

1 **Efficacy of serious games in healthcare professions education: a systematic review and meta-**
2 **analysis.**

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38 **SUMMARY STATEMENT**

39 Serious games (SGs) are interactive and entertaining software designed primarily with an educational
40 purpose. This systematic review synthesizes evidence from experimental studies regarding the efficacy of
41 SGs for supporting engagement and improving learning outcomes in healthcare professions education.
42 Randomized controlled trials (RCTs) published between January 2005 and April 2019 were included.
43 Reference selection and data extraction were performed in duplicate, independently. Thirty-seven RCTs
44 were found and 29 were included in random effect meta-analyses. Compared with other educational
45 interventions, SGs did not lead to more time spent with the intervention (mean difference 23.21 minutes
46 [95% confidence interval (CI) -1.25, 47.66]), higher knowledge acquisition (standardized mean difference
47 (SMD) 0.16 [95%CI -0.20, 0.52]), cognitive (SMD 0.08 [95%CI -0.73, 0.89]) and procedural skills
48 development (SMD 0.05 [95%CI -0.78, 0.87]), attitude change (SMD -0.09 [95%CI -0.38, 0.20]) nor
49 behavior change (SMD 0.2 [95%CI -0.11, 0.51]). Only a small SMD of 0.27 [95%CI 0.01, 0.53]) was
50 found in favor of SGs for improving confidence in skills.

51 **ABBREVIATED TITLE**

52 Serious games in health professions education

53

54 INTRODUCTION

55 Serious games (SGs) are interactive and entertaining software designed primarily with an educational
56 purpose. Popularized in the beginning of the 2000s, SGs quickly became integrated into healthcare
57 professions education as their entertaining factor showed the potential to engage learners and support their
58 learning process.¹ SGs are thought to fulfill the needs of adult learners, such as autonomy, control, and a
59 sense of achievement.^{2,3} Moreover, authors report that learners are receptive to the visual and the
60 interactive aspects of SGs, traditionally associated with video games.⁴ Thus, their use by healthcare
61 educators is expected to rise in both initial and continuing education.⁵

62 Learning in SGs typically occurs through a gameplay experience that combines challenges with
63 various playful design elements, which can be seen as features or building blocks of SGs (e.g., scoring
64 system, content unlocking, integration of a storyline).⁶ Challenges allow learners to be actively involved in
65 a decision-making process for which they can receive immediate feedback and see the results of their
66 decisions.⁷ For example, an SG can challenge learners to provide the correct management plan for a
67 virtual patient. Points can be awarded, and learners can unlock a new game level if they provide the
68 correct management plan. As such, SGs are often associated with a constructivist learning perspective
69 where the learning progression is fueled by an interaction cycle between learners and the SG, and where
70 the reception of feedback allows learners to reflect on new or better ways to take on a challenge.⁶ Thus,
71 one of the main objectives in designing SGs is to ensure that they support learners' engagement to take on
72 the various challenges that are expected to lead to significant learning outcomes.⁸

73 Engagement can be defined as a bi-dimensional concept: a behavioral dimension (i.e., the extent of the
74 learners' involvement while taking on the challenges; e.g., the total amount of time invested by learners'
75 in the SG), and an experiential dimension (i.e., the subjective experience of the learners while taking on

76 the challenges; e.g., learners' affect while using the SG).⁹ Proper integration of the challenges with the
77 playful design elements while designing SGs can ensure that learners remain engaged towards the
78 challenges they take on.¹⁰

79 Systematic reviews on the use of SGs in the healthcare professions report that their efficacy in
80 supporting engagement and improving learning outcomes varies greatly.^{1,11-15} However, reasons as to why
81 SGs produce heterogeneous results have been left unexplored. Heterogeneity is often the product of
82 diversity in the combination of studies with different research designs, populations, intervention designs,
83 comparators, or outcomes evaluated.¹⁶ Previous reviews of SGs combined the findings of quasi-
84 experimental studies with experimental ones which could have induced biases in the results reported
85 through the lack of a control group or randomization.^{12,13} Other reviews combined studies evaluating SGs
86 to ones evaluating gamification interventions (i.e., the application of gaming elements to non-gaming
87 contexts) or commercial off-the-shelf games (i.e., games designed specially for entertainment but used for
88 educational purpose) which could have induced heterogeneity in the results reported due to the different
89 design of each of these interventions.^{14,15}

90 Thus, in this systematic review, we focused on identifying, appraising, and synthesizing the results of
91 experimental studies evaluating the efficacy of SGs on engagement and learning outcomes in healthcare
92 education. Since the development of an SG can be expensive and time-consuming,¹⁴ findings from this
93 review will thus provide guidance to educators regarding the design and the adoption of SGs, and to
94 researchers in the conduct of future works.

