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The Prevalence of Anxiety Disorders in Older Adults with Chronic Somatic Illnesses: A Meta-Analysis

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Abstract

Previous studies have found that the prevalence of anxiety disorders declines with age in otherwise healthy people. However, it is not yet clear whether this phenomenon can be found in populations with chronic somatic illnesses as well. In view of this uncertainty, a meta-analysis was conducted. We hypothesized that a decline of the prevalence of anxiety disorders is limited to otherwise healthy people and cannot be observed in people with chronic somatic illnesses. Furthermore, we assumed more chronically and somatically ill females than males to be diagnosed with an anxiety disorder regardless of their ages. We included 29 studies in the meta-analysis, which we found through an article search in the online database Medline using PubMed. The results of the meta-analysis showed that a decrease in the prevalence of anxiety disorders can also be observed in people with chronic somatic illnesses, although this decline was not statistically significant. Strikingly, gender differences in the prevalence of anxiety disorders were not found. Apart from that, we found a higher prevalence of anxiety disorders in our population than in otherwise healthy populations as reported in current literature. This suggests that chronic somatic diseases and anxiety disorders are associated to a great extent. However, we suggest that our findings to be interpreted with caution, as they are suspect to various biases that are common in meta-analyses.

Keywords: old age, anxiety disorder, chronic illness, meta-analysis

The Prevalence of Anxiety Disorders in Older Adults with Chronic Somatic Illnesses: A Meta-Analysis

Anxiety disorders refer to a spectrum of disorders that generally develop in childhood and tend to persist if not treated (American Psychiatric Association (APA), 2013). Their current global prevalence has been reported to be about 7%, with a range from 5% in African cultures to 10% in Euro/Anglo cultures (Baxter, Scott, Vos, & Whiteford, 2013). Anxiety disorders have often been found to co-occur with chronic somatic illnesses, such as coronary artery disease and cancer (Fleet, Lavoie, & Beitman, 2000; National Breast Cancer Centre and the National Cancer Control Initiative, 2003). A study by the Harvard Medical School and the Lown Cardiovascular Research Institute found that men and women with an established heart disease are more likely to suffer a heart attack when having an anxiety disorder than those without an anxiety disorder (Harvard Health Publications, 2008).

Research has suggested that the prevalence of anxiety disorders decreases with age in otherwise healthy people. To give an example, Kessler, Petukhova, Sampson, Zaslavsky, and Wittchen (2012) have reported a decrease in anxiety prevalence of almost 19% when comparing an adult to an elderly population diagnosed with an anxiety disorder. A decrease has also been observed in a study by Schaub and Linden (2000), in which the prevalence of anxiety disorders was lower in those over than those under 85 years of age. One of the reasons for this decrease may be that the process of ageing simply brings about an intrinsic reduction in susceptibility to anxiety (Jorm, 2000). For instance, older people may have developed strengths and coping skills throughout their lives that enable them to deal more effectively with crises and to experience fewer negative emotional reactions than younger people. Therefore they may perceive the symptoms of anxiety disorders to a lesser extent (Wolitzky-Taylor, Castriotta, Lenze, Stanley, & Craske, 2010).

However, the decrease of anxiety prevalence might not occur in every population. It has been found that the overall prevalence of anxiety disorders is higher in older adults with chronic somatic illnesses than in otherwise healthy older people (Junginger, Phelan, Cherry, & Levy, 1993). Furthermore, up to 40% of the elderly population with chronic somatic conditions report anxiety symptoms. These reported anxiety symptoms may not only be associated with the usual ageing process that brings about memory difficulties, low levels of physical activity, increased dependence on others and an overall poorer perception of health (Brenes et al., 2005; Chapman, Perry, & Strine, 2005; Kunik et al., 2005; Wu, 2014). In fact,

they may rather be intrinsically associated with chronic somatic conditions. Considering this, the question may arise if anxiety prevalence decreases in older populations with chronic somatic conditions as well or if this observation is limited to otherwise healthy populations. Existing literature cannot give an accurate answer to this question, as there are mixed findings on this topic. On the one hand, research has reported a higher prevalence of anxiety disorders in older chronically and somatically ill populations when compared to younger affected populations (Sharma et al., 2013; Vögele & von Leupoldt, 2007). On the other hand, a lower prevalence of anxiety disorders has been shown in older compared to younger patients with chronic somatic illnesses (Demyttenaere et al.; 2007). Considering that current research is not yet clear on the decrease of anxiety prevalence in chronically and somatically ill ageing people, we believed that this issue represents an important venue for further investigation. Therefore our first study aim was to answer the question if the prevalence of anxiety disorders also decreases in ageing people suffering from a chronic somatic illness.

Anxiety has been shown to be more prevalent in women than in men (APA, 2013; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; McLean, Asnaani, Litz, & Hofmann, 2011). Regier, Narrow, and Rae (1990) have investigated the gender difference in the prevalence of anxiety disorders and even found that it persists regardless of age. The wide evidence of a gender difference in the prevalence of anxiety disorders led us to believe that gender is an important factor to include in our research. It may have main effects on the prevalence of anxiety disorders or may act as a moderator of the relationship between age and anxiety.

Although the terms chronic somatic illness, old age, anxiety disorder and prevalence are frequently used, it is essential to define them more precisely for the purpose of this research. *Chronic somatic illnesses* cover a wide range of somatic illnesses that are non-transmittable. They are generally characterized by a long duration and slow progression, and require management over years or even decades (World Health Organization (WHO), 2014). They bring about permanent changes in health status, which are oftentimes accompanied by psychological distress, such as anxiety (Wu, 2014). Respiratory- and cardiovascular diseases, cancers and diabetes represent the most frequent chronic somatic illnesses (WHO, 2014). Another term discussed in the literature is *old age*, which refers to the later part of life. There is no official standard cutoff that differentiates between younger and older adults; however, the suggested cutoffs reside around the age of 55 (WHO, 2015). For this reason, we have

