

Effect of age on treatment outcomes in benign paroxysmal positional vertigo: A systematic review

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1 **Effect of age on treatment outcomes in benign paroxysmal positional vertigo: a systematic**
2 **review.**

3

4 **Running Title: Effect of age on treatment results in BPPV**

5 Gwen Laurent^a MBS*, Luc Vereeck^b PhD*, Evi Verbecque^{a,b} PhD, Nolan Herssens^{b,c} PhD,
6 Laura Casters^a PT, Joke Spildooren PhD^a

7 *Joint first author – both authors contributed equally to the work

8

9 ^aRehabilitation Research Center (REVAL), Department of Rehabilitation Sciences, Hasselt
10 University, Agoralaan Gebouw A, 3590 Diepenbeek, Belgium.

11 ^bDepartment of Rehabilitation Sciences and Physiotherapy/MOVANT, Faculty of Medicine
12 and Health Sciences, University of Antwerp, Wilrijk, Belgium.

13 ^cDepartment of Rehabilitation Sciences, Gent university, Gent, Belgium

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19 Corresponding author:

20 Joke Spildooren

21 Agoralaan Gebouw A, 3590 Diepenbeek, Belgium

22 +32 11 269178

23 Joke.spildooren@uhasselt.be

24 @JSpildooren

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31 **KEY POINTS**

- 32 • *Treating older adults with BPPV is more complex, requires more CRP's and the risk for*
33 *recurrence is higher*
- 34 • *Age does not affect the ability to recover from BPPV*

35 **WHY DOES THIS MATTER?**

36 *Musculoskeletal and motivational changes hamper the treatment of older adults with BPPV*
37 *but this does not affect overall treatment outcome*

38

39 ABSTRACT

40 **Background:** Benign paroxysmal positional vertigo (BPPV) can lead to an increased fall risk in
41 older adults. Therefore, we examined the influence of age on the effectiveness of canalith-
42 repositioning procedures (CRPs) for the treatment of BPPV.

43 **Methods:** Pubmed, Web of Science, and the bibliographies of selected articles were searched
44 for studies conducted before September 2020 that examined the effectiveness of treatments
45 for BPPV in various age groups. Meta-analyses were performed to compare treatment
46 effectiveness and recurrence rates for younger and older adults. Odds ratios were calculated
47 in a random-effects model. Mean differences were calculated using a fixed-effects model. A
48 significance level of $p < 0.05$ (95% confidence interval) was set. The risk of bias and the
49 methodological quality of all included articles were examined.

50 **Results:** Forty-five studies were retrieved after full-text screening, of which 29 studies were
51 included for a qualitative review. The remaining 16 studies were eligible for inclusion in the
52 meta-analysis (3,267 participants with BPPV). The success rate of a single CRP was higher in
53 the younger group (72.5% vs. 67%, $p < 0.001$). An average of 1.4 and 1.5 CRPs was needed for
54 complete recovery in the younger and older groups, respectively ($p = 0.02$). However, global
55 treatment success did not differ between these groups (97.5% vs. 94.6%, $p = 0.41$). The
56 recurrence rate was higher in the older population (23.2% vs. 18.6%, $p = 0.007$).

57 **Conclusions:** Although more CRPs are needed, the rate of complete recovery in older adults
58 is similar to that observed in younger adults.

59 **KEY WORDS:** benign paroxysmal positional vertigo, treatment efficacy, recurrence, older
60 adults, aging

61 _____

62

63 INTRODUCTION

64 Vertigo and dizziness occur in 15–35% of the adult population, increasing up to 50% in people
65 aged 80 and older^{1,2}. In vestibular clinics, benign paroxysmal positional vertigo (BPPV) is
66 responsible for one-third of the cases in which vertigo or dizziness is the main complaint^{1,3,4}.
67 Additionally, BPPV is a common condition, with a known 1-year prevalence of 0.5% in the
68 population aged 18–39, 1.7% in the people aged 40–59, and 3.4% in the population 60 years
69 and older⁵.

70 Usually, BPPV is characterized by intense feelings of positional vertigo lasting about one
71 minute^{1,6}. However, adults aged 65 or over often complain of disequilibrium or imbalance,
72 without reporting vertigo^{7,8}. These complaints are often misdiagnosed and attributed to
73 other medical, neurological, or age-related changes^{9,10,11}. This may lead to the unnecessary
74 use of healthcare services, such as redundant diagnostic testing procedures and therapeutic
75 measures, resulting in an inefficient approach to this problem^{4,12}. Moreover, in older adults,
76 BPPV symptoms may also contribute to reduced social and daily activities and reduced
77 physical function, which are associated with increased fall risk^{1,13,14}. The timely and accurate
78 diagnosis and treatment of BPPV are important for preventing this decline in quality of life in
79 older adults.

80 Because the symptom presentation differs between age groups, it is plausible that the
81 effectiveness of the treatment may also differ. Recently, Sim et al. (2019) performed a
82 systematic review and meta-analysis of the treatment outcomes of BPPV in young and old
83 age groups¹⁵. Improvement in vertigo was shown in both groups, but in the older group, the
84 recovery of dynamic balance was worse, and an increased perception of disability was
85 reported¹⁵. For the meta-analysis, studies were allocated to either the young or older age

86 group according to the average age of the study population (above or below 60 years).
87 Consequently, due to the age spread in those studies, some older adults may have been
88 misplaced in the young age group, and *vice versa*, which may have negatively impacted the
89 significance of their results (e.g., similar recurrence rates in both groups)¹⁵.

90 The aim of the current systematic review and meta-analysis is to investigate the effect of age
91 on treatment efficacy, i.e., global success rate, success rate after one maneuver, the presence
92 of residual dizziness, and recurrence.

93 **METHODS**

94 **Protocol and registration**

95 This systematic review was registered in PROSPERO (CRD42020166194) and conducted
96 following the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA)
97 guidelines¹⁵.

98 **Data sources and searches**

99 Two researchers (JS, LV) performed a systematic search in Pubmed and Web of Science (last
100 search update on October 26th 2020) using keywords related to Benign Paroxysmal Positional
101 Vertigo, Epley, Sémont, Gans, or Brandt-Daroff. The filter “human” and language filters
102 German, English, Dutch, and French were applied. The specifics regarding the search queries
103 are available in *Supplementary Text S1*.

104 **Eligibility and study selection**

105 Original studies with a cohort, case-control, or controlled study design were considered
106 relevant. Conference proceedings/reports, editorials, case studies/series, abstracts only,
107 (systematic) reviews, and meta-analyses were excluded.

108 To be included, treatment efficacy and/or recurrence had to be compared between patients
109 with BPPV of different ages. For this analysis the pre-determined age cutoff was between 60
110 and 79 years, because the prevalence, because the prevalence of BPPV is almost seven times
111 higher in this age group⁵. Age effects could be investigated by defining age groups *a priori*
112 (e.g., comparing a group of younger versus older BPPV patients), using age *as a covariate in*
113 *the statistical analysis* (e.g., an analysis of variance or regression analysis), or performing *a*
114 *retrograde univariate analysis* (e.g., group composition based on recurrence rates and
115 comparing their mean ages). Treatment efficacy or recurrence after the canalith-
116 repositioning procedure (CRP) had to be measured using appropriate positional tests
117 corresponding to the canals to be tested, and CRPs were defined as all therapeutic maneuvers
118 to remove otoconia from the semicircular canals with/without postural restrictions. Studies
119 using only self-reported treatment, purely medication-based treatment, or surgery were
120 excluded. Finally, studies dealing exclusively with anterior or horizontal canal involvement
121 were excluded.

122 Two independent researchers (JS, LV) applied the selection criteria for the title and abstract
123 (phase 1), followed by a full-text screening (phase 2) in the same sequence: design,
124 population, comparison, and outcome. After each phase, the selection process was discussed
125 in a consensus meeting. To ensure that no relevant articles were missed, the references of all
126 studies included after phase 2 were screened and included if eligible. Global treatment

127 efficacy was defined as symptom resolution and conversion to a negative positional test after
128 treatment. Residual dizziness was defined as the sensation of lightheadedness or unsteadiness
129 without vertigo or nystagmus during positional testing after successful treatment. The
130 recurrence rate was defined as the reappearance of positional vertigo and nystagmus after
131 remission.

132 **Risk of bias in individual studies**

133 The risk of bias in the individual studies was identified with a modified version of the Scottish
134 Intercollegiate Guidelines Network (SIGN) checklist for cohort trials. Because the effect of age
135 on treatment outcome was rarely the primary research goal of the included studies, the
136 questions were modified to increase the identification of selection, detection, and attrition
137 bias (in relation to our research question). The specifics of the modified checklist are
138 presented in *Supplementary Text S2*.

139 **Data extraction**

140 Information regarding *general population characteristics* (number of subjects, age, and
141 gender), *specific population characteristics* (diagnostic test, canalolithiasis/cupulolithiasis,
142 affected canal, and time since onset of complaints), *the applied treatment procedure*, and *the*
143 *assessment of treatment efficacy and recurrence rate* (i.e., definition of success and number
144 of maneuvers) was extracted. Unclearities were discussed with the team in a consensus
145 meeting.

146 **Data Synthesis and Analysis**

147 If there was a sufficient number of articles describing treatment effectiveness or recurrence
148 rate as influenced by age (i.e. ≥ 5 studies¹⁶), meta-analyses were performed using Review
149 Manager 5.3. (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).
150 Odds ratios (ORs) were calculated for dichotomous data, such as the absence of vertigo and/or
151 nystagmus after performing a positional test for measuring treatment effectiveness or the
152 reappearance of vertigo symptoms for measuring recurrence. Between-group comparisons
153 were made using the Mantel-Haenszel method with a random-effects model. Mean
154 differences in the number of CRP maneuvers were calculated using a fixed-effects model.
155 Overall weighted estimates and 95% confidence intervals (95% CIs) were calculated for the
156 individual studies. Significance was set at $p < 0.05$.

157 **RESULTS**

158 **Study selection**

159 The selection process is presented in a flowchart (Supplementary Figure S1). The search
160 query revealed 792 unique citations. Data from 16 studies were included in the meta-
161 analysis. Twenty-nine additional studies were only used for descriptive data.