95 **METHODS**

96 **Protocol and registration**

97 This systematic review was based on the Cochrane Handbook for Systematic Reviews of
98 Interventions.¹⁶ We report this systematic review according to the Preferred Reporting Items for
99 Systematic review and Meta-Analysis (PRISMA) standards.¹⁷ We prospectively registered
100 (#CRD42017077424) and published the detailed review protocol.¹⁸

101 **Eligibility criteria**

102 We included randomized controlled trials (RCTs), cluster-RCTs, and crossover-RCTs published in
103 English or in French from January 1, 2005, to April 24, 2019. An SG had to be assessed, as a stand-alone
104 intervention or as part of a multi-component intervention, among healthcare professionals or students,
105 from any level of education, either in an initial or a continuing education setting. For the purpose of this
106 review, we defined SGs as interactive and entertaining software with a primary educational purpose that
107 engage learners through challenges.¹⁹⁻²² All types of comparator interventions were considered for
108 inclusion. Studies had to report at least one measure of a learning outcome or one measure of
109 engagement—behavioral (i.e., the duration of the educational intervention usage) or experiential (i.e., self-
110 reported measures of learners' experience in using the educational intervention). Learning outcomes were
111 defined after Kirkpatrick's model.²³ We considered all short-term and long-term measures of knowledge
112 acquisition, skill development (subdivided as confidence in skills, cognitive skills, and procedural skills),
113 attitude and behavior change, as well as clinical outcomes in healthcare system users.

114 **Information sources and search**

115 A librarian searched six bibliographical databases using keywords and MeSH terms related to:
116 SGs (e.g., serious game(s), game-based learning/training, applied game(s)) healthcare
117 professionals/healthcare students (e.g., physician(s), clinician(s), trainee(s)), and effect on engagement and

118 learning outcomes (e.g., efficacy, skills development, knowledge acquisition). These bibliographical
119 databases were: Cumulative Index of Nursing and Allied Health (EBSCO), EMBASE (OVID), ERIC
120 (ProQuest), PsycINFO (APA PsycNET), PubMed (NCBI), and Web of Science – SCI and SSCI (ISI –
121 Thomson Scientific). We performed an initial search in these databases on December 13, 2017, and we
122 updated our search on April 24, 2019 (see Text, Supplementary Digital Content 1, all search strategies are
123 reported). To find additional articles, hand-searching was performed in scientific journals specialized in
124 SGs (Games for Health Journal, Games, G|A|M|E The Italian Journal of Game Studies, International
125 Journal of Computer Games Technology, International Journal of Serious Games, and JMIR Serious
126 Games), in previous systematic reviews,^{13,24} and in the reference lists of identified studies.

127 Identified references were imported and managed in EndNote (Version X8, Clarivate Analytics).
128 We screened all references independently and in pairs, and all disagreements were resolved through
129 discussion with a third author.

130 **Data extraction process**

131 We performed the data extraction process by using the Effective Practice and Organisation of Care
132 template.²⁵ The extraction form was piloted by all review authors involved in this step using a single
133 article. Authors then met to discuss issues they might have had while using the form. As no significant
134 disparity was found between forms during the piloting phase, one author performed the initial data
135 extraction and another one validated it.

136 **Data items**

137 For descriptive purposes, we extracted the following items: study aim; study design; population;
138 attrition rate; name of SGs evaluated; theoretical framework used for the SGs development; cost and

139 duration of the SGs development; clinical topics addressed; methods of delivery of the comparator
140 intervention (i.e., classroom learning, written material, e-learning, another serious game, simulation/virtual
141 simulation); duration and frequency of use of the interventions; unit of measurement; time points
142 measured; instruments; validity and reliability of the instruments.

143 For quantitative synthesis purposes, we extracted the following items: sample size; outcome data; risk
144 of bias data.