decided on categorizing people aged 55 years or over as old. The third term, namely *anxiety disorder*, refers to a category of mental disorders characterized by excessive fear and anxiety. The two official classification systems used to diagnose anxiety disorders are the *International Statistical Classification of Diseases and Related Health Problems* (ICD; WHO, 1992) and the *Diagnostic and Statistical Manual of Mental Disorders* (DSM; APA, 2013). What needs to be mentioned at this point is that the DSM is not of one mind when it comes to anxiety disorders. Even though the newest version of the DSM, the DSM-V (APA, 2013), has already been around for two years, the former version (DSM-IV; APA, 2000) is still widely used. There are several differences between the two versions in terms of the classification of anxiety disorders. Firstly, the DSM-IV differentiates panic disorder into two categories (with/without agoraphobia), while the DSM-V does not. Furthermore, the DSM-IV presupposes agoraphobia to be a sole diagnosis only if a history of panic disorder is not given. Secondly, the DSM-IV includes obsessive-compulsive disorder, posttraumatic stress disorder and acute stress disorder in the category of anxiety disorders. The DSM-V, however, does not include these conditions in the anxiety category, but rather classifies them into new categories of mental disorders (obsessive-compulsive and related disorders, respectively trauma- and stressor-related disorders). Thirdly, the DSM-IV has listed selective mutism and separation anxiety disorder under the category of disorders usually first diagnosed in infancy, childhood or adolescence. However, they can now be found in the category of anxiety disorders in the DSM-V. What needs to be mentioned though is that selective mutism as well as separation anxiety disorder are not of importance for our research, since our focus lays on anxiety disorders of elderly instead of young people (APA, 2000, 2013).

We have worked towards combining the literature from the past decades. Therefore it was likely that we would encounter both versions of disorder classification. We have decided to include all of the disorders that are mentioned in the DSM-IV, as they represent the wider range of anxiety disorders. Thus, we will consider the following conditions as anxiety disorders in our further investigation: panic disorder with/without agoraphobia, agoraphobia without history of panic disorder, specific phobia, social phobia, obsessive-compulsive disorder, posttraumatic stress disorder, acute stress disorder, generalized anxiety disorder, anxiety disorder due to a medical condition, anxiety disorder not otherwise specified and substance-induced anxiety disorder (APA, 2000).

Considering the topic of our study, *prevalence* describes the number of people with an anxiety disorder in a population of chronically and somatically ill people. Prevalence can be divided into three time specifications, namely period- (a specific time period), point- (a specific point in time) and lifetime prevalence (Gerstman, 2013; National Institute of Mental Health, n.d.). Most studies of mental illness report the lifetime prevalence; however, there are some disadvantages to this parameter. First of all, lifetime prevalence is cumulative over time, thus by definition not useful for the investigation of age differences in the prevalence of anxiety disorders (Patten, 2015). Furthermore, the parameter of lifetime prevalence is unaffected by the number of people who have already recovered. Respectively, subjects are included even though they may not meet criteria for an anxiety disorder anymore (Warner, 2004). Moreover, a recall bias may hinder valid measurement, as the assessment of lifetime prevalence asks subjects to provide information that is based solely on their recollection (Marchevsky, 2000). On the whole, it has been suggested that lifetime prevalence is a useless parameter that should not provide a definite basis for comparison (Murray, Hill, McGuffin, & Birley, 1997; Patten, 2015). Therefore we have decided not to include information or data that reports on lifetime prevalence but rather to focus on the period- and point prevalences. Specifically, we were interested in the investigation of 12-month period prevalence and point prevalence.

In view of uncertainties about the prevalence of anxiety disorders in chronically and somatically ill older people, we have aimed at systematically summarizing the literature on this topic. For this reason, we have decided on conducting a meta-analysis. Thereby, we assume that a decrease of anxiety prevalence in old age is an observation limited to otherwise healthy people and cannot be found in chronically and somatically ill populations. Furthermore, we expect to find a gender difference in the chronically and somatically ill population in terms of anxiety disorders. Specifically, we assume more affected females than males to be diagnosed with an anxiety disorder, regardless of their ages.

Method

Research Design

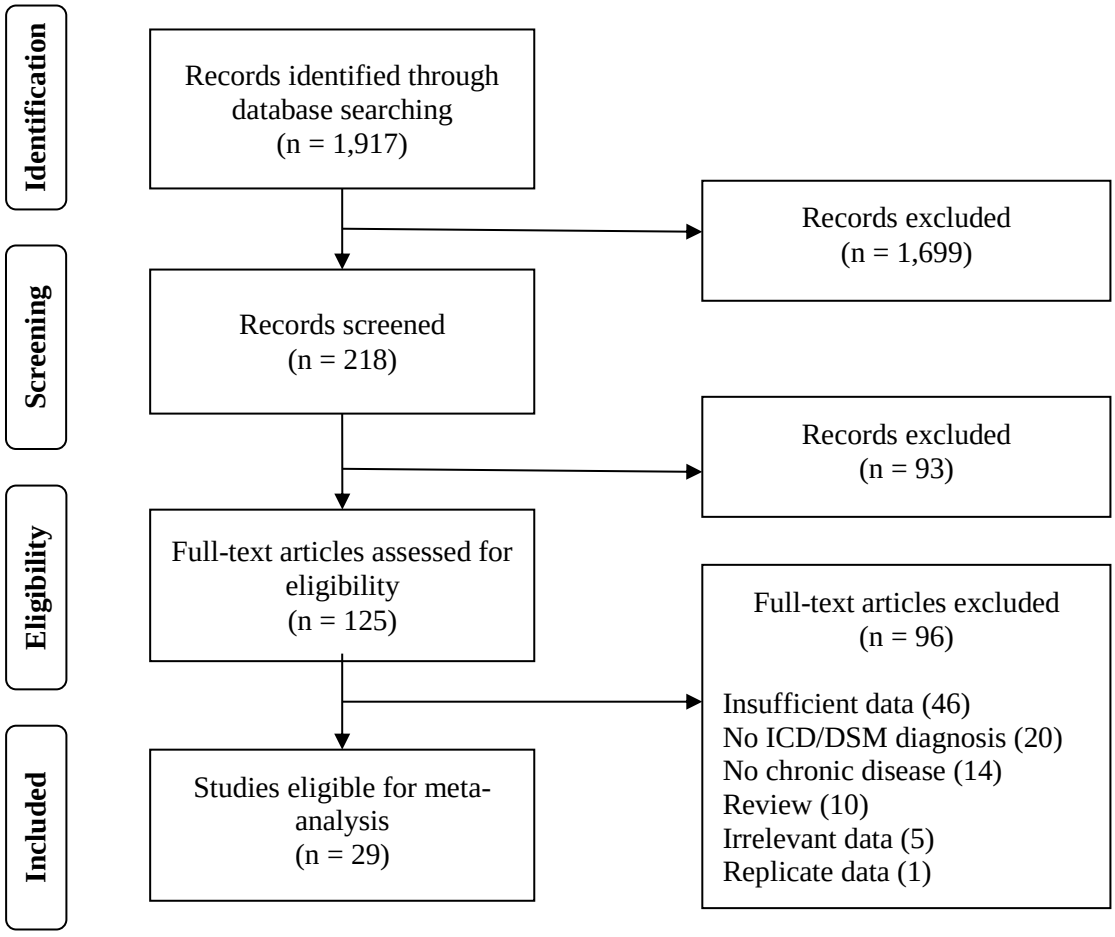
For our current research, we aimed at systematically summarizing and evaluating published research results on our topic of interest. Therefore we performed an epidemiological study, more precisely a meta-analysis (Biostat Inc., n.d.; Greco, Zangrillo, Biondi-Zoccai, & Landoni, 2013). We preferred a meta-analysis over an individual observational study, because