162 **Risk of bias in individual studies**

163 Seventeen prospective studies¹⁷⁻³³, four randomized controlled trials³⁴⁻³⁷, one non-
164 randomized controlled trial³⁸, two randomized trials^{39,40}, and 21 retrospective studies were
165 included^{8,25,41-59}. An overview of the methodological quality assessment is provided in
166 *Supplementary Table S1*. In 20 studies, the effect of age on treatment outcome or recurrence
167 was the primary research aim^{8,18,23,25,26,29-31,42,43,48-52,54-57,59}. The statistical procedure was well
168 described in 22 of 45 studies. The assessment of treatment efficacy and recurrence rate was
169 described in 29 and 23 studies, respectively. Fifteen studies only included canalolithiasis-type

170 BPPV^{19,20,23,25,27,31-33,38,40,41,44-47}, eleven studies also included cupulolithiasis-type BPPV^{8,18,22,24,}
171 ^{28,39,48,50,55,57,59}, and 19 studies did not specify the type of BPPV.

172 **Subject and study characteristics**

173 Across the 45 included studies, a total of 11,451 BPPV patients were included. Their mean age
174 ranged from 48³⁸ to 72³² years (Table 1, Supplementary Table S2). In 25 studies, only BPPV of
175 the posterior canal was included^{17,19,20,23,25,27-29,32-37,39-41,45-47,51,53,54,56,60}, while 18 studies also
176 included horizontal and/or anterior canal BPPV^{8,18,21,22,24,26,30,31,38,42,43,48-50,55,57-59}, and two
177 studies did not report information on canal involvement^{44,52}. Based on the diagnostic tests
178 (i.e., Dix-Hallpike) it could reasonably be assumed that posterior canal BPPV was included in
179 these articles^{44,52}. In 23 studies, a diagnosis of BPPV was confirmed via Dix-Hallpike maneuver
180 (DH)^{17,19-21,23,27-29,32,34,35,37,39,41,42,44-47,53,54,56,60}, while fourteen studies used both DH and the roll
181 test^{7,18,25,26,32,31,38,43,49,50,55,57-59}. One study did not specify the diagnostic maneuver²². Eleven
182 studies used Frenzel goggles to confirm diagnosis^{18,22,28,29,36,39-41,46,49,60}, while ten studies used
183 other visual-suppression systems^{21,30,31,35,42,48,50,55,59,60}.

184 **Characteristics of the treatment procedure**

185 The time between the onset of symptoms and the start of therapy ranged, on average, from
186 less than 24 hours²³ to 20 months⁴⁵. The Epley maneuver or modified Epley maneuver was
187 performed in 14^{8,23-26,35,37,39,44,55-58} and 10 studies, respectively,^{18-20,23,33,38,39,50,54,59}, sometimes
188 in combination with medication⁵⁵, vibrations¹⁸, or Brandt-Daroff exercises^{39,59}. Seven studies
189 used a Semont Maneuver^{18,28-30,32,41,51}, of which one occurred in combination with medication
190 intake³². One study combined a Semont maneuver with a Galletti-Contrino maneuver²¹. Five
191 studies chose between the Epley and Semont maneuver^{17,36,40,43,49}, and five studies did not
192 specify which CRP was used^{27,42,45,52,53}. The total number of CRPs varied from

193 one^{23,24,27,28,35,37,41,45,46,55} to seven⁴² maneuvers. *Table 1 and Supplementary Table S2* provide
194 a detailed description of the study and treatment characteristics.

195 **The influence of age on treatment success**

196 *Treatment efficacy after one maneuver*

197 Sixteen studies evaluated the effect of age on the success rate after one maneuver
198 (*Supplementary Table S3*), of which ten could be included in a meta-analysis (Figure 1A).

199 A significantly higher success rate was found in the younger age group (OR 1.47; 95% CI 1.23
200 – 1.77). Non-significant heterogeneity was found ($p=0.64$), as well as consistency between the
201 studies ($I^2=0\%$).

202 Of the six articles without numeric age-group data, five studies found no influence of age on
203 treatment outcome after one CRP^{23,28,36,41,60}. Korres *et al.* (2005) found a better initial
204 response to treatment in the younger age group ($p<.001$)⁵⁰.

205

206 *Number of maneuvers needed for successful treatment*

207 Ten studies reported the influence of age on the number of maneuvers needed for successful
208 treatment^{8,20,22,31,38,42,48,49,54,59} (*Supplementary Table S3*), of which seven could be used in a
209 meta-analysis (Figure 1B). An average of 1.4 and 1.5 maneuvers were needed for complete
210 resolution in the younger and older groups, respectively ($p=0.02$). Non-significant
211 heterogeneity was found ($p=0.16$), as well as consistency between the studies ($I^2=36\%$).
212 Batuecas *et al.* (2014) showed that adults aged 70 and older had twice the chance of requiring
213 three or more CRPs as compared to younger adults ($p=0.02$)⁸. In contrast, two studies found
214 no relation between the number of CRPs and age^{22,38}.

215 *Global treatment efficacy*

216 The influence of age on general treatment efficacy was reported in 21 studies
217 (*Supplementary Table S3*)^{18,21,29,32-37,39,40,44,48-51,53-55,58,59}, of which eight could be used in a
218 meta-analysis (Fig. 1C). A scoring correction was applied for studies in which a 100%
219 treatment efficacy was found (n=4)^{48,49,54,59} to enable their inclusion in the meta-analysis. A
220 detailed description of this correction can be consulted in Supplementary Text S3. The
221 overall treatment efficacy did not differ between the two groups (p=0.41), even though the
222 implemented scoring correction was slightly (but negligibly) in favor of the younger age
223 group. In the younger age group, 97.5% of patients were treated successfully, whereas
224 94.6% of the older age group was treated successfully. Non-significant heterogeneity was
225 found (p=0.19), as well as consistency between the studies (I²=30%).

226 *Residual dizziness after successful treatment*

227 Five studies reported residual dizziness, i.e., unsteadiness or lightheadedness without
228 positional nystagmus, after successful treatment for BPPV^{24,25,27,30,58}. The influence of age on
229 residual dizziness is inconclusive. Two studies found a significantly higher incidence of residual
230 dizziness with increasing age using a regression analysis^{25,30}. Also, the duration of residual
231 dizziness increased with age³⁰. Three studies did not find an age-related effect on residual
232 dizziness^{24,27,58}.

233 **The influence of age on recurrence rate**

234 The effect of age on recurrence rate was evaluated in 20 studies^{8,17-19,22,26,29,31,38,43-48,50,52,55-57}
235 (see *Supplementary Table S3*), of which seven could be included in a meta-analysis (Fig. 1D).

236 A lower recurrence rate was significantly associated with younger age (OR 0.75; 95% CI
237 0.61;0.92). Non-significant heterogeneity was found ($p=0.46$), as well as consistency between
238 the studies ($I^2=0\%$).

239 Two studies supported these findings^{26,50}. Korres *et al.* (2005) did not specify age cut-off value,
240 while Prokopakis *et al.* (2013) had an age cut-off value of 70 years. Eleven studies found no
241 significant relationship between age and recurrence rate^{17-19,22,29,44-47,52,55}.

242 Two studies reported no association between time to recurrence and increasing age^{45,46},
243 whereas Kao *et al.* (2009) found a longer symptom-free duration before recurrence with
244 higher age⁴⁸.

245

246 **DISCUSSION**

247 This is the first systematic review and meta-analysis examining the effect of age, based on
248 precisely defined age groups, on treatment efficacy and recurrence rate in people with BPPV.
249 The success rate of a single CRP was significantly higher in the younger group as compared to
250 the older group. Overall, the younger group needed 0.1 fewer CRPs as compared to the older
251 group to obtain complete recovery. Even though this discrepancy is statistically significant, the
252 difference is minimal and not clinically important. Indeed this result indicates that only one in
253 ten older adults will require an additional CRP to obtain complete recovery from BPPV as
254 compared to the younger adults. In addition, the rate of complete recovery (i.e., global
255 treatment efficacy) is equal for older and younger adults. However, likely due to the more
256 accurate and reliable division of age groups in our study, we were able to demonstrate that

257 the recurrence rate is significantly higher for older adults as compared to younger adults, in
258 contrast to the study of Sim et al. (2019).

259 This is the first meta-analysis examining the effect of age on the success of a single CRP and
260 the total number of CRPs needed for recovery. The findings were supported by some^{8,50} but
261 not all articles used in the qualitative review. A major part of the included articles did not find
262 an age-related effect. The discrepancy may be related to the large variation in the applied
263 protocols, a potential lack of power, and the moderate quality of these studies. The statistical
264 procedure was not well described in 23 of 45 studies, and none of the included articles
265 performed a power calculation *a priori*. Furthermore, studies that did not find an age-related
266 effect on treatment outcome had a shorter follow-up time, ranging from 1h to 96hrs^{35,39},
267 whereas the guidelines recommend performing a re-assessment after one month¹¹.

268 This is the first systematic review examining the effect of age on residual dizziness. The results
269 regarding residual dizziness were inconclusive. The two studies indicating that older adults
270 were prone to residual dizziness measured this outcome 2 to 3 days^{25,28} after the treatment,
271 whereas the other studies evaluated residual dizziness after one week^{24,27,58}. Maas et al.
272 (2019) reported that, specifically in older adults, nausea could indeed be a side effect of the
273 Epley maneuver in the first days post-treatment⁶¹.

274 **Potential Explanations for Age Differences in BPPV Treatment Success**

275 Despite the fact that BPPV is the most common vestibular disorder, it has a low recognition
276 rate in primary healthcare, particularly in older adults^{4,8,62}. Older adults report disequilibrium
277 or imbalance as the clinical presentation of BPPV, without reporting vertigo. The patient often
278 attributes these symptoms to “ageing” and also takes longer to seek medical attention as

279 compared to younger adults^{7,8,10}. These complaints are often misdiagnosed and attributed to
280 other medical, neurological, or age-related changes, resulting in a delayed diagnosis of BPPV
281 in older adults^{9,10,11}. The effect of this delayed diagnosis on treatment effectiveness is still
282 unclear. Batuecas et al. (2013) found that the success rate of the treatment of BPPV decreases
283 the longer the symptoms remain untreated⁸. Others claim that symptom duration is irrelevant
284 to treatment outcome^{24,39,50}.