145 **Assessment of risk of bias**

146 Two authors independently assessed the risk of bias of each included study using the Cochrane
147 Collaboration’s tool for assessing risk of bias²⁶ and all disagreements were resolved with the help of a
148 third author. A high risk of bias diminishes the reliability of the study results. The following aspects are
149 considered during assessment: random sequence generation, allocation concealment, measurement of
150 study group characteristics and baseline outcomes, incomplete outcome data, blinding, contamination, and
151 selective outcome reporting. For each criterion, we judged studies at “low risk”, “high risk”, or “unclear
152 risk” of bias. We considered studies at high risk of bias if they were judged at high or unclear risk of bias
153 on either of these three criteria: randomization sequence generation, allocation concealment, or blinding of
154 assessors to participants’ group assignment as these criteria are likely to significantly bias the results.²⁷

155 **Assessment of selective reporting of outcomes**

156 We compared the outcomes reported in the articles with the outcomes reported in the research
157 protocol or, if no protocol was available, with the trial prospective registration form. If the trial was not
158 prospectively registered, we compared the outcomes presented in the methods section with the ones
159 reported in the results section.

160 **Assessment of reporting biases**

161 We constructed a funnel plot in RevMan 5.3 (The Cochrane Collaboration, Copenhagen,
162 Denmark) and visually inspected it to assess reporting biases (e.g., due to publication, language, or
163 citation biases) at the body of literature level. We considered an asymmetrical funnel plot at visual
164 inspection as an indicator of reporting biases.

165 **Data synthesis**

166 **Efficacy of serious games in supporting behavioral and experiential engagement**

167 To evaluate the efficacy of SGs in supporting behavioral engagement, we used meta-analytical
168 methods to compare the duration of SG use versus the comparator intervention use. All meta-analyses in
169 this systematic review were performed in RevMan 5.3 (The Cochrane Collaboration, Copenhagen,
170 Denmark) using an inverse variance approach with random-effect models to combine continuous data. At
171 least two studies had to contribute to a single meta-analysis for it to be conducted.²⁸ No minimal number
172 of participants was required. All results are expressed with 95% confidence intervals (CIs) and statistically
173 significant results are defined as a two-sided alpha of 0.05.

174 Regarding the efficacy of SGs to support behavioral engagement, the result is expressed as a mean
175 difference (in minutes). Moreover, we compared narratively the expected frequency and duration of SG
176 use, according to study authors, to the observed ones.

177 Regarding experiential engagement, this concept encompasses many aspects of the learners'
178 experience with SGs, and we expected that authors would measure a diverse set of these aspects. As such,
179 we employed an analysis approach where we let these aspects emerged from the data (and not from
180 prespecified categories). This allowed us both to identify all aspects of experiential engagement that were

181 evaluated in included studies, and to compare between studies the results obtained regarding each
182 identified aspect. First, we extracted the items composing each instrument used to assess and to compare
183 the experiential engagement in learners between groups. Second, two authors independently analyzed and
184 categorized all items into aspects that were refined iteratively through the data analysis process. Third, the
185 proposition of each author was contrasted to reach a consensus on aspects of experiential engagement that
186 were measured. The efficacy of SGs on experiential engagement was finally evaluated for each aspect.

187 **Efficacy of serious games in improving learning outcomes**

188 We conducted meta-analyses to evaluate the efficacy of SGs compared to any other educational
189 intervention in improving learning outcomes. Meta-analyses included all studies with enough data to
190 compute a standardized mean difference (SMD) regarding at least one outcome (i.e., post-test means,
191 medians, or odds ratios; standard deviations, first and third quartiles, standard errors, p values, or t value;
192 number of participants in each group).

193 We also performed meta-analyses of studies evaluating the efficacy of SGs versus passive
194 comparators. However, the emphasis was kept on studies with active education comparisons as educators
195 usually seek to find the best educational intervention, and not if an educational intervention is better than
196 doing nothing. As such, results of these analyses are not reported here but online (see Figures,
197 Supplementary Digital Content 2, meta-analyses are presented there).