it yields more precise population estimates. It also has the advantage that one can examine the variability and heterogeneity in study results, as well as their generalizability. Additionally, a meta-analysis is more cost-effective, as participants do not have to be recruited and potentially be reimbursed (Grady, 2005). Finally, it might be essential to summarize existing literature before conducting an observational research on a topic of interest, so that one can assess whether conducting an individual study would actually contribute valuable knowledge to the existing literature (Haidich, 2010).

Procedure

In order to ensure the quality and similarity of the included articles, we decided on selecting them based on stringent inclusion and exclusion criteria (see Appendix, Table 1; Field & Gillett, 2010). Firstly, a paper should report on the prevalence of DSM or ICD diagnosed anxiety disorders in persons with chronic somatic illnesses (APA, 2000, 2013; WHO, 1992). Secondly, the study should report necessary data, for instance the number of female participants. Thirdly, the findings should have been published in a peer-reviewed journal. Exclusion criteria included data that was presented in abstracts, reviews, editorials, comments, or meta-analyses. Furthermore, a paper was excluded if it was not written in Dutch, English, French, German, or Spanish. A search term combination of anxiety, illness and old age ((anxiety disord*) AND (prevalen* OR inciden*) AND (somatic* OR medical* OR hospital* OR inpatient) AND (elderly OR late life OR midlife)) was used to find suitable literature in the online database Medline using *PubMed* on November 16, 2015. The idea was to conduct several decision rounds, in which the number of articles would be narrowed down more and more based on their eligbility. Thus, in the first round, we included 218 of 1,917 articles that we found with our search terms, based on their fitting titles and keywords. After conducting three decision rounds in the time frame from November 16, 2015, until January 26, 2016, and after requesting additional information from some authors, we found 29 articles to be eligible for the meta-analysis (see Figure 1). Throughout the decision process, my colleague S. Brinkman and I independently performed the assessment of eligibility. Afterwards we had a consensus meeting to discuss the excluded articles and to assure that no essential ones would be discarded, as this could lead to several biases (Haidich, 2010). Questions that arose during the process were also discussed with our thesis supervisors (Dr. Molendijk and Prof. dr. Spinhoven). An institutional review board approval was not required, as our meta-analysis only involved data from published studies (Lu et al., 2012).

Figure 1. *Flow Diagram of the Article Selection (November 16, 2015 – January 26, 2016)*



Note. ICD = International Statistical Classification of Diseases and Related Health Problems. DSM = Diagnostic and Statistical Manual of Mental Disorders. Design adapted from Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., & PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Public Library of Science Medicine, 6*(7): e1000097.

Data Extraction

The following data were extracted from the eligible articles: names of the authors, publication date of the study, the total sample size of the study, age of the subjects, type of chronic somatic condition of the subjects, the proportion of female subjects and the 12-month/point prevalence of one or more anxiety disorders. Here, the two types of prevalence were not differentiated any longer, since only four of the 29 included studies reported the 12-month prevalence (while the remaining studies either reported the point prevalence or did not differentiate between the two at all). The prevalences did therefore not come into consideration for a subsequent test of statistical difference and were lumped together. Unfortunately, the included studies did not report the prevalence of anxiety disorders seperately for males and females. For the sake of being able to make any assumptions about

gender differences, we stated the overall prevalence of anxiety disorders and the proportion of females for each individual study. If data from more than one sample was reported in an article, the samples were treated as separate studies and identified with a, b, c, etc. In order to test the significance of age differences in the prevalence of anxiety disorders, we divided the variable of age into three age categories: younger than 55 years (young), 55-75 years (old) and older than 75 years (very old). The study samples were then assigned to one of the categories depending on the age of the assessed subjects. Gender was expressed by a continuous variable (proportion of females). Afterwards, all data was integrated into an Excel file and then transferred to the Comprehensive Meta-Analysis Software (CMA) Version 3.0 (Borenstein, Hedges, Higgins, & Rothstein, 2014) and SPSS Version 23.0 (IBM Corp., 2015).

Statistical Analysis

For the sake of testing whether the prevalence of anxiety disorders was the same in all age groups, we performed a random effects meta-analysis in CMA Version 3.0. In contrast to a fixed effect meta-analysis that assumes the same effect across all studies, a random effects meta-analysis hypothesizes heterogeneity among study results. We strongly presupposed that the collected studies illustrated varied results, which is why we decided on using a random-effects model (DerSimonian & Kacker, 2007; Haidich, 2010).