285 The degeneration of the vestibular system may lead to deformities of the semicircular canals
286 in older adults. Furthermore, the continuous demineralization of otoconia that causes
287 detachment from the otoconial membrane can make treatment less effective in older adults⁶³.

288 An insufficient ability to rotate and hyperextend the neck may also be one of the reasons older
289 adults require a higher number of maneuvers to obtain complete resolution^{8,31}. More
290 precisely, limited neck rotation, spinal arthritis, or other illnesses that require some
291 modification of the standard CRP can impair the effectiveness of the repositioning⁴².

292 Older adults (>70 years) experience significantly more discomfort, nausea, and pain in the
293 neck and back directly after the Epley maneuver and are approximately 2.5 times more likely
294 to refuse potential retreatment as compared to younger adults (<70 years)⁶¹. Older adults may
295 refuse retreatment due to anxiety, nausea, and a lack of faith in the effectiveness of the
296 treatment, while younger adults may refuse retreatment because of logistic problems and the
297 belief that retreatment would be more incapacitating than their remaining symptoms.
298 Therefore, education on treatment benefits and the impact of BPPV on both daily activities
299 and quality of life is extremely important, especially in older adults because retreatment is
300 often necessary in this group.

301 **Explanations for age differences in recurrence rate**

302 In general, older adults are less mobile and physically active than younger adults, spending
303 longer time periods in a lounging or lying down position, resulting in a higher probability of
304 developing BPPV and a higher risk of recurrence³¹. Also, older adults are less frequently
305 exposed to symptom-provoking movements, potentially explaining the longer symptom free
306 duration before BPPV recurred⁴⁸.

307 In addition, osteoporosis and the protracted state of vitamin D deficiency, which are
308 inevitably related to one another, are significantly associated with a higher recurrence of
309 BPPV^{4,38}. Low vitamin D levels affect the bone and the inner ear directly by opening the
310 calcium channels in the gut, stimulating the absorption of calcium, and indirectly via
311 parathyroid hormone (PTH) release^{4,64,65}. The release of PTH stimulates the absorption of
312 calcium in the entire body. In the inner ear, calcium carbonate will be absorbed from the
313 otoconia, potentially leading to the fragmentation of the otoconia⁴. In turn, the
314 displacement of these otoconial fragments into the SCCs may cause a recurrence of BPPV^{4,}
315 ⁶⁵. Furthermore, due to the increased calcium resorption in the inner ear, the endolymphatic
316 free-calcium concentration rises, resulting in a diminished capacity to dissolve these
317 dislodged otoconial fragments⁶⁵.

318

319 **Strengths and limitations**

320 This review has several strengths. First, the study selection was performed by two
321 independent reviewers in two databases (i.e., Web of Science and Pubmed). Second, a
322 detailed methodological quality assessment was carried out by three independent reviewers.
323 In both cases, the reviewers discussed the results until a consensus was reached. In addition

324 to English, articles in Dutch, French, and German were also included. However, some
325 additional information may have been missed due to the remaining language limitations.

326 Treatment effectiveness and recurrence rate were analyzed using young and old age groups
327 within each article, if such were present, whereas Sim *et al.* (2019) attributed complete articles
328 to either the young or old age group¹⁵. However, not all included articles investigated the
329 effect of age as a primary goal, and only a minority of studies defined age groups *a priori*. This
330 negatively influenced the assessment of methodological quality in terms of our research
331 question. Still, for most outcome variables, sufficient studies could be included in a meta-
332 analysis. The included studies had a great range in sample size. However, none of the articles
333 performed a power calculation *a priori*. Differences in functional limitations, symptomatology,
334 or time between the onset of symptoms and the diagnosis between younger and older adults
335 on the one hand and a lack of high-quality articles with age as a primary outcome on the other
336 hand make it difficult to provide additional recommendations regarding the appropriate
337 treatment approach in older adults.

338 **Future directions**

339 The results show that the rate of complete recovery in older adults is similar to that in
340 younger adults, even though older adults are more exposed to the disease and require more
341 treatment sessions³⁹. The longer treatment duration keeps older people longer at risk of
342 falling. This adds to the already increased risk of falling in older adults as compared to
343 healthy older adults^{8,10}. However, balance improves after BPPV with positioning
344 maneuvers³⁵ and normalizes again to the balance of healthy controls. Still, dynamic balance
345 recovery takes longer for older adults⁶⁶, which is highly important in fall prevention. Correct

346 and timely BPPV diagnosis can decrease the risk of falling. Therefore, future studies should
347 focus on a rapid diagnosis of BPPV in older adults with an increased fall risk.

348 To limit fall risk, a follow-up should be provided, especially for older adults because they are
349 at a higher risk of recurrence. Parham et al. (2016) stated that the management of BPPV will
350 need to evolve beyond the treatment of acute episodes. It should evolve into global
351 management with education and the prevention of recurrence via monitoring and treating
352 risk factors related to the recurrence of BPPV (i.e., Vitamin D deficiency)⁴. Patients should be
353 educated about predictive symptoms indicating a recurrence of BPPV (i.e., positional vertigo
354 lasting ≤ 1 minute, nausea, and the feeling of being “off balance”) and what to do when they
355 experience a recurrence¹¹. Moreover, treating physicians should keep in mind that older
356 adults require a longer time to recover from BPPV and the chances of recurrence are higher.
357 Future studies should examine the effect of post-treatment physical activity in older adults on
358 recurrence rate in this population.

359 **Conclusion**

360 The overall treatment efficacy for BPPV is similar in younger and older adults. Nevertheless,
361 the recognition of the condition in the older population is more complex, treatment requires
362 more CRPs (due to degeneration of the vestibular system, decreased neck mobility and
363 cooperation), and the risk of recurrence is greater.

364

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Conflict of Interest Checklist:

Elements of Financial/Personal Conflicts	GL		LV		NH		EV		LC		JS	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Employment or Affiliation		X		X		X		X		X		X
Grants/Funds		X		X		X		X	X			X
Honoraria		X		X		X		X		X		X
Speaker Forum		X		X		X		X		X		X

Consultant		X		X		X		X		X		X
Stocks		X		X		X		X		X		X
Royalties		X		X		X		X		X		X
Expert Testimony		X		X		X		X		X		X
Board Member		X		X		X		X		X		X
Patents		X		X		X		X		X		X
Personal Relationship		X		X		X		X		X		X

*Authors can be listed by abbreviations of their names

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TABLES

Table 1 – Simplified study characteristics table

GENERAL STUDY CHARACTERISTICS					TREATMENT CHARACTERISTICS	
AGE GROUPS DEFINED A PRIORI						
Author	Type of study	n =	Mean age (years) ± SD	% PSCC	Treatment	Max # CRPs
Anagnostou et al. (2007) ¹⁷	Prospective study	70	59.5 ± 13.3	100	Epley/Semont	N.S.
Batuecas-Caletrio et al. (2013) ⁸	Retrospective cohort study	404	N.S.	82.5	Epley/Lempert/Yacovino	>3
Jang et al. (2009) ³⁸	Prospective study	78	48,0	39	Modified Epley + PR/ Barbecue + PR	5
Simoceli et al. (2005) ³⁷	Randomized prospective study	50	60.9 ± 15.3	100	Epley (2X) with/without PR	1
Yeo et al. (2018) ³¹	Prospective study, record review	370	59.5 ± 12.3	54.6	Reverse Epley/modified Epley /360° Barbecue	N.S.
Zhu et al. (2019) ⁴³	Retrospective study	1012	N.S.	76.2	Epley / Semont/ Lempert / Barbecue + Gufoni / modified Semont	N.S.
AGE AS A COVARIATE						
Author	Type of study	n =	Mean age (years) ± SD	% PSCC	Treatment	Max # CRPs
Beynon et al. (2000) ¹⁹	Prospective consecutive series	51	60 ± 13	100	Modified Epley	2

Bruintjes et al. (2014)³⁴	Randomized, double-blind, sham-controlled trial	44	59.1 ± 13	100	Epley + PR/ Sham intervention + PR	2
Ciodaro et al. (2018)²¹	Prospective cohort study	408	N.S.	100	Galletti-Contrino/ Semont	2
Cohen et al. (2005)³⁵	Prospective, randomized, sham-controlled	124	58.3 ± 12.8	100	Modified CRP/ modified liberatory maneuver/ Brandt-Daroff exercises/ vertigo habituation exercises/sham maneuver	1
Do et al. (2011)²²	Prospective study	138	51.6 ± 16.4	55.8	Modified Epley/Barbecue	N.S.
Hain et al. (2000)⁴⁵	Retrospective case review	94	58 ± 16	100	CRP with/without vibration + PR	1
Korkmaz et al. (2016)⁴⁹	Retrospective study	153	53.6	87.6	Semont/ Epley/Barbecue + PR	5
Levrat et al. (2003)⁵¹	Retrospective study	278	Median age 55.5	100	Semont	4
Martellucci et al. (2016)²⁵	Prospective cohort study	86	58.2 ± 15	100	Epley	4
Oh et al. (2017)³⁶	Prospective randomized controlled trial	506	64 ± 12	100	Epley/Semont	2
Radtke et al. (2004)⁴⁰	Prospective randomized study	70	60 ± 12	100	Epley/Semont	3x daily
Tanimoto et al. (2008)⁵⁷	Retrospective chart review	145	60	72	Epley/Lempert/no treatment	N.S.
Teggi et al. (2011)³⁰	Prospective study	60	72 ± 4	76.7	Semont/Gufoni + Lempert/Modified Epley	>3
Wei et al. (2018)⁵⁸	Retrospective study	127	53.9 ± 13.9	84.2	Epley/Barbecue	N.S.
Wolf et al. (1999)³⁹	Prospective study	41	N.S.	100	Epley	N.S.
Yoon et al. (2018)⁵⁹	Retrospective study	1426	54.9	39.1	Modified Epley with/without Brandt-Daroff +PR/ Barbecue with vibrations + PR	7
AGE AS A UNIVARIATE FACTOR						