198 **Subgroup and sensitivity analyses**

199 Statistical heterogeneity was assessed using the I^2 statistic. A value superior to 50% was
200 considered as a high level of heterogeneity for all meta-analyses. We explored statistical heterogeneity by
201 performing subgroup and sensitivity analyses. Subgroup analyses were conducted regarding the study

202 population (i.e., healthcare professionals v. healthcare students), the comparator intervention (i.e.,
203 classroom-learning, written material, e-learning, simulation or virtual simulation, or a non-active
204 comparator), and the publication year. As for this last subgroup analysis, we prospectively retained 2014
205 as a cut-off year (i.e., before or in 2014 v. after 2014) as the New Media Consortium declared that year
206 that SGs were to be greatly developed and evaluated by educational institutions in the next 2 to 3 years.²⁹
207 Sensitivity analyses were performed to restrict meta-analyses to studies with larger sample sizes. Smaller
208 studies tend to be associated with larger standard errors and different intervention effects, which could
209 introduce statistical heterogeneity.^{16,30,31} We considered a study “small” if its sample size fell under the
210 first quartile when looking at the distribution of all study sample sizes included in a single meta-analysis.
211 The median threshold from which we considered a study sample size “small” was 46 participants and the
212 range varied between 28 and 74.

213 **Assessment of the overall quality of the evidence**

214 The overall quality of the evidence regarding the efficacy of SGs on each outcome was assessed
215 by using the Grading of Recommendations Assessment, Development and Evaluation (GRADE)
216 approach.³² GRADE formalizes the evaluation of the overall quality of evidence and the formulation of
217 recommendations. Quality of evidence depends on risks of bias, inconsistencies, imprecisions, and
218 indirectness in the results of the studies. For each outcome, there are four levels of quality of evidence
219 (very low, low, moderate, high) which represent our confidence in the pooled SMDs (i.e., the findings of
220 this review). Two authors independently assessed the quality of the evidence and all disagreements were
221 resolved through consensus.

222 **RESULTS**

223 **Descriptive results of included studies**

224 From a pool of 3173 unique references, 37 studies were included in the systematic review, and 29
225 studies (78%; all percentages presented are out of the 37 studies included) provided enough data to be
226 included in a meta-analysis (see Figure 1). Descriptive data regarding included studies are reported in
227 Table 1 (see Text, Supplementary Digital Content 3 and 4, the lists of included studies and of excluded
228 studies at the full-text assessment stage are reported).

229 The median publication year was 2017. Twenty-eight studies (76%) were conducted exclusively
230 among healthcare students, eight studies (22%) exclusively among healthcare professionals, and one study
231 (3%) among both healthcare professionals and students. Regarding the professions, many studies were
232 conducted in the medical profession (n=24; 65%). The median sample size was 91 participants
233 (interquartile range (IQR) 99). Median attrition rates were 6.61% (IQR 20.89) at post-test assessment and
234 20% (IQR 25.28) at a follow-up period (i.e., between 6-week and 6-month post-intervention). E-learning
235 interventions (n=14; 38%) were the most frequent types of comparator intervention.

236 Three studies (8%) compared SGs between one another. It was shown in one of the included studies
237 that a voluntarily poor decision-making in an SG compared to a “normal” one did not influence the
238 improvement of cognitive skills (SMD 0.00 [95%CI -0.31, 0.31]).³³ Another study showed that more
239 frequent, but lighter sessions of SG usage, led to higher knowledge acquisition than fewer but more
240 intensive sessions of SG usage (SMD 0.43 [95%CI 0.30, 0.56]).³⁴ The last one focused on the evaluation
241 of two similar SGs; the experimental group received a SG an educational content aligned with the
242 learning objectives as the control group received a SG with a similar, but irrelevant educational content, to
243 avoid compensatory equalization in this group.³⁵ The group that received the SG that was aligned with the
244 learning objective had significantly higher procedural skills compared with the control group (SMD 1.30
245 [95%CI 0.85, 1.74]).

246 Otherwise, in ten studies (27%), the control group received no intervention or no intervention other
247 than one shared with the experimental group (e.g., both experimental and control groups shared the same
248 classroom-learning activity).

249 **Risk of bias, selective reporting of outcomes in included studies, and reporting biases**

250 Seven studies (19%) were judged at low risk of bias. The risk of bias graph is presented in Figure
251 2 (also see Figure, Supplementary Digital Content 5, the risk of bias summary for each study is presented).
252 Other studies were judged at high risk of bias, mainly due to reporting or methodological issues at study
253 level regarding the randomization sequence generation (n=17; 46%), and the allocation concealment
254 (n=29; 78%). Only six studies (16%) were prospectively registered or had published a protocol before the
255 publication of the results.

256 A funnel plot was constructed for the “Knowledge” outcome (see Figure, Supplementary Digital
257 Content 6, the funnel plot is presented). Visual inspection of the funnel plot revealed no serious reporting
258 biases at the body of literature level.