The first step of the meta-analysis was to create and inspect a forest plot, which shows an estimate of the overall prevalence of the meta-analysis and its 95% confidence interval (*CI*; depicted by a diamond shape at the bottom of the plot). It allows a visual assessment of the amount of heterogeneity between the results of the studies (Akobeng, 2005). Additionally, the forest plot gives information from the individual included studies, such as their event rates (depicted by squares) and their 95% *CI*s (depicted by horizontal lines). The second step of the meta-analysis was to assess the risk of publication bias, which arises when it is more likely that studies with statistically significant rather than non-significant results are published and cited (Jüni, Holenstein, Sterne, Bartlett, & Egger, 2002). The assessment was done with a funnel plot and an Egger's *t*-test (Egger, 1997). The funnel plot was examined for its shape and any outliers that may suggest the possibility of publication bias (Haidich, 2010). Specifically, an unsymmetrical inverted funnel and scatter that falls outside the triangular region of the funnel suggest the presence of publication bias (Sterne, 2011). We also conducted an Egger's *t*-test, which tests the null hypothesis of no publication bias across the studies. If the results of both, the funnel plot and the Egger's *t*-test, are significant and hereby

reveal the risk of publication bias, then corrective measures can be taken to impute missing studies and to subsequently estimate an adjusted prevalence (Duval & Tweedie, 2000). After testing for publication bias, we determined the prevalence of anxiety disorders for each age category. *CI*s set at 95% were used in order to determine statistical signficance of the prevalences.

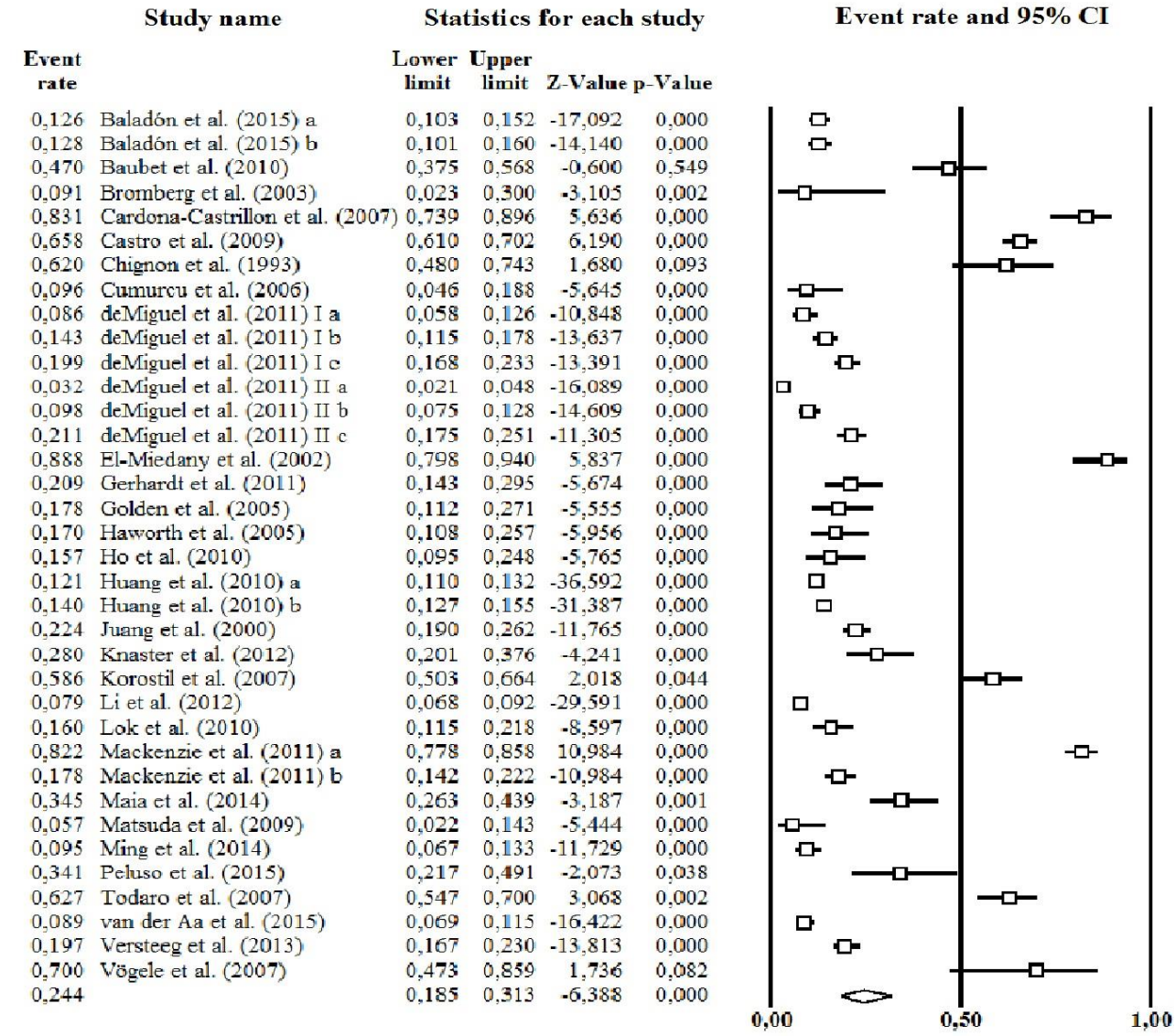
Heterogeneity between studies was evaluated with the Cochran's *Q*-test and a value of significance at 5% ($p \leq .05$; Hardy & Thompson, 1998). The *Q*-test assumes that all studies share a common prevalence. Thus, a rejection of this hypothesis means that the excess variance of the prevalences falls outside the range that could be attributed to random variation alone. While the *Q*-test only informs us about the presence or absence of heterogeneity, the I^2 statistic also informs us about its extent (Huedo-Medina, Sanchez-Meca, Marin-Martinez, & Botella, 2006). It expresses between-study heterogeneity through a percentage of total variation across studies and is calculated by subtracting the degrees of freedom from the *Q*-value, dividing the result by the original *Q*-value and then multiplying the result of this by 100% ($I^2 = [Q\text{-}df]/Q \times 100\%$). I^2 values of 25% indicate low, 50% indicate moderate and 75% indicate high heterogeneity (Haidich, 2010; Higgins, Thompson, Deeks, & Altman, 2003; Lu et al., 2012).