Author	Type of study	n =	Mean age (years) ± SD	% PSCC	Treatment	Max # CRPs
Albera et al. (2018) ⁴¹	Retrospective cohort study	113	62.6 ± 12	100	Semont	1
Babac et al. (2014) ¹⁸	Prospective cohort study	400	58.7 ± 12	86	Modified Epley/semont/ barbecue /inverted Gufoni / Kim Maneuver	4
Casqueiro et al. (2008) ²⁰	Prospective double-blind consecutive case study	391	57.2	100	Epley with/without PR	5
Cavaliere et al. (2005) ³²	Prospective study	103	N.S.	100	Semont with/without betahistine. Brandt-Daroff with/without betahistine.	N.S.
Dominguez-Duran et al. (2017) ²³	Observational prospective multicenter study	234	62	100	Epley + PR	1
Dornhoffer et al. (2000) ⁴⁴	Retrospective study	52	63	N.S. ^a	Epley + PR	3
Helminski et al. (2005) ⁴⁶	Retrospective study (and random sample of convenience)	116	57 ± 16	100	Epley with/without vibrations + PR Brandt-Daroff exercises	1
Kansu et al. (2010) ⁴⁷	Retrospective study	118	51.8 ± 14.7	100	CRP with mastoid oscillation + PR	6
Kao et al. (2009) ⁴⁸	Retrospective study	218	68.1 ± 14.4	78.4	Epley/Semont/Barbecue	3
Kim et al. (2014) ²⁴	Prospective study	58	55.8 ± 10	36.2	Epley/Barbecue Maneuver with/without mastoid vibrations + PR/Reverse Epley	1
Korres et al. (2006) ⁵⁰	Retrospective study	155	59.9 ± 12.6	82.6	Moddified Epley/Vannucchi	2
Luryi et al. (2018) ⁵²	Retrospective study	1105	64.6 ± 14.6	N.S. ^a	CRP appropriate for the SCC	≥3
Macias et al. (2000) ⁴²	Retrospective study	259	58.6	93.1	CRP appropriate for the SCC	7
Martellucci et al. (2019) ⁶⁰	Retrospective study	47	62.1 ± 13.1	100	Epley	4

Monobe et al. (2001)⁵³	Retrospective study	62	Median age of 63	100	CRP + PR	2
Moreno et al. (2009)⁵⁴	Retrospective study	71	54.9	100	Modified Epley	4
Otsuka et al. (2013)⁵⁵	Retrospective study	357	60	65	Epley/Medication/Lempert/non-specific physical techniques	1
Prokopakis et al. (2013)²⁶	Prospective study	965	range 18 - 87 years	88	Modified Epley + vibrations+ PR/ modified Barbecue + PR	>3
Radtke et al. (1999)³³	Prospective study	54	54.8 ± 11.7	100	Brandt-Daroff exercises /Modified Epley.	3x daily BD
Seo et al. (2017)²⁷	Prospective study	44	N.S.	100	CRP	1
Soto-Varela et al. (2011)²⁸	Prospective study	135	60.9	100	Semont	1
Soto-Varela et al. (2012)²⁹	Prospective study	412	58	100	Semont/Epley/Brandt-Daroff exercises	4
Su et al. (2016)⁵⁶	Retrospective study	247	57.5 ± 13.9	100	Epley	6

Note: ^aBased on the diagnostic tests (i.e. Dix-Hallpike) it could be assumed that posterior canal BPPV was included in these articles.

Abbreviations: SD: standard deviation; SCC: semicircular canal; PSCC: posterior semicircular canal; CRP: canalith repositioning procedure; max #

CRPs: maximum number of canalith repositioning procedures; PR: postural restrictions

LEGENDS

Figure 1: Impact of age on treatment efficacy after one CRP, number of CRPs and recurrence rate.

A. Impact of age on treatment efficacy after one CRP: comparison of success rate after one maneuver between younger adults (<70 years) and older adults (≥70 years).

*Legend: * Articles with an age cut-off value of 65 years, defining younger adults as persons <65 years and older adults as persons ≥65 years old. ** Articles with an age cut-off value of 60 years, defining younger adults as persons <60 years and older adults as persons ≥60 years old. A significant result is visualized by the diamond shape not crossing the central vertical line. CI confidence interval, M-H Mantel-Haenszel.*

B. Impact of age on number of maneuvers: comparison of number of CRP between younger (<70 years) adults and older adults (≥70 years)..

*Legend: ** Articles with an age cut-off value of 65 years, defining younger adults as persons <65 years and older adults as persons ≥65 years old. CI confidence interval, M-H Mantel-Haenszel.*

C. Impact of age on global treatment efficacy: comparison of global success rate between younger adults (<70 years) and older adults (≥70 years).

*Legend: * Articles with an age cut-off value of 65 years, defining younger adults as persons <65 years and older adults as persons ≥65 years old. ** Articles with an age cut-off value of 60 years, defining younger adults as persons <60 years and older adults as persons ≥60 years old. CI confidence interval, M-H Mantel-Haenszel*

D. Impact of age on recurrence rate: comparison of recurrence rate between younger adults (<70 years) and older adults (≥70 years).

*Legend: * Articles with an age cut-off value of 65 years, defining younger adults as persons <65 years and older adults as persons ≥65 years old, ** Articles with an age cut-off value of 60 years, defining younger adults as persons <60 years and older adults as persons ≥60 years old.*

CI confidence interval, M-H Mantel-Haenszel

Supplementary Text S1 - Search string

Supplementary Text S2 – Modified version of the SIGN checklist for cohort studies

Supplementary Text S3– Detailed description of the correction for studies reporting 100% global treatment efficacy

Supplementary Figure S1 – Flow chart of the selection process

Supplementary Table S1 – Risk of bias assessment

Supplementary Table S2 – Detailed description characteristics of the included studies

Supplementary Table S3: Treatment efficacy and recurrence rate influenced by age.

Supplementary Table S4 – PRISMA 2009 Checklist

SUPPLEMENTARY MATERIALS

Supplementary Text S1 - Search string

Pubmed

("Benign Paroxysmal Positional Vertigo"[MeSH] OR "Benign Paroxysmal Positional Vertigo"[title/abstract] OR "BPPV"[title/abstract]) AND ("Epley"[title/abstract] OR "Sémont"[title/abstract] OR "Gans"[title/abstract] OR "Reposition"[title/abstract] OR "hybrid"[title/abstract] OR "liberatory"[title/abstract] OR "habituation"[title/abstract] OR "Brandt-Daroff"[title/abstract])

Web of Science

TS=(("Benign Paroxysmal Positional Vertigo" OR "BPPV") AND ("Epley" OR "Sémont" OR "Gans" OR "Reposition"[title/abstract] OR "hybrid"[title/abstract] OR "liberatory" OR "habituation" OR "Brandt-Daroff")) OR TI=(("Benign Paroxysmal Positional Vertigo" OR "BPPV") AND ("Epley" OR "Sémont" OR "Gans" OR "Reposition"[title/abstract] OR "hybrid"[title/abstract] OR "liberatory" OR "habituation" OR "Brandt-Daroff"))

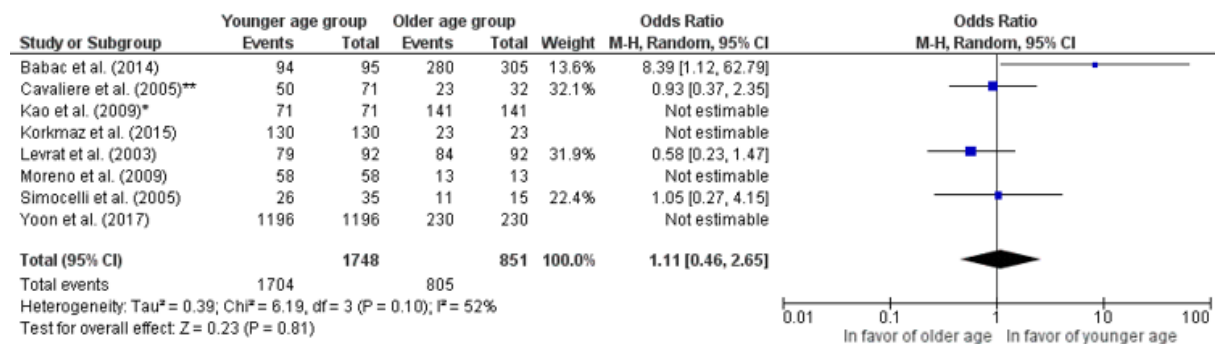
Supplementary Text S2 – modified version of the SIGN checklist for cohort studies

1. Was the effect of age on treatment outcome or recurrence the primary goal or clearly stated as a secondary goal of the study?
 - a. Yes
 - b. No
2. How was the effect of age investigated?
 - a. Anterograde composition of age groups
 - b. Covariate (analysis of variance, regression analysis)
 - c. Retrograde univariate analysis – E.g. recurrence rate used as a grouping variable and mean age/ age groups is compared between outcome groups.
3. Was the statistical procedure to study the age effect well described in the methods section?
 - a. Yes
 - b. No, but available in results or tables
 - c. No, not available in results or tables
4. Which type of BPPV was included (cupulo- versus canalolithiasis)?
 - a. Only canalolithiasis
 - b. Canalolithiasis and cupulolithiasis
 - c. Not reported
5. Which canals were included (studies dealing with anterior or horizontal canal involvement only were excluded a priori)?
 - a. Only posterior canal
 - b. Posterior canal and horizontal and/or anterior canal
 - c. Not reported
6. Were the type of BPPV and the affected canals accounted for in the statistical analysis?
 - a. Yes
 - b. No
 - c. Not applicable (only PSCC canalolithiasis studies)
7. Was the treatment procedure clearly described?
 - a. Yes
 - b. No
8. Was the assessment of treatment efficacy clearly defined in the methods section?
 - a. Yes
 - b. No
 - c. Not applicable (treatment efficacy not studied)
9. Was the assessment of recurrence clearly defined in the methods section?
 - a. Yes
 - b. No
 - c. Not applicable (recurrence not studied)
10. Were the number of recruited and included participants reported?
 - a. Yes: ... % included
 - b. No
 - c. Not applicable (in case of retrospective analysis)
11. Were the dropouts reported?
 - a. Yes: ... % dropout
 - b. No (Q12, N/A)
 - c. Not applicable (in case of retrospective analysis)
12. Were dropouts compared to the full participants?