259 **Description of the serious games**

260 Most SGs were exclusively available on a computer (n=24; 65%), seven (19%) were offered
261 exclusively on a portable or a handheld device, four (11%) were available on more than one platform, and
262 two (5%) were available on an unspecified platform. Clinical topics were diverse; cardiac resuscitation
263 (n=5; 14%), triaging (n=3; 8%), and anatomy (n=3; 8%) were the most frequent. About half of the
264 included studies reported the expected frequency of using the SG (n=19; 51%) or its duration (n=23;
265 62%). In those, the median expected frequency of usage was one session (IQR 3) and the median expected
266 duration of usage was 60 minutes (IQR 150). Data related to the cost and time of development of the SG

267 was not reported in any study (also see Table, Supplemental Digital Content 7, key information of the SGs
268 assessed are presented).

269 Ten studies (27%) cited the theoretical framework that guided the design or the development of the
270 SG; no theoretical framework was cited more than once across the 37 included studies. Two (5%) studies
271 reported the use of a game-based learning theory to guide the design of the SG. The most frequent
272 challenges in SGs included the assessment and/or management of a virtual patient presenting a health-
273 related illness condition (n=17; 46%) and answering questions on a clinical topic (n=10; 27%).

274 **Efficacy of serious games in supporting behavioral and experiential engagement**

275 Our confidence in the results of all meta-analyses is presented in Table 2. Our confidence ranges from
276 very low to low for almost all meta-analyses conducted due mostly to serious risks of bias in included
277 studies, inconsistencies, and imprecisions in results.

278 Five studies (14%) were included in a meta-analysis (see Figure 3) to evaluate the efficacy of SGs on
279 behavioral engagement (i.e., minutes spent with the interventions). A non-statistically significant result
280 favoring SGs was found (mean difference (in minutes) 23.21 [95%CI -1.25, 47.66; I₂= 91%]).
281 Heterogeneity remained high (> 50%) when conducting planned subgroup and sensitivity analyses (see
282 Figures, Supplementary Digital Content 8, subgroup and sensitivity analysis graphs are presented).

283 Five studies (14%) reported enough data to allow a comparison between the expected behavioral
284 engagement in the SG and the actual one in terms of time spent using the SG. In three studies, the actual
285 time spent was shorter than expected,³⁶⁻³⁸ in one it was longer,³⁹ and in one it was as expected.⁴⁰

286 Experiential engagement was contrasted between groups in 11 studies (30%). Aspects of experiential
287 engagement that were assessed are the following: perceived learning efficacy (n=9; 24%), enjoyment

288 (n=7; 19%), satisfaction (n=6; 16%), usability (n=5; 14%), appropriateness (n=4; 11%), focus (n=4; 11%),
289 fidelity (n=4; 11%), difficulty (n=2; 5%), perceived learning efficiency (n=2; 5%), and stress (n=1; 3%).
290 Results regarding the efficacy of SGs on each aspect of experiential engagement are reported in Table 3.
291 Results were highly heterogeneous overall; SGs were rarely regarded as systematically superior to other
292 educational interventions for any of the aspects identified.

293 **Efficacy of serious games in improving learning outcomes**

294 **Knowledge**

295 Fifteen studies (41%) assessed participants' acquisition of knowledge and eleven (30%) were
296 included in meta-analysis (Figure 4). We observed a negligible and non-statistically significant SMD of
297 0.16 (95%CI -0.20, 0.52; $I_2=86\%$) in favor of SGs. The number of included studies in this meta-analysis
298 allowed for subgroup and sensitivity analyses. Statistical heterogeneity remained high ($I^2 \geq 50\%$) in all
299 subgroup analyses. However, a statistically significant difference ($p=0.006$) was found between the pooled
300 SMD of studies conducted with healthcare students (SMD -0.19 [95%CI -0.66, 0.28]; $I_2=85\%$) compared to
301 the pooled SMD of studies conducted with healthcare professionals (SMD 0.80 [95%CI 0.27, 1.32],
302 $I_2=84\%$). When removing the studies falling under the first quartile in term of sample size (less than 48
303 participants) statistical heterogeneity also remained high. However, the result became statistically
304 significant (SMD 0.48 [95%CI 0.19, 0.78], $I_2=77\%$). Two studies (5%) assessed participants' retention of
305 knowledge, one after a follow-up period of six weeks and the other one after six months. At six weeks, a
306 negligible and non-statistically significant difference between a SG and written material was found (SMD
307 0.05 [95%CI -0.74, 0.83]).⁴¹ At six months, a negligible and non-statistically significant difference
308 between a SG and an e-learning intervention was found (SMD -0.14 [95%CI -0.60, 0.32]).⁴²