In order to investigate whether gender has any influence on the prevalence of anxiety disorders or the direction and strength of the relationship between age and anxiety prevalence, we performed a moderated regression. Here, the proportion of females (*PropFem*) was either used as the independent variable or as the moderator with age category as the independent variable (*AgeCat*). In both cases, the prevalence of anxiety disorders was the dependent variable (*PropAnx*). Before the actual regression, a listwise deletion was employed, so that the complete data of every study that did not report on the proportion of females was deleted. Afterwards, the assumptions of multiple regression were checked in SPSS to assure that there was no need to transform the data. However, it was important to remember that a violation of an assumption should not always result in a transformation of data (Hogg & Tanis, 1977). According to the basic moderation path model by Baron and Kenny (1986), a moderation analysis is conducted by testing the significance of the interaction term between the independent variable and the moderator over and above their main effects. Therefore, we created an interaction term (*IntAgexGen*) by multiplying the age category with the proportion

of females and tested the significance of this variable in CMA (Baron & Kenny, 1986; Jose, 2013). *CI*s set at 95% and *F*-tests ($p \leq .05$) were used to determine statistical significance.

Results

Figure 2. *Forest Plot of the Included Studies*



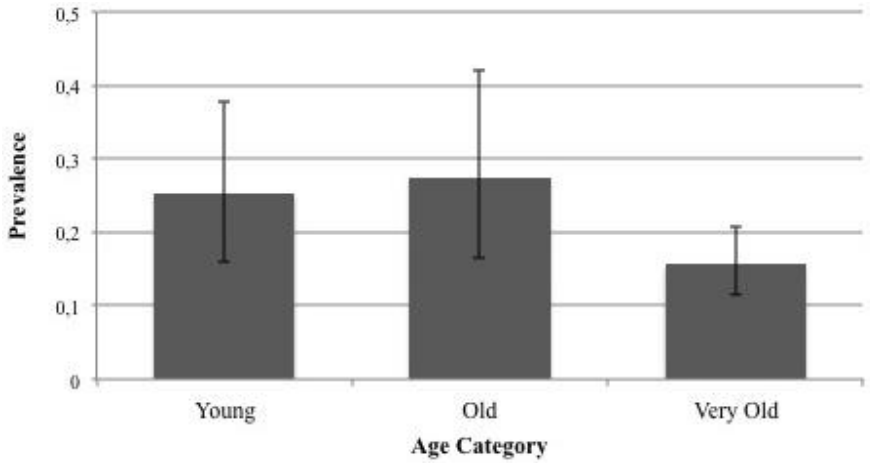
Note. Studies included = 29 (three articles reported the prevalence of more than one sample, therefore n = 36).

In the forest plot, the results of 29 studies have been pooled (see Figure 2). A visual inspection of the plot revealed event rates between .021 and .888. Furthermore, a funnel plot of the event rate in logits against the standard error was assessed (see Appendix, Figure 1). Firstly, the funnel plot was inspected visually. It seemed like most of the scatter fell outside the triangular region and was missing in the lower parts of the plot. However, the funnel did not give a clear

visual impression of asymmetry. Secondly, the Egger's *t*-test (see Appendix, Table 2) was run and identified the funnel plot as symmetrical, since the null hypothesis could not be rejected at a significance level of $p \leq .05$, intercept $b = 4.442$, $t(34) = 1.881$, 95% *CI* (-.357, 9.240), $p = .069$.

The overall prevalence of anxiety disorders in our meta-analysis turned out to be .244, $p < .001$, 95% *CI* (.185, .313; see Figure 2). When the sample was split and divided into the corresponding age groups, the following prevalence proportions were found: .253 for the young age group ($p < .001$, 95% *CI* [.159, .378]), .274 for the old age group ($p = .003$, 95% *CI* [.165, .419]) and .156 for the very old age group ($p < .001$, 95% *CI* [.115, .208]; see Appendix, Table 3).

Figure 3. *Bar Chart of the Prevalences in the Different Age Categories*



Note. Error bars represent the 95% confidence interval.

The Cochran's *Q*-test determined that the null hypothesis of the same prevalence of anxiety disorders in all age categories could not be rejected at a significance level of $p \leq .05$, $Q(2) = 5.361$, $p = .069$ (see Appendix, Table 3). The I^2 value of 62.694 (63%) pointed to the presence of moderately high between-study heterogeneity.

Before conducting the moderated regression, we employed a listwise deletion. The data of nine out of 36 cases was deleted due to missing information about the female proportion of the sample. Afterwards, the assumptions of multiple regression were checked. Linearity was established by visual inspection of a scatterplot. The assumption of multicollinearity was met, as the variance inflation factor (VIF) of *AgeCat* and *PropFem* was 1.003, and therefore smaller than 2.500. When the interaction term was added to the model, the VIFs rose,

VIF_{AgeCat} = 13.991, $VIF_{PropFem}$ = 2.381, $VIF_{IntAgexGen}$ = 14.938. However, this did not entail a transformation of data, because the high VIFs were most likely caused by the inclusion of the interaction term (Allison, 2012). Homoscedasticity was determined by visual inspection of the studentized residuals plotted against the unstandardized predicted values. The assumption of normality was violated, as was shown by a statistically significant result of the Shapiro-Wilk's test, $p < .001$. Nevertheless, a data transformation was not essential, because our sample size was greater than 25 (Hogg & Tanis, 1977; Elliot & Woodward, 2007). The Durbin-Watson test revealed independence of residuals, as $d = 2.211$ and, therefore, $1.5 < d < 2.5$ (Cohen, Cohen, West, & Aiken, 2003).

A meta-regression was then conducted with the help of the increments option in CMA (Biostat; see Table 1). The main effects of *PropFem* and *AgeCat* were neither statistically significant nor approached significance. Consequently, the model containing only the main effects *PropFem* and *AgeCat* was not statistically significant as well, $Q(3) = 2.110$, $p = .550$. Furthermore, a moderator effect could not be found, as evidenced by a statistically non-significant addition of the interaction term *IntAgexGen* to the model, $Tau^2_{Change} = .108$, $R^2_{change} < .001$, $Q(1) = .080$, $p = .782$.

Table 1. *Results of the Meta-Regression*

	Current Model		Test of Model			Change from Prior		Test of Change		
Model	Tau^2	R^2	Q	df	p-value	Tau^2_{Change}	R^2_{Change}	Q	df	p-value
1[a]	1.899	< .001	2.110	3	.550	-.023	< .001	.040	1	.844
2[b]	2.007	< .001	2.070	4	.722	.108	< .001	.080	1	.782

Note. Tau^2 = Estimated standard deviation of effects across studies. R^2 = Multiple correlation squared. R^2_{Change} = Change in multiple correlation. Q = Test statistic of the Cochran's Q-test. df = Degrees of freedom.
[a]Predictors: (Constant), *PropFem, AgeCat*
[b]Predictors: (Constant), *PropFem, AgeCat, IntAgexGen*

Discussion

We conducted a meta-analysis in order to systematically summarize research results on the prevalence of anxiety disorders in a population of people with chronic somatic illnesses. In doing so, we pooled data from individual studies and reanalyzed them using established statistical methods (Muir Gray, 2001).