- a. Yes
- b. No
- c. Not applicable

Supplementary Text S3– Detailed description of the correction for studies reporting 100% global treatment efficacy

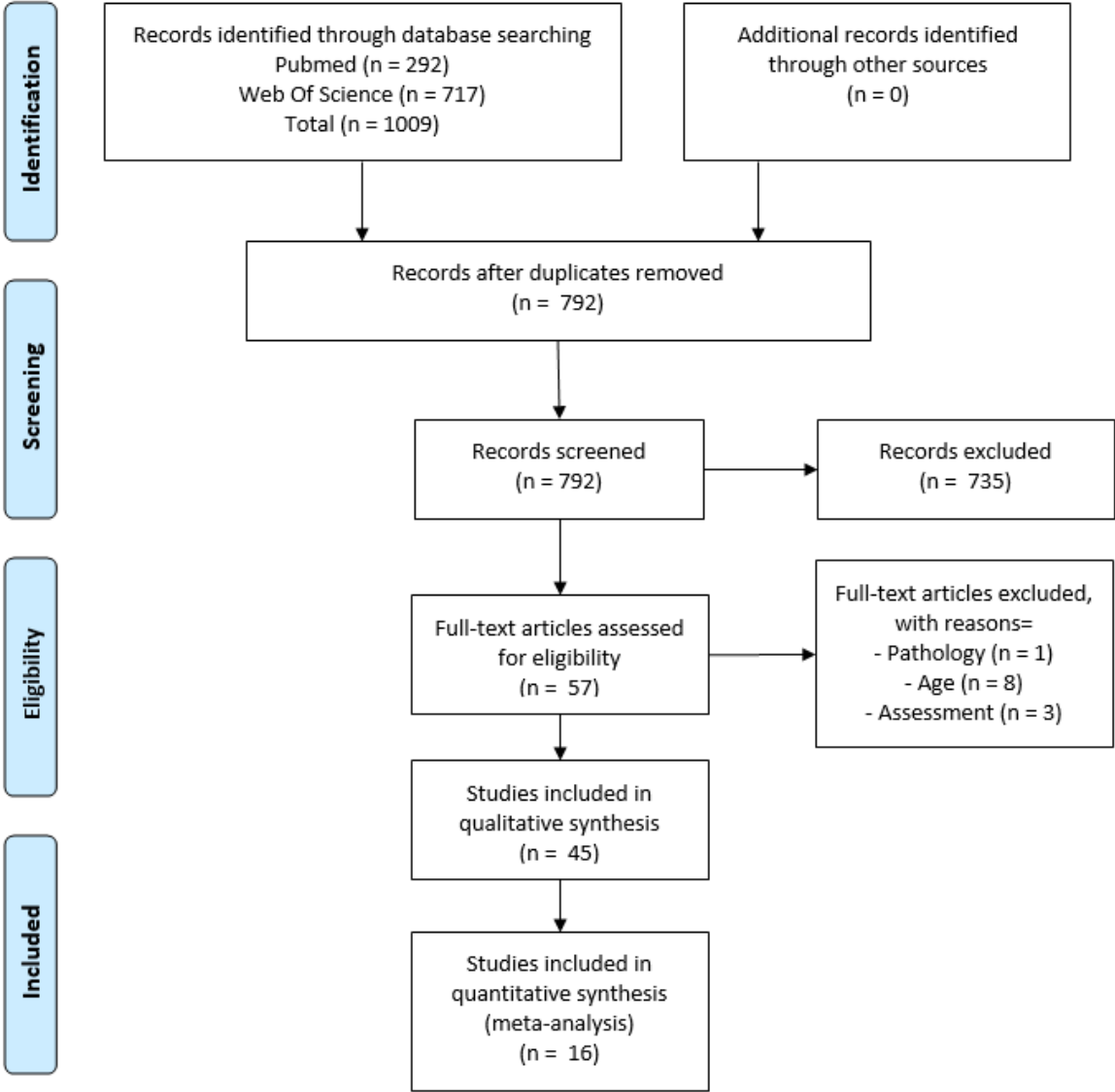
Four of the included studies reported a treatment effectiveness of 100% in the older and the younger group^{48, 49, 54, 59}. The odds ratio cannot be calculated for studies if there are no events, therefore a scoring correction of -1 was applied to these studies in both groups based on the Revman handbook chapter 9.2.2.2. Leading to 1 event in the younger and older age group^{48, 49, 54, 59}. This correction was unfavorable for the older age group, because the proportion of older adults was smaller (n=851). Although the treatment correction was in favor of the younger age group, the global treatment efficacy did not differ (OR 1.35; 95% CI 0.66 – 2.74).



Supplementary Figure S1 – Flow chart of the selection process



PRISMA 2009 Flow Diagram



Supplementary Table S1 – Risk of bias assessment

Author	Question number											
	1	2	3	4	5	6	7	8	9	10	11	12
Albera et al. (2018) ⁴¹	B	C	B	A	A	C	A	A	C	C	C	C
Anagnostou et al. (2007) ¹⁷	B	A	B	C	A	B	B	C	A	100	B	C
Babac et al. (2014) ¹⁸	A	C	B	B	B	B	A	A	A	B	B	C
Batuecas-Caletrio et al. (2013) ⁸	A	A	A	B	B	A	A	A	A	C	C	C
Beynon et al. (2000) ¹⁹	B	B	A	A	A	C	A	A	A	100	0	C
Bruintjes et al. (2014) ³⁴	B	B	A	C	A	C	A	A	C	7.3	13.6	A
Casqueiro et al. (2008) ²⁰	B	C	B	A	A	C	A	A	B	100	5.9	B
Cavaliere et al. (2005) ³²	B	C	B	A	A	C	A	A	A	100	B	C
Ciodaro et al. (2018) ²¹	B	B	A	C	B	A	A	A	C	B	B	C
Cohen et al. (2005) ³⁵	B	B	A	C	A	C	A	A	C	B	16.2	B
Do et al. (2011) ²²	B	B	B	B	B	A	A	A	A	100	B	C
Dominguez-Duran et al. (2017) ²³	A	C	B	A	A	C	A	A	C	61	12.7	B
Dornhoffer et al. (2000) ⁴⁴	B	C	B	A	A	C	A	A	A	100	A	C
Hain et al. (2000) ⁴⁵	B	B	B	A	A	C	A	A	A	C	C	C
Helminski et al. (2005) ⁴⁶	B	C	B	A	A	C	A	C	A	B	B	C
Jang et al. (2009) ³⁸	B	A	A	A	B	A	A	A	C	68	20	B
Kansu et al. (2010) ⁴⁷	B	C	B	A	A	C	A	A	A	73.3	C	C
Kao et al. (2009) ⁴⁸	A	C	A	B	B	B	A	A	A	B	C	C
Kim et al. (2014) ²⁴	B	C	A	B	B	A	A	A	C	64.5	0	C
Korkmaz et al. (2016) ⁴⁹	A	B	A	C	B	A	A	A	C	C	C	C
Korres et al. (2006) ⁵⁰	A	C	A	B	B	A	A	A	A	100	89.6	B
Levrat et al. (2003) ⁵¹	A	B	A	C	A	C	A	A	C	C	C	C
Luryi et al. (2018) ⁵²	A	C	A	C	C	B	B	C	A	36.7	B	C
Macias et al. (2000) ⁴²	A	C	B	C	B	A	B	A	C	C	C	C
Martellucci et al. (2016) ²⁵	A	B	A	A	A	C	A	A	C	100	11.3	B
Martellucci et al. (2019) ⁶⁰	B	C	B	C	A	C	A	A	C	100	0	C
Monobe et al. (2001) ⁵³	B	C	B	C	A	C	A	A	C	C	C	C
Moreno et al. (2009) ⁵⁴	A	C	A	C	A	B	A	A	C	C	C	C
Oh et al. (2017) ³⁶	B	B	A	C	A	B	A	A	C	92	0	C
Otsuka et al. (2013) ⁵⁵	A	C	B	B	B	A	A	B	A	9.4	0	C
Prokopakis et al. (2013) ²⁶	A	C	A	C	B	B	A	A	B	B	7.3	B
Radtke et al. (1999) ³³	B	C	B	A	A	C	A	A	C	87.1	0	C
Radtke et al. (2004) ⁴⁰	B	B	B	A	A	C	A	A	C	100	11.4	B
Seo et al. (2017) ²⁷	B	C	B	A	A	C	A	A	C	72.1	9.1	B
Simoceli et al. (2005) ³⁷	B	A	B	C	A	C	A	A	C	B	0	C
Soto-Varela et al. (2011) ²⁸	B	B	A	B	B	B	A	A	A	75.7	1.7	B
Soto-Varela et al. (2012) ²⁹	A	C	A	C	A	C	A	A	C	100	0	C
Su et al. (2016) ⁵⁶	A	B	A	C	A	C	a	A	A	C	1.6	B
Tanimoto et al. (2008) ⁵⁷	A	B	B	B	B	A	A	A	A	98	8.3	B
Teggi et al. (2011) ³⁰	A	B	A	C	B	A	A	A	C	100	0	C
Wei et al. (2018) ⁵⁸	B	B	A	C	B	A	A	A	A	92.7	3.8	B

Wolf et al. (1999) ³⁹	B	B	B	C	A	C	A	A	B	82	B	C
Yeo et al. (2018) ³¹	A	A	A	A	B	B	A	A	A	41	0	B
Yoon et al. (2018) ⁵⁹	A	B	B	B	B	A	A	A	A	C	B	C
Zhu et al. (2019) ⁴³	A	A	A	C	B	B	A	A	A	96.7	3.3	B

Supplementary Table S2 – detailed description characteristics of the included studies