309

310 **Skills**

311 Ten studies (27%) assessed participants' cognitive skills and five of them (11%) were included in
312 a meta-analysis (see Figure 6). We observed a negligible and non-statistically significant SMD of 0.08
313 (95% CI -0.73, 0.89; $I_2= 95\%$) in favor of SGs. Heterogeneity remained high (> 50%) when exploring the
314 potential effect of study population, and publication year. Two studies included a follow-up period. At
315 three months, a small and non-statistically significant difference (SMD 0.23 [95% CI -0.11, 0.57])
316 favoring the SG compared to a classroom learning intervention was found and, at a follow-up period of 6
317 months, a small and statistically significant difference (SMD 0.46 [95% CI 0.32, 0.68]) favoring the SG
318 compared to an e-learning intervention was reported.^{43,44}

319 Twelve studies (32%) assessed participants' procedural skills. Four studies (11%) were included
320 in this meta-analysis (see Figure 7). We observed a negligible and non-statistically significant SMD of
321 0.05 (95%CI -0.78, 0.87; $I_2= 88\%$). The heterogeneity remained high (>50%) when exploring the potential
322 effect of the comparator intervention, study population, and publication year. One study (3%) included a
323 four-month follow-up period and a negligible and non-statistically significant difference (SMD -0.16
324 [95%CI -0.62, 0.29]) favoring the e-learning intervention was found.⁴⁵

325 Six studies (16%) assessed participants' confidence in their skills and four of them (11%) were
326 included in a meta-analysis (see Figure 5). We observed a small and statistically significant SMD of 0.27
327 (95% CI 0.01, 0.53; $I_2= 0\%$) in favor of SGs. Non-significant differences between groups were found
328 while exploring the potential effect of study population, publication year, and the comparator intervention.

329 **Attitude**

330 Five studies (14%) assessed participants' attitude. Three studies (8%) were included in this meta-
331 analysis (see Figure 8). We observed a negligible and non-statistically significant SMD of -0.09 (95%CI -
332 0.38, 0.20; I₂= 47%) in favor of comparator educational interventions. The low number of included studies
333 in the main meta-analysis precluded us from conducting other subgroup or sensitivity analyses.

334 **Behavior**

335 Three studies (8%) assessed the perception of behavior change in practice. Two studies (5%) were
336 included in this meta-analysis (see Figure 9). We observed a negligible and non-statistically significant
337 SMD of 0.2 (95%CI -0.11, 0.51; I₂= 0%) in favor of SGs.

338 **Clinical outcomes**

339 Only one study (3%) included the assessment of a clinical outcome in healthcare system users (i.e.,
340 number of days to blood pressure target in the patients who were taken care by the healthcare providers
341 participating in the study) and the authors reported a statistically significant difference (p=0.018) favoring
342 the SG compared (median = 142 days) to another e-learning intervention (median = 148 days).⁴⁶

343 **DISCUSSION**

344 This systematic review examined the efficacy of SG in healthcare professions education. Most studies
345 were published in the last three years, among students, in the medical profession, and compared an SG
346 with another e-learning intervention. We found negligible and non statistically significant differences
347 between SGs and other educational interventions **regarding their effects** on knowledge **acquisition**,
348 cognitive and procedural skill **development** in a test setting, behavior **change** in clinical practice, or
349 **supporting** engagement during the **learning activities**. Additionally, heterogeneous results were found

350 regarding the efficacy of SGs to support any of the identified aspects of experiential engagement. This
351 systematic review adds to previous reviews on SGs in healthcare professions education by synthesizing
352 the latest evidence of their efficacy, by evaluating the assumption that SGs are more engaging than other
353 educational interventions, by quantifying their efficacy, and by exploring various sources of heterogeneity
354 through meta-analytic methods.