Main findings

Heterogeneity. A forest plot of the 29 included studies showed that the majority of the

prevalences of anxiety disorders was below 50%. Furthermore, most confidence intervals were narrow, which indicated that the prevalence estimates were rather precise. Some outliers could be detected, but overall, the forest plot did not give the impression of substantially heterogeneous data. Nevertheless, we investigated heterogeneity further in our statistical analysis in order to increase the certainty of a meaningful prevalence estimate. On that account, we made use of two statistical methods, namely the *Q*-test and the I^2 inconsistency index. The result of the first statistical method led us to reject the null hypothesis of statistically significant differences between the observed prevalences of the individual studies, which supported our notion of homogeneous data (Cuijpers, 2016). The second statistical test revealed that the percentage of total variance that can be explained by heterogeneity was 62.7%, thus indicating moderately high heterogeneity (Higgins et al., 2003). On the whole, the statistical methods supported the observations made from the forest plot: the data does show hints of heterogeneity but these do not seem to be substantial. What needs to be mentioned is that even though both statistical methods are considered key components in meta-analyses, they should be interpreted with caution, meaning that a non-significant result of the statistical test of heterogeneity should not be equated with the complete absence of heterogeneity (Cuijpers, 2016). Regarding our analysis, it might have been the case that the number of included studies simply did not have enough power to identify heterogeneity even though it was present. In sum, we tested for heterogeneity and found the data to be rather homogeneous. Therefore, we did not see the necessity for employing any corrective actions.

Publication bias. Furthermore, we evaluated the presence of publication bias. The graphical evaluation method, namely the funnel plot, is based on the assumption that large studies appear toward the top of the plot and small studies toward the bottom (Rothstein, Sutton, & Borenstein, 2005; Cuijpers, 2016). In our case, the funnel plot showed gaps in the lower part. This suggested a bias towards the inclusion of large studies, respectively the presence of publication bias. As no definite conclusions should be drawn from visual inspection alone, we also employed a statistical method to detect publication bias, namely the Egger's regression. It yielded a non-significant result and, therefore, did not support our notion of publication bias. Merging the results of these two evaluation methods together, we came to the conclusion that the presence of a publication bias was rather unlikely and should not be of great concern in the interpretation of our results.

Prevalence of anxiety disorders. The overall prevalence of anxiety disorders in our data

was .244. In other words, 24.4% of the assessed chronically and somatically ill population has met the criteria for at least one anxiety disorder within the past 12 months or on the date of assessment. As we were also interested in age differences in the prevalence of anxiety disorders, we assessed the prevalences for three distinct age categories. The prevalence of anxiety disorders was 25.3% for people younger than 55 years (young age category), 27.4% for people between 55 and 75 years (old age category) and 15.6% for people older than 75 years (very old age category). The prevalence of anxiety disorders therefore increased 2.1% from the young to the old age category and decreased 11.8% from the old to the very old age category. However, the result of a random effects analysis revealed that the prevalences of the age categories were not significantly different from each other.

Effects of gender. Finally, we investigated the potential main or moderating effect of gender on the prevalence of anxiety disorders, respectively on the relationship between age and the prevalence of anxiety disorders. Firstly, it was striking that the model containing the two main effects (gender and age) was not statistically significant, meaning that the prevalence of anxiety disorders could neither be predicted from the gender nor the age of the chronically and somatically ill population. Secondly, the addition of the interaction term to the model was not significant as well, which reveals that gender did not act as a moderator of the relationship between age and the prevalence of anxiety disorders.

Implications of the results

Our first hypothesis was that the previously observed decrease of anxiety prevalence in otherwise healthy older populations could not be found in older populations with chronic somatic illnesses (Kessler et al., 2012; Schaub & Linden, 2000). However, we did find a decline of 11.8% in the prevalence of anxiety disorders from the old to the very old age category of chronically and somatically ill people. Even though this decrease was not statistically significant, it showed a trend towards significance. We subsequently hypothesized possible reasons for this almost significant decline. Firstly, older people may experience an age-related intrinsic reduction of anxiety symptoms, as they may have developed better coping skills and consequently can deal more effectively with crises, such as the worsening of their chronic conditions (Jorm, 2000; Wolitzky-Taylor et al., 2010). Secondly, many older people suffer from dementia, which has a high symptom overlap with some of the anxiety disorders. For instance, generalized anxiety disorder and dementia both include symptoms like restlessness, concentration difficulties and fatigue. Thus, symptoms of

an anxiety disorder may easily be mistaken for symptoms of dementia. On top of that, symptoms anxiety disorders are often wrongly assigned to difficulties associated with the normal ageing process (Lenze & Wetherell, 2011; Seignourel, Kunik, Snow, Wilson, & Stanley, 2008). Thirdly, many older adults tend to deny psychological problems and focus on somatic complaints instead (Lenze et al., 2005). Fourthly, one may observe a lower prevalence of anxiety disorders simply because older adults with anxiety disorders do not engage in studies or do not acknowledge their anxiety symptoms in the first place. Finally, anxiety disorders may also be associated with excess mortality among the young and middle-aged, which then contributes to a lower prevalence of anxiety disorders in older people (Byrne, 2002).