GENERAL STUDY CHARACTERISTICS						TREATMENT CHARACTERISTICS				
AGE GROUPS DEFINED A PRIORI										
Author	Type of study	Included (nr) (%women)	Mean age (years) ± SD	Affected SCC (%)	Diagnostic test	Treatment	Max # CRPs	Definition success	Definition recurrence	Definition RD
Anagnostou et al. (2007) ¹⁷	Prospective study	70 (61.4)	59.5 ± 13.3 Group 20-39 years Group 40-59 years Group >59 years	PSCC 100%	DH	Epley Semont	N.S.	N.S.	N.S.	N.S.
Batuecas-Caletrio et al. (2013) ⁸	Retrospective cohort study	404 (61)	Group <70 years: 53.8 (n=193) Group ≥70 year: 77.7 (n=211)	PSCC 82.5% HSCC 10.4% ASCC 5.9% Multiple 1% Can 84.9% / Cup 15.10%	DH+RT	PSCC: Epley HCSS: Lempert ACSS: Yacovino	>3	Negative HD or RT (after 7-11 days)	N.S.	N.S.
Jang et al. (2009) ³⁸	Prospective study	78 (100)	48 Group A: 20-39 years (n=20) Group B: 40-49 years (n=21) Group C: 50-59 years (n=18) Group D: 60-69 years (n=19)	PSCC 71.8% HSCC 28.2%	DH / lateral head turn	PSCC: modified Epley + avoid bending over, sleep with the head elevated HSCC: Barbecue maneuver + lie on 1 side (affected ear up)	5	No vertigo and negative provocative test	Condition in which patients had intermittent episodes of position-induced vertigo of at least 1 month before the first visit.	N.S.
Simoceli et al. (2005) ³⁷	Randomized prospective study	50 (68)	60.9 ± 15.3 <40 years (n=3) 40-60 years (n=16) 60-70 years (n=16) >70 years (n=15)	PSCC 100%	DH	Epley (2X) with/without restrictions (sleep with head elevated using two pillows; not perform sudden head movements, ; not to sleep over the affected ear)	1	Absence of dizziness and/or nystagmus in Dix-Hallpike test	Partial improvement or absence of improvement and positive DH	N.S.
Yeo et al. (2018) ³¹	Prospective study,	370 (67)			DH/RT video	ASCC= reverse Epley PSCC: modified Epley	N.S.	N.S.	N.S.	N.S.

	reviewing records		59.6 ± 12.3 ≥65 years (n=136) <65 years (n=234)	PSCC 54.6% HSCC 41.4% ASCC 4%	nystagmogram (ambiguous results)	HSCC: 360° Barbecue maneuver				
Zhu et al. (2019)⁴³	Retrospective study	1012(67.2)	Group 18-45 years: 37.1 ± 6.5 (n=208)Group 45-60 years: 53.6 ± 4.2 (n=489)Group >60 years: 67.7 ± 5.9(n=315)	PSCC 76.2% HSCC 23.8%(Of which 4% both)	DH+RT	PSCC: Epley / Semont HSCC: Lempert / Barbecue + Gufoni / modified Semont	N.S.	The absence of vertigo and nystagmus on positional testing.	Recurrence positional vertigo + nystagmus (DH/RT) after successful treatment for 1 week	N.S.
AGE AS A COVARIATE										
Author	Type of study	Included (nr) (% women)	Mean age (years)	Affected SCC (%)	Diagnostic test	Treatment	Max # CRPs	Definition success	Definition recurrence	Definition RD
Beynon et al. (2000)¹⁹	Prospective consecutive series	51 (67)	60 ± 13	PSCC 100%	DH	Modified Epley	2	Negative DH (after 1-2 weeks)	Recurrence of positional provoked vertigo after a negative DH	N.S.
Bruintjes et al. (2014)³⁴	Randomized, double-blind, sham- controlled trial	44 (59)	59.1 ± 13	PSCC 100%	DH	Epley / Sham intervention Both groups postural restrictions: sleep with the head elevated (48 h) and avoid lying down on the affected side (48 h)	2	Negative DH	N.S.	N.S.
Ciodaro et al. (2018)²¹	Prospective cohort study	408 (57)	Overweight: 55.5 ± 4.1 non-overweight: 54.2 ± 3.4	PSCC 91% ASCC 9%	DH + videonystagmoscopy	Galletti-Contrino/ Semont	2	N.S.	N.S.	N.S.
Cohen et al. (2005)³⁵	Prospective, randomized, sham- controlled	124 (61.3)	58.3 ± 12.8	PSCC 100%	DH + Electro-oculography	The five treatment groups : 1) modified CRP (n = 24) 2) modified liberatory maneuver (LM) (n = 25) 3) Brandt-Daroff exercise (n = 25) 4) Vertigo habituation exercises (n = 25) 5) Sham maneuver (n = 25).	1	The absence of vertigo on positional testing (DH).	N.S.	N.S.

Do et al. (2011)²²	Prospective study	138 (66.7)	51.56 ± 16.39	PSCC 55.8% HSCC 34.8% (Can 58.3%/ Cup 41.6%) Multiple 9.4%	Positional testing, Frenzel glasses of video image	PSCC: Modified Epley HSCC: Barbecue maneuver	N.S.	Disappearance of vertigo and nystagmus during positional maneuver	The reappearance of a similar whirling dizziness or similar rotating nystagmus.	N.S.
Hain et al. (2000)⁴⁵	Retrospective case review	94(77)	58 ± 16	PSCC 100%	DH	CRP without vibration (1991 - 1997) CRP with vibration (1994 - 1996) Both groups -- > Avoid the following: sleeping with the ear in a dependent position, rapid head movements, extreme flexion and extension of the neck, and provoking po- sitions.	1	Relieving symptoms	BPPV in the same ear or opposite ear redeveloped BPPV symptoms (25-day to 5.25 year follow- up)	N.S.
Korkmaz et al. (2016)⁴⁹	Retrospective study	153 62.1% women	53.6	PSCC 87.6% HSCC 7.8% ASCC 3.3% Multiple 1.3%	DH+RT Frenzel glasses	PSCC+ASCC: Semont/ Epley HSCC: Barbecue maneuver Both groups postural restrictions: sleep with the head elevated (48 h) and avoid up and down movements of the head (48 h)	5	Absence of both nystagmus and vertigo during DH or RT.	N.S.	N.S.
Levrat et al. (2003)⁵¹	Retrospective study	278 (65)	Median age 55.5 (range, 13.5 to 91.5 years).	PSCC 100%	Triggering maneuver of Brandt-Daroff	Semont	4	Symptoms had completely disappeared	N.S.	N.S.
Martellucci et al. (2016)²⁵	Prospective cohort study	86 (62)	58.23 ± 14.98	PSCC 100%	DH + RT (to exclude HSCC BPPV)	Epley	4	Absence of both vertigo and positional nystagmus	N.S.	Residual dizziness (i.e. unsteadiness and/or light- headedness and/or dizziness) without true vertigo and nystagmus.

Oh et al. (2017)³⁶	Prospective randomized controlled trial	506(59.9)	64 ± 12	PSCC 100%	DH + straight head hanging test Frenzel glasses or video-oculography	1st Maneuver: Epley (n=506)2nd Maneuver non-responders: Epley/Semont	2	Absence of both vertigo and positional nystagmus	N.S.	N.S.
Radtke et al. (2004)⁴⁰	Prospective randomized study	70 (86)	60 ± 12	PSCC (100%)	Lateral head hanging position Frenzel glasses	Self-treatment at home using Epley or Semont (3 times a day, until positional vertigo had ceased for at least 24 hours)	3x daily	Absence of both vertigo and positional nystagmus	N.S.	N.S.
Tanimoto et al. (2008)⁵⁷	Retrospective chart review	145 (63)	60	PSCC 72% HSCC 25.9% (Can 73.6% /Cup 26.3%) Multiple 1.4%	DH+RT	PSCC: Epley HSCC: Lempert (Can), no treatment (Cup)	N.S.	Absence of both vertigo and positional nystagmus	History of nystagmus and BPPV in both the same ear and the other ear.	N.S.
Teggi et al. (2011)³⁰	Prospective study	60 (70)	72 ± 4	PSCC 76.7% HSCC 15% ASCC 3.3% Multiple 5%	DH + Pagnini-McClure test Videonystagmography system	PSCC: Semont HSCC: Gufoni + Lempert ASCC: Modified Epley	>3	Absence of positional nystagmus		The sensation of unsteadiness or light headedness without rotational and/or positional vertigo.
Wei et al. (2018)⁵⁸	Retrospective study	127 (64)	53.9 ± 13.93	PSCC (84.2%) non-PSCC (15.8%)	DH + RT	PSCC +ASCC: Epley HSCC: Barbecue Maneuver	N.S.	Absence of both vertigo and positional nystagmus	Confirmed relapse of vertigo and nystagmus according to DH or RT after successful treatment.	N.S.
Wolf et al. (1999)³⁹	Prospective, study	41 (56)	Group 1: 46.2 ± 13.1 Group 2: 44.7 ± 14.4 Group 3: 45.5 ± 15.5	PCSS (100%)	DH Frenzel glasses	Epley	N.S.	Absence of both vertigo and positional nystagmus	Recurrent episodes through telephone questionnaire	N.S.

Yoon et al. (2018)⁵⁹	Retrospective study	1426(66.1)	54.9	PSCC 39.1% HSCC 30.6% bilateral 14% Multiple 16.3%	DH + RT Videonystagmography	PSCC: Modified Epley with/without Brandt-Daroff HSCC (can): 360° Barcebecue maneuver HSCC(cup): Barbecue maneuver vibration was first applied to the affected ear for 10 seconds. Then the head was immediately rotated through 360 degrees. All groups: avoid rapid head movement, extreme neckflexion and extension, and positions that provoked vertigosymptoms, for 48 hours.	7	Absence of positional nystagmus for ≥ 1 months, within 4 CRP session.	Recurrence of symptoms and nystagmus, combined with a positive positional test, following complete recovery.	N.S.
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AGE AS A UNIVARIATE FACTOR

Author	Type of study	Included (nr) (% women)	Mean age (years)	Affected SCC (%)	Diagnostic test	Treatment	Max # CRPs	Definition success	Definition recurrence	Definition RD
Albera et al. (2018)⁴¹	Retrospective cohort study	113 (64%)	62.6 ± 12	PSCC 100%	DH Frenzel glasses or videonystagmography	Semont	1	Absence of both vertigo and positional nystagmus	N.S.	N.S.
Babac et al. (2014)¹⁸	Prospective cohort study	400 (70.2%)	58.75 ± 12	PSCC 86% HSCC 12.25% ASCC 1.75% Bilateral 0.5% Multiple 0.7%	DH + RT Frenzel glasses	PSCC: Modified Epley/semont (with mastoid vibrations) HSCC: Barbecue maneuver (Can), inverted Gufoni (Cup) ASCC: Kim Maneuver	4	Negative DH or RT (after 4 maneuvers)	Recurrent symptoms along with positive diagnostic tests, after a successful recovery	N.S.
Casqueiro et al. (2008)²⁰	Prospective double-blind consecutive case study	391 (70.6)	57.2	PSCC (100%)	DH	Epley with/without postural restrictions	5	Negative DH (absence of both vertigo and positional nystagmus)	Number of patients that came back with another episode of vertigo after resolution of their previous episode.	N.S.

