disorder (Self-rating Anxiety Scale;SAS) with vaccination readiness, revealed an association between mild to moderate levels of anxiety (SAS score \geq 60) and a decreased vaccination readiness. (p = 0,087; n = 440).

Regarding vaccination readiness against seasonal influenza, Eyllon et al. (2022) reported a significant decrease in vaccination readiness in persons with a diagnosed generalized anxiety disorders (OR:1.45 95 % CI: [1.20–1.7] $p \le 0.001$), other anxiety disorders (OR: 1.41 95 % CI: [1.24–1.59] $p \le 0.001$), as well as a major depressive disorder (OR: 1.44 (95 % CI: [1.25–1.6] p < 0.001).

3.5. Associations between CMDs and vaccination rates

Keppeler et al. (2024) reported that symptoms of depression in chronically ill were not significantly associated with vaccination rates against Covid-19 and seasonal influenza behavior($\beta=0.007, p\geq0.999, 95\%$ CI [-0.052, 0.067], n=514). Lawrence et al. (2020) showed a that a diagnosis of depression or anxiety among patients with any physical comorbidities were associated with increased vaccination rates against seasonal influenza (aOR = 1.77; 95 % CI [1.22-2.57]). On the contrary, Bazargan et al. (2020) found that individuals with more depressive symptoms were less likely to be vaccinated against seasonal influenza (OR: 0.92 95 % CI: [0.84-0.99] p=0.002).

3.6. Risk of Bias assessment

Since all included studies were observational studies, six of the seven included studies might entail a medium to high risk of bias.

Most studies showed a selection bias, as the number of study centres for the recruitment of potential study participants were limited, resulting in relatively small numbers of study participants (Risk of bias domain D3). As there were no interventional studies included, bias arising from measurement of the exposure or bias due to post-exposure interventions had not to be considered (Risk of bias domains D2 and D4).

Three studies demonstrated an overall low to moderate risk of bias, particularly those by Lawrence et al. (2020), Sanftenberg et al. (2024) and Keppeler et al. (2023), which used validated measurement instruments and mostly objective vaccination status data (e.g., from electronic medical health records). They utilized proper adjustment for relevant confounders (e.g., socioeconomic factors, comorbidities, healthcare utilization) and the use of validated psychiatric diagnoses or scoring systems.

The studies by Bouloukaki et al. (2024), Bazargan et al. (2020) and Eyllon et al. (2021) showed a moderate to severe risk of bias, primarily due to selection bias resulting from low response rates or non-representative samples. The exclusively self-reported vaccination and diagnostic data was also identified as a possibly biased limitation. The study by Ionescu et al. (2021) showed the highest risk of bias, owing mostly to the lack of adjustment (see Fig. 2).

4. Discussion

This review aimed to identify associations between CMDs and vaccination readiness against seasonal influenza and Covid-19 of chronically ill adult patients in primary care. Regarding Covid-19, a significant association between depressive symptoms and decreased vaccination readiness could be identified. In terms of anxiety, the findings were not congruent and seem to depend on the severity of the symptoms. In the context of seasonal influenza, an association between symptoms of CMDs and decreased vaccination readiness could be identified. None of the identified publications addressed the impact of somatoform disorders on vaccination readiness.

The studies showed high diversity in terms of applied instruments, data sources and outcomes, leading to reduced comparability and difficulties to draw consistent conclusions. In many cases, either only vaccination readiness or vaccination rates have been reported, limiting

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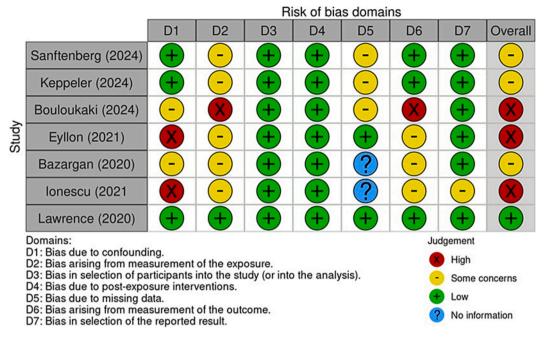


Fig. 2. risk of bias assessment.

the understanding of relation between vaccination readiness and vaccination behavior. However, it has to be assumed that there is a gap between vaccination readiness and actual vaccination rates [24,27].

This leads to the question if there might be another influencing factor in between the vaccination readiness of the individual and the lastly taken action of vaccination behavior. In Keppeler et al. (2024) e.g., it is mentioned that factors such as patient activation and the doctor-patient relationship also played a role in the individual's decision on taking the vaccination. In the publication of Lawrence et al. (2020) it is described that the high visit utilization of health care in individuals suffering from chronic physical conditions and mental illnesses, might foster an increased number of opportunities for vaccinations. [28]. Various models attempt to explain the discrepancy between the intention to get vaccinated and the followed through action. The intention-behavior gap describes the failure to translate intentions into action. According to this theory, it can be assumed that vaccination rates are usually lower than the assessed vaccination readiness indicates [29].

The studies of Keppeler et al. (2024) and Chu et al. (2024) considered different factors of the TPB in the context of vaccination behavior and concluded that a doctor's influence was one of the most impactful subjective norms affecting the individual patient behavior [11]. This influence included personal recommendations, encouragement, and the information provided during medical consultations. This suggests that primary care physicians can play a crucial role in improving vaccination uptake even if vaccination readiness among patients with CMDs is affected. By fostering a relationship of trust, making strong recommendations, and providing thorough information, they can positively influence their patients' vaccination behavior [17,30]. It has already been shown, that conversation-based interventions referring to the principles of shared decision-making, are effective to increase vaccination rates among adults in primary care [31–33].

4.1. Strengths and limitations

To our knowledge, this is the first systematic review to explore the associations between CMDs and vaccination readiness among chronically ill adults in primary care. The focus on this specific setting is highly appropriate, as primary care simultaneously addresses vaccination, CMDs, as well as chronic physical conditions. Although a comprehensive

literature search was conducted, only a small number of relevant studies could be identified. The included studies showed considerable variation in methodology, outcome measures, and the assessment and diagnosis of CMDs, resulting in high heterogeneity and limited comparability of findings. The variability in study quality further raises concerns regarding the validity of some results.

4.2. Implications for practice

Special attention should be given to patients with CMDs, emphasizing trust-building and individualized communication based on the principles of shared decision making to enhance adherence to vaccination recommendations.

5. Conclusions

CMDs tend to show an association with decreased vaccination readiness, however vaccination rates are not automatically affected as well. According to the TPB model, this variance can be explained by a variety of intra- and interpersonal factors.

CRediT authorship contribution statement

Linda Sanftenberg: Writing – original draft, Supervision, Investigation, Conceptualization. Laura Kraeker: Writing – review & editing, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation. Fabian Walter: Writing – review & editing, Methodology, Investigation, Formal analysis. Ioanna Tsiligianni: Writing – review & editing, Project administration, Investigation. Izolde Bouloukaki: Writing – review & editing, Project administration, Investigation. Marco Roos: Writing – review & editing, Resources, Conceptualization. Jochen Gensichen: Writing – review & editing, Resources, Conceptualization.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Due to the study design, no ethics vote was necessary and no personal primary data was collected.

Funding statement

There was no external funding to conduct this review.

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.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2025.127682.

Data availability

Data will be made available on request.

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