Our second hypothesis was that there are more chronically and somatically ill females than males with an anxiety disorder, regardless of age. Strikingly, our results opposed that hypothesis. The prevalence of anxiety disorders did not depend on the gender of the subjects, meaning that there were not significantly more females than males with an anxiety disorder in our sample. This finding is rather unexpected, considering that previous research has found ample evidence of a gender difference in the prevalence of anxiety disorders that even persists regardless of age (e.g. McLean et al., 2011; Regier et al., 1990). However, this might suggest that chronically and somatically ill populations differ from otherwise healthy populations in regard to anxiety disorders. Chronically and somatically ill males with anxiety disorders might experience the same kind of anxiety symptoms as chronically and somatically ill females with anxiety disorders. For instance, the three leading causes of death (heart disease, cancer and stroke) are the same in chronically and somatically men and women, which might cause the same severity of anxiety in both genders. Moreover, men and women's overall mental health is described to be the same. This suggests that men and women also have the same abilities to cope with anxiety disorders and chronic somatic illnesses (Kessler et al., 2003). Finally, it could be that more chronically and somatically ill women than men suffer from anxiety disorders but that this is limited to younger age. In older age however, the prevalence of anxiety disorders for males may increase in a way that it gets on the same level as females. For instance, men's anxiety levels may rise because of their lower life expectancy and higher proneness to life-threatening chronic diseases (Rieker & Bird, 2005).

Previous research has shown that the current, respectively the point and 12-month, global prevalence of anxiety disorders is about 7%, with the highest prevalence values found for

Euro/Anglo cultures (Baxter et al., 2013; Kessler, Chiu, Demler, Merikangas, & Walters, 2005). The current global prevalence of anxiety disorders is therefore 17.4% lower than the overall current prevalence we found for our sample of people with chronic somatic illnesses. This finding suggests that anxiety disorders occur more often in chronically and somatically ill people. Literature in support of this suggestion has indicated that somatic symptoms often occur in reaction to stressful, anxiety-inducing situations, which may account for the association between anxiety and chronic somatic illness (Feder, n.d.). Furthermore, anxiety has been associated with more frequent hospitalization and distress in people with chronic somatic illnesses. Even therapies designed to treat anxiety disorders have shown success in easing the symptoms of chronic somatic illnesses, such as respiratory and heart diseases (Harvard Health Publications, 2008).

In sum, our data showed a decrease in the prevalence of anxiety disorders in older populations with chronic somatic illnesses. However, this decline was not statistically significant. In contrast to otherwise healthy populations, we did not find any gender differences in the prevalence of anxiety disorders in chronically and somatically ill populations. Apart from that, we found a much higher prevalence of anxiety disorders in our population than in otherwise healthy populations, which might suggest that chronic somatic disease and anxiety are associated to a great extent.

Strengths

Research design. Our central aim was to investigate the prevalence of anxiety disorders in older adults with chronic illnesses. We chose a systematic review to do so and reanalyzed existing research results on the topic of interest. In comparison to narrative reviews, systematic reviews are more powerful in combining several individual results. They apply scientific strategies that limit the risk of bias, enhance statistical power and improve the precision of estimates (Cook, Mulrow, & Haynes, 1997; Lang & Secic, 1997; Biondi-Zoccai, Landoni, & Modena, 2011). Furthermore, contemporary research is being accused of neglecting methods that integrate results from existing studies in order to reveal patterns of underlying relationships between variables. We took notice of that deficit and therefore conducted a systematic review instead of an individual observational study. In doing so, we also assured high external validity, as we pooled data from samples including different genders, ages, races and chronic illnesses (Hunter, Schmidt, & Jackson, 1982).

Research methods. We stated a predetermined method for assessing the eligibility of

studies and thereby followed the PRISMA guidelines for systematic reviews (Moher et al., 2009). By evaluating the eligibility of the articles independently, we minimized the risk of discarding any relevant studies (Clarke & Oxman, 2003). Furthermore, we did not ignore interaction effects at the expense of main effects, which is said to be a drawback of many contemporary studies (Cook & Leviton, 1980). Specifically, we looked at a possible moderation effect of gender on the relationship between age and the prevalence of anxiety disorders on top of investigating the main effects of these variables. Finally, many meta-analyses do not consider publication bias as an influential factor. Compared to that, we did screen for publication bias and would have taken corrective measures if the bias had shown to be substantial (Cuijpers, 2016).

Limitations

The four categories of limitations in meta-analyses. Glass, McGaw and Smith (1981) mentioned four categories of limitations in meta-analyses. Firstly, the so-called „apples and oranges problem“ can present a threat to the validity of meta-analyses. Whenever data from dissimilar studies is pooled, problems such as nonlinear correlations, multifactorial effects or heterogeneous data that fails to connect with the hypothesis can be created (Greco et al., 2013). These problems make it difficult to derive logical conclusions from the comparison of studies (Glass et al., 1981). Secondly, meta-analyses include results of well-designed studies along with results of poorly-designed studies, which may then result in a meta-analysis that appears to be poorly designed even though it is not. Thirdly, meta-analyses run the risk of being biased if they include biased research in the first place. To counter that, we have investigated the most frequent bias in meta-analyses, namely the publication bias. Publication bias represents a great problem in current research, as an estimated 92% of studies in psychology and psychiatry publish only positive results, while negative results are rarely published (Fanelli, 2010). Besides publication bias, location-, language- and availability bias could have had effects on the results of our meta-analysis as well (Egger, 1997; Rothstein et al., 2005). For instance, we only included articles that were either in English, Spanish, Dutch, German or French and discarded articles in any other language (language bias). Additionally, we have only searched the online database *PubMed* (Medline) for studies on the topic of question (availability bias). However, the exclusive reliance on one database has been shown to retrieve a set of studies that are unrepresentative of the totality of studies that would have been identified through a search of multiple databases. Hence, the search of a single online

database lacks sensitivity, results in the omission of including relevant articles and increases the overall threat of selection bias (Akobeng, 2005). Fourthly, the use of multiple results from the same study may bias or invalidate the meta-analysis in a way that the results appear more reliable than they really are (Glass et al., 1981). In sum, it is important to keep these potential biases in mind when interpreting our findings.

Methods and Statistical Analysis. The so-called PRISMA checklist suggests a set of items that should be reported in meta-analyses. The statement suggests to assess the risk of bias of individual studies in addition to the risk of bias across studies in order to investigate the extent to which the authors of the included studies conducted their research to the highest possible standards (Moher et al., 2009). However, we only assessed the risk of bias across studies and, therefore, failed to investigate whether well-designed and poorly designed studies yield similar conclusions. One of the limitations regarding the statistical analysis was that the old age category only included the data of five studies compared to 19 studies of the young age category. Even though this makes sense in a way that the young age category comprised a larger age span, this disparity may have affected the validity of our results. Another limitation regarding the statistical analysis was that the design of our study did not allow the assessment of causality, but rather only the investigation of potential relations between variables (Greco et al., 2013).