Cavaliere et al. (2005)³²	Prospective study	103 (65)	LM group 51.6 ± 10.6 LM-BE group: 48.6 ± 9.7 BD group: 49.6 ± 11.4 BD-BE group: 50.5 ± 9.1	PSCC (100%)	DH	LM: Semont without betahistine LM-BE: Semont with betahistine BD: Brandt-Daroff (3X/day) with betahistine. BD-BE: Brandt-Daroff (3X/day) without betahistine	N.S.	Evaluated using Epley's criteria: disappeared, improved, partially resolved, unchanged	N.S.	N.S.
Dominguez-Duran et al. (2017)²³	Observational prospective multicenter study	234 (71)	62	PSCC 100% Can 100%/Cup 0	DH	Epley + sleep with head elevated (30°)	1	Lack of nystagmus in DH, regardless of the presence of vertigo symptoms in that position.	N.S.	N.S.
Dornhoffer et al. (2000)⁴⁴	Retrospective study	52 (75)	63	N.S. Bilateral 7%	DH	Epley + sleep with head elevated at least 30° (48h)	3	Complete response (elimination of nystagmus and symptoms), improved response (elimination of nystagmus but with some residual symptoms), or no response (continued nystagmus and symptoms).	Complete initial response to repositioning followed by a later return of symptoms.	N.S.

Helminski et al. (2005)⁴⁶	Retrospective study (and random sample of convenience)	116 (72)	57 ± 16	PSCC 100% 28%	DH video-Frenzel system	Epley with/without vibrations Postural restrictions: sleep with head elevated (48 h), avoid rapid head movements, extreme flexion and extension of the neck, and positions that provoke symptoms of vertigo, such as placing the involved ear in a dependent position while sleeping (for 1 week) Brandt-Daroff exercises (daily)	1	Cured	Sporadic periods of BPPV symptoms over time.	N.S.
Kansu et al. (2010)⁴⁷	Retrospective study	118 (62.7)	51.8 ± 14.7	PSCC 100% Bilateral 4.2%	DH	CRP with mastoid oscillation. Postural restrictions: avoid abrupt head movements, sleep with head elevated, avoid turning to the affected ear during sleep (48 h)	6	Negative DH (absence of both vertigo and positional nystagmus)	Episodes of BPPV	N.S.
Kao et al. (2009)⁴⁸	Retrospective study	218(66)	68.1 ± 14.4	PSCC 78.4% HSCC 3.7% Bilateral 12.8% Sub BPPV: 4.1% Multiple 0.9%	DH + RT Infra-red video fixation goggles	PSCC: Epley (Can), Liberatory maneuver (Cup) HSCC: Barbecue (Can), Liberatory maneuver (Cup)	3	No signs of BPPV	As recurrent symptoms of vertigo with a positive Dix-Hallpike test after at least one month of symptom free status.	N.S.
Kim et al. (2014)²⁴	Prospective study	58 (69)	55.8 ± 10	PSCC 36.2% HSCC 48.3% ASCC 12.1% Multiple 3.4%	DH + supine head turning test	PSCC: Epley HSCC (Can): Barbecue Maneuver + sleep on healthy side (24 h) HSCC (Cup): Barbecue Maneuver + mastoid vibration/ Brandt-Daroff exercise ASCC: Reverse Epley	1	Absence of positional vertigo and nystagmus during the maneuver.	N.S.	The sensation of light headedness or unsteadiness without positional vertigo or nystagmus at

										the time of testing .
Korres et al. (2006)⁵⁰	Retrospective study	155 (57.4)	59.9 ± 12.6	PSCC 82.6% HSCC 9% ASCC 1.9% Bilateral 4.5% Multiple 1.9%	DH + RT Electro-nystagmography	PSCC+ASCC: Modified Epley HSCC: Vannucchi	2	Negative DH (absence of both vertigo and positional nystagmus)	Recurrence of symptoms	N.S.
Luryi et al. (2018)⁵²	Retrospective study	1105 (71.5)	64.6 ± 14.6	N.S. Bilateral 17.40%	DH or other diagnostic maneuver	CRP	≥3	Complete relief from symptoms or relief from the majority of symptoms with conversion to a negative diagnostic maneuver.	Recurrence of subjective symptoms with a diagnostic maneuver positive for subjective vertigo and objective nystagmus in either ear.	N.S.
Macias et al. (2000)⁴²	Retrospective study	259 (72)	58.6	PSCC 93.1% HSCC 1.9% Multiple 5.0%	Dix-Hallpike Electronystagmogram	CRP appropriate for the SCC	7	Negative DH (absence of both vertigo and positional nystagmus)	Recurrence of any positional symptoms	N.S.
Martellucci et al. (2019)⁶⁰	Retrospective study	47 (57)	62.1 ± 13.1	PSCC 100%	Dix-Hallpike Infrared video-frenzel goggles	Epley	4	Negative DH (absence of both vertigo and positional nystagmus)	After successful CRP, positive DH in the same side	N.S.

Monobe et al. (2001)⁵³	Retrospective study	62(66)	Median age of 63	PSCC 100%	DH	CRP Postural restrictions: keep head upright for 10 h, not sleep on the affected ear for 2 weeks	2	1) all vertigo (and nystagmus) resolved. 2) BPPV resolved but other vertigo remains.3) Partially resolved, non-positional nystagmus remains	N.S.	N.S.
Moreno et al. (2009)⁵⁴	Retrospective study	71 (65)	54.9	PSCC 100%	DH	Modified Epley	4	Symptom resolution and negative Dix-Hallpike	N.S.	N.S.
Otsuka et al. (2013)⁵⁵	Retrospective study	357 (68.1)	60	PSCC 65% HSCC 32% (Can 60%/ Cup 40%) Multiple 2.80%	DH + RT Infrared charge-coupled device camera	PSCC: Epley (group 1), medication (group 2) HSCC (Can): Lempert (group 1), medication (group 2) HSCC (Cup): medication + non-specific physical techniques such as Brandt-Daroff exercises/head shaking	1	Cured	Reappearance of symptoms after a symptom-free interval or more than 21 days.	N.S.
Prokopakis et al. (2013)²⁶	Prospective study	965 (50.2)	range 18 - 87 years	PSCC 88% HSCC 10% ASCC 2%	DH +RT	PSCC+ASCC: Modified Epley + ipsilateral mastoid vibration (80 Hz) at second position of CRP/ manually shaking the head or tapped the cranium during CRP. HSCC: variant of Barbecue maneuver Postural restrictions: don't bend over, move their head up or down, or lie supine (48 h)	>3	No vertigo or nystagmus provoked during RT or DH.	Positive result on provoking maneuver	N.S.
Radtke et al. (1999)³³	Prospective study	54 (72)	54.8 ± 11.7	PSCC 100%	Lateral head hanging position	Self-treatment at home using Brandt-Daroff exercises/ Modified Epley. Both 3 times daily until positional vertigo had subsided for 24 hours.	3x daily BD	Absence of both positional vertigo and positional nystagmus on DH after 1 week	N.S.	N.S.

Seo et al. (2017)²⁷	Prospective study	44 (59)	non-RD: 48.8 ± 9.6 RD group: 46.1 ± 9.3	PSCC 100%	DH	CRP	1	No positional nystagmus or vertigo present	N.S.	Persistent and non-positional atypical dizziness.
Soto-Varela et al. (2011)²⁸	Prospective study	135(65)	60.9	PSCC 100%	DH Frenzel goggles videonystagmography (in doubtful cases)	Semont	1	Negative DH (absence of both vertigo and positional nystagmus)	N.S.	N.S.
Soto-Varela et al. (2012)²⁹	Prospective study	412 (65)	58	PSCC (100%)	DH Frenzel goggles videonystagmography (in doubtful cases)	Semont (1x) → not cured: Epley (max. 3x) → not cured Brandt-Daroff ex.	4	Negative DH (absence of both vertigo and positional nystagmus)	After a cure compatible symptoms and a positive Dix–Hallpike test	N.S.
Su et al. (2016)⁵⁶	Retrospective study	247 (80.7)	57.5 ± 13.9	PSCC (100%)	DH	Epley	6	Negative DH (absence of both vertigo and positional nystagmus)	Vertigo evoked by changing position 3 months after successful treatment with Epley	N.S.

Supplementary Table S3: Treatment efficacy and recurrence rate influenced by age.