355 Educators should be aware of the limited evidence supporting the engaging nature of SGs with
356 healthcare professionals and students. Mixed findings regarding engagement are surprising considering
357 that the decision to use an SG is often motivated by their potential to improve learners' engagement.^{37,47,48}
358 The concept of engagement has a large scope that makes it almost an umbrella term for multiple emotional
359 or cognitive states and numerous behaviors.⁹ As such, we remained inclusive of all measures used by
360 authors that were linked either to the behavioral or experiential dimension of engagement while using the
361 intervention. However, these findings are impeded by the small number of studies reporting engagement
362 outcomes and the lack of information regarding the validity or the reliability of the assessment tools used
363 in half of the studies. Authors should consider assessing learners' engagement across educational
364 interventions using validated and reliable assessment tools, such as the evaluation questionnaire developed
365 by Dankbaar et al.⁴⁹ in their study, or the usability questionnaire developed by Zaharias &
366 Povlymenakou⁵⁰.

367 Non-significant differences between SGs and other educational interventions were found for most
368 learning outcomes. Our findings are in line with the ones reported in previous reviews regarding the
369 efficacy of SGs in improving learning outcomes.¹²⁻¹⁴ Authors of these previous reviews underlined the
370 mixed efficacy of SGs to improve learning outcomes compared to other educational interventions. Our
371 meta-analyses showed that, for most learning outcomes and no matter what the comparator educational

372 intervention was, the overall body of the evidence did not support the claim that SGs were significantly
373 more effective. The lack of theoretical framework to support SG design could serve as an explanation for
374 these results as most authors did not explicate a theoretical framework for the design of their SGs and only
375 two explicitly referred to a game-based learning theory.^{6,20,46,51} Designing an SG through a theoretical lens
376 holds the potential to greatly improve learners' engagement and learning outcomes.⁵² Theoretical works
377 should be undertaken and synthesized to explain the mechanisms through which SGs are expected to lead
378 to learning outcomes.

379 Furthermore, authors of recent RCTs underlined the ongoing difficulty in identifying empirical data
380 to support their design choices.^{49,53} We had initially planned in the published protocol to evaluate the
381 individual impact of SG design elements on engagement and learning outcomes.¹⁸ Unfortunately, scarce
382 data prevented us from doing so. Few included studies compared different versions of an SG between one
383 another which is essential to isolate the impact of individual design choices.^{33,35,46,54} Future studies should
384 focus on evaluating the efficacy of different versions of a SG on engagement and learning outcomes.

385 Regarding the long-term retention of learning outcomes, only five studies included a follow-up
386 period and three of them reported non-significant differences between groups. It should be noted that the
387 median expected frequency and duration of usage is a single 60-minute session, and that learners have
388 been shown in some studies to use the SGs less than expected^{36,37}. It could be hypothesized that the
389 duration of SG use is not enough to bring greater long-term changes in learning outcomes compared to
390 other educational interventions. Future studies should consider assessing participants' long-term retention
391 of learning outcomes, as there is insufficient evidence to support SG efficacy in the long-term compared to
392 other educational interventions.

393 As the development of an SG can be a resource-intensive endeavor and as some SGs are
394 commercialized following their evaluation, researchers should consider prospectively registering their trial
395 or publishing their research protocol to improve the transparency in the reporting of their results and to
396 avoid any suspicion of potential conflicts of interest.⁵⁵ This would facilitate the evaluation of the selective
397 reporting of outcomes in result papers. Moreover, regarding the reporting, most studies were judged at
398 high risk of bias as the reporting of the randomization sequence generation and the allocation concealment
399 were unclear. Future studies should make sure to report all elements necessary to their assessment. The
400 adoption of reporting grids, such as the CONSORT grid, by journals, and the use of them by researchers,
401 could greatly improve the reporting of these trials.⁵⁶

402 Strengths of this systematic review include the prospective publication of the protocol,¹⁸ and the
403 reporting of the results according to the PRISMA guidelines, enhancing the transparency of the research
404 process.⁵⁷ Furthermore, the data extraction process was piloted, and all data extraction forms were
405 validated by a second review author. Limits of this review include the selection of RCTs only and their
406 relatively low number. Following the Cochrane guidance, we restricted this review to RCTs to minimize
407 threats to internal validity, and as we were aware that the efficacy of SGs had already been evaluated in
408 multiple RCTs.²⁸ Another limit include a potential language bias as only studies published in English and
409 in French were considered. However, the visual inspection of the funnel plot did not allow for the
410 identification of a significant language bias or other types of reporting biases. Furthermore, as the nature
411 of what constitute an SG and how it differs from interventions such