Anxiety disorders as a variable in general. Anxiety disorders may generally be underdiagnosed because physicians fail to identify them (Benjamin, Morris, McBeth, MacFarlane, & Silman, 2000; Lenze et al., 2005). For instance, anxiety has a high co-occurrence with other mental disorders. This may complicate the identification of anxiety symptoms independent of other mental disorders in the first place (Seltzer, 2010). Also chronic illnesses have been found to be highly associated with anxiety disorders, for example by producing symptoms that mimick anxiety (e.g. hyperthyroidism; Calleo & Stanley, 2008). Furthermore, many older patients focus on physical complaints and thereby deny psycho-social problems (Lenze et al., 2005).

The bottom line is that the general limitations of meta-analyses and the specific limitations of our study may have had effects on the results of our meta-analysis. In our defence though, it has been suggested that the human mind is unable to perfectly conduct a meta-analysis given the enormous amount of data that must be gathered, combined and synthesized in many disciplines (Glass et al., 1981).

Suggestions for further research

Firstly, it would be interesting to create narrower age categories. In that way, one could make more meaningful conclusions about age differences in the prevalence of anxiety disorders. Secondly, it would be desirable to avoid publication bias in the first place instead of correcting for it (Lau, Ionnaidis, Terrin, Schmid, & Olkin, 2006). This could be done by including studies in all kinds of languages, unpublished studies and studies with negative results. Thirdly, our search strategy could be extended by searching additional databases (Akobeng, 2005). Hereby, backward snowballing (the scanning of references of retrieved studies) and grey literature (literature not formally published in books or journal articles) should also play a role (Greco et al., 2013). Fourthly, the inclusion of more than 29 studies of anxiety in chronically and somatically ill populations will help in approaching the true population prevalence of anxiety disorders.

Our results suggest that chronic somatic illnesses may be highly associated with anxiety disorders. As therapies for anxiety disorders have already been shown to be successful in easing the symptoms of chronic somatic conditions, it would be interesting to investigate this association further (Harvard Health Publications, 2008).

Conclusion

Previous studies have found ample evidence for a decreasing prevalence of anxiety disorders in otherwise healthy older adults (Kessler et al., 2012; Schaub & Linden, 2000). However, it is not yet clear whether this phenomenon is to be found in populations with chronic somatic illnesses as well, which is why we chose to systematically review studies on the topic of interest. We found a decrease in the prevalence of anxiety disorders in older populations with chronic somatic illnesses, but it was non-significant. Strikingly, a gender difference in the prevalence of anxiety disorders could not be established in the chronically and somatically ill population. Apart from that, we compared our assessed prevalence to the prevalence of otherwise healthy populations reported in current research and found our prevalence to be higher. In sum, we contributed evidence to the phenomenon of an age-related decline of anxiety disorders in chronically and somatically ill populations.

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Appendix

Table 1. *Eligibility Criteria of the Article Selection*

Inclusion Criteria
• The paper reports on the prevalence of DSM or ICD diagnosed anxiety disorders in persons with chronic somatic illnesses. • The investigators report the necessary data. • The findings are published in a peer-reviewed journal.
Exclusion Criteria
• When data is presented in abstracts, reviews, editorials, comments, or meta-analyses. • When studies are not written in Dutch, English, French, German, or Spanish

Figure 1. *Funnel Plot of Standard Error by Logit Event Rate*

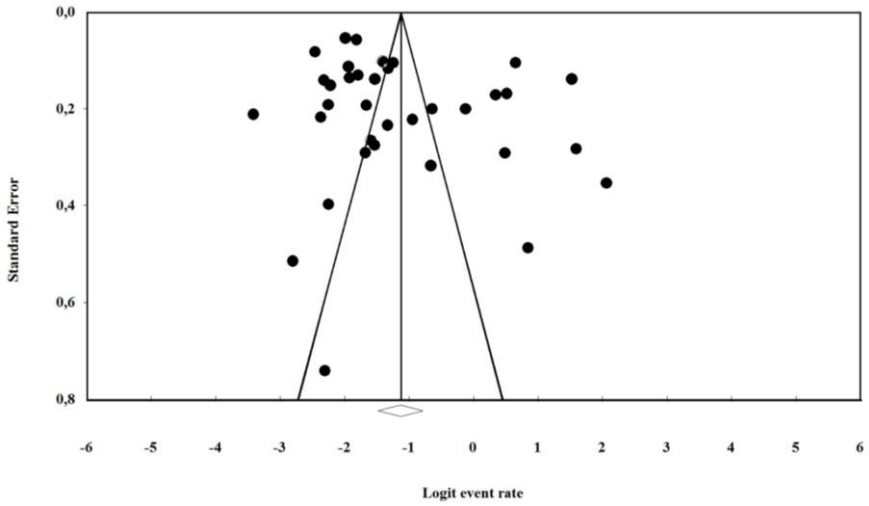

Table 2. *Results of the Egger's* t-*test*

Intercept	4.442
Standard error	2.361
95% lower limit (2-tailed)	-.357
95% upper limit (2-tailed)	9.240
t-value	1.881
df	34
p-value (1-tailed)	.034
p-value (2-tailed)	.069

Note. *df* = Degrees of freedom.

Table 3. *Results of Random Effects Analysis with Subgroups of Age*

	Effect size and 95% interval			Test of null (2-tail)		Heterogeneity			
Group	*n*	Prevalence	95% *CI*	*Z*-score	*p*-value	*Q*	*df*(Q)	*p*-value	I^2
Young (< 55 y)	19	.253	[.159, .378]	-3.637	<.001**				
Old (55-75 y)	12	.274	[.165, .419]	-2.960	.003**				
Very old (> 75 y)	5	.156	[.115, .208]	-9.351	<.001**				
Total between						5.361	2	.069	62.694
Overall	36	.194	[.154, .240]	-10.201	<.001**				

Note. *n* = Number of studies. *CI* = Confidence interval. *Q* = Test statistic of the Cochran's *Q*-test. I^2 = statistic of the inconsistency index.
* $p < .05$, two-tailed. ** $p < .01$, two-tailed