Author	N =	1CRP	Number of CRPs	Global treatment efficacy	Recurrence rate	Time to recurrence	Residual Dizziness	Duration Residual dizziness
AGE GROUPS DEFINED A PRIORI								
Anagnostou et al. (2007) ¹⁷	70				=			
Batuecas-Caletrio et al. (2013) ⁸	404	↓	↑		↑			
Jang et al. (2009) ³⁸	78	=	=		↑↑↑			
Simoceli et al. (2005) ³⁷	50	=						
Yeo et al. (2018) ³¹	370		=		=			
Zhu et al. (2019) ⁴³	1012				=			
AGE AS A COVARIATE								
Beynon et al. (2000) ¹⁹	51				=			
Bruintjes et al. (2014) ³⁴	44			=				
Ciodaro et al. (2018) ²¹	408			=				
Cohen et al. (2005) ³⁵	124			=				
Do et al. (2011) ²²	138		=		=			
Hain et al. (2000) ⁴⁵	94				=	=		
Korkmaz et al. (2016) ⁴⁹	153	=	=					
Levrat et al. (2003) ⁵¹	278			=				
Martellucci et al. (2016) ²⁵	86						↑↑	
Oh et al. (2017) ³⁶	506	=		↓↓				
Radtke et al. (2004) ⁴⁰	70			=				
Tanimoto et al. (2008) ⁵⁷	145				=			
Teggi et al. (2011) ³⁰	60						↑	↑
Wei et al. (2008) ⁵⁸	127			=			=	
Wolf et al. (1999) ⁴⁰	41			=				

Yoon et al. (2018) ⁵⁹	1426	↓↓	↑					
AGE AS A UNIVARIATE FACTOR								
Albera et al. (2018) ⁴¹	113	=						
Babac et al. (2014) ¹⁸	400			↓	=			
Casqueiro et al. (2008) ²⁰	391	=	=					
Cavaliere et al. (2005) ³²	103	=		=				
Dominguez-Duran et al. (2017) ²³	234	=						
Dornhoffer et al. (2000) ⁴⁴	52			=	=			
Helminski et al. (2005) ⁴⁶	116				=	=		
Kansu et al. (2010) ⁴⁷	118				=			
Kao et al. (2009) ⁴⁸	218	=	=		=	↑		
Kim et al. (2014) ²⁴	58						=	
Korres et al. (2006) ⁵¹	155	↓↓↓		=	↑↑↑			
Luryi et al. (2018) ⁵²	1105				=			
Macias et al. (2000) ⁴²	259	↓↓	=	-				
Martellucci et al. (2019) ⁶⁰	47	=						
Monobe et al. (2001) ⁵³	62			=				
Moreno et al. (2009) ⁵⁴	71	=	=					
Otsuka et al. (2013) ⁵⁵	357			↓	=			
Prokopakis et al. (2013) ²⁶	965				↑↑↑			
Radtke et al. (1999) ³³	54			=				
Seo et al. (2017) ²⁷	44						=	
Soto-Varela et al. (2011) ²⁸	135	=						
Soto-Varela et al. (2012) ²⁹	412			=	=			
Su et al. (2016) ⁵⁶	247				=			
Total	11451	16	10	16	20	3	5	1

Abbreviations: N: number of study participants; 1CRP: 1 canalith repositioning procedure; #CRPs: number of canalith repositioning procedures;

RR: recurrence rate; RD: residual dizziness

Note: =, No significant impact of age on outcome

↓, Significantly less effective in the older group compared to the younger group ($p < 0.05$)

↓↓, Significantly less effective in the older group compared to the younger group ($p < 0.01$)

↓↓↓, Significantly less effective in the older group compared to the younger group ($p < 0.001$)

↑, Significantly higher in the older group as compared to the younger group ($p < 0.05$)

↑↑, Significantly higher in the older group as compared to the younger group ($p < 0.01$)

↑↑↑, Significantly higher in the older group as compared to the younger group ($p < 0.001$)

Supplementary Table S4 – PRISMA 2009 checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5 {76-98}
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5 {96-98}
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5 {100-103}
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6 {111-126}
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5 {105-108}
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary Text S1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6 {111-126}
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7 {145-150}

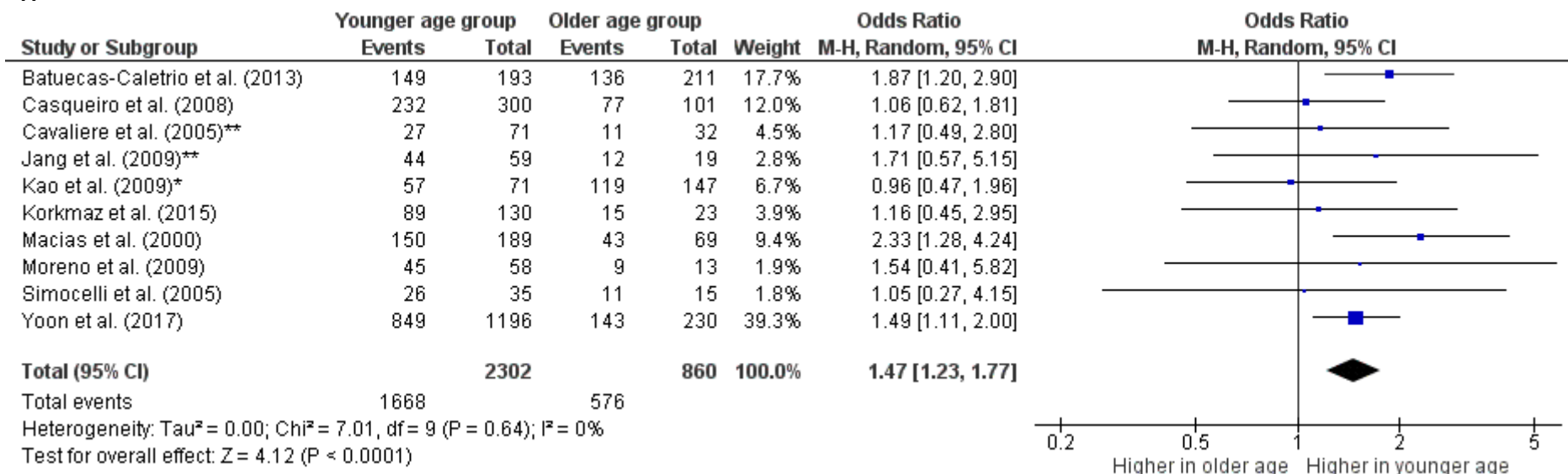
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6-7 {118-143}
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7 {144-150}
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7 {158-168}
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7 {158-168}

Page 1 of 2

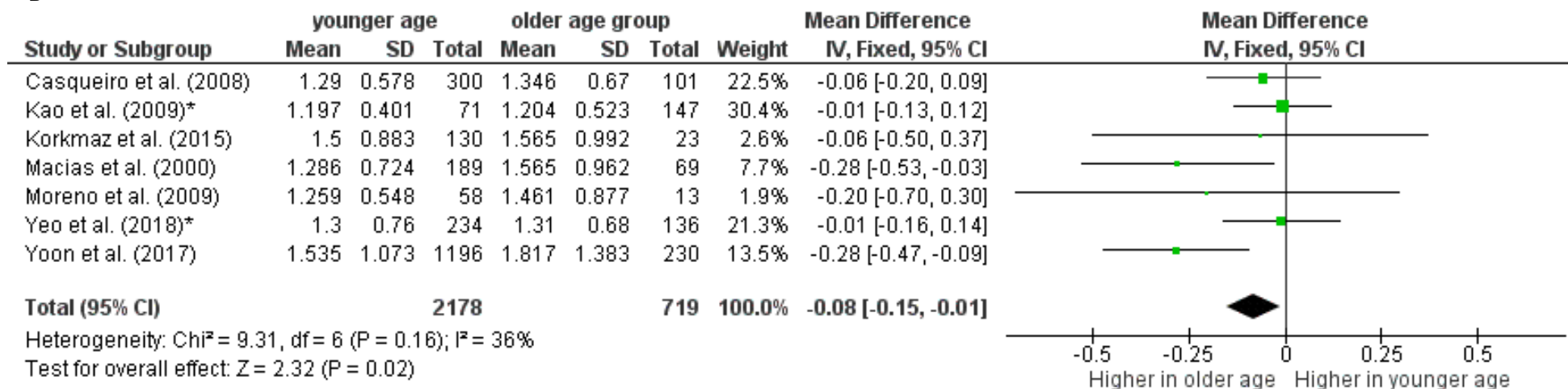
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	16 {328-330}
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	/
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8 {163-166} Supplementary Figure S1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9 {177-188} Table 1 Supplementary Table S2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8 {168-176} Supplementary Table S1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-12 {200-249} Figure 1

Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10-12 {200-249} Figure 1
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15 {335-337}
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	/
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-13 {258-285}
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16 {328-330}
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16 {331-342}
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1 {26-27} 21

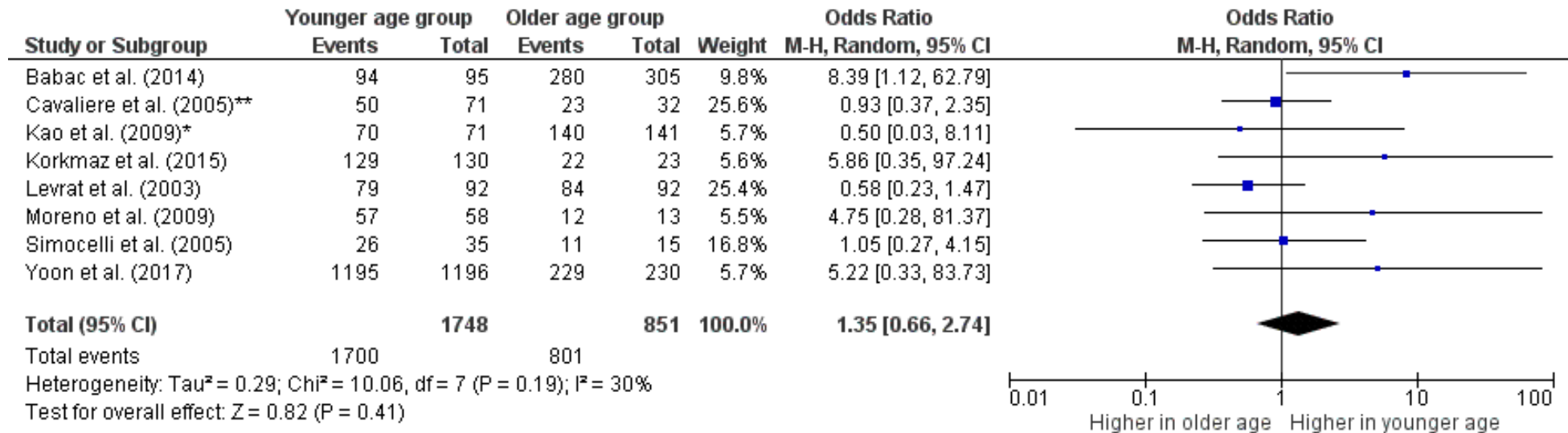
A



B



C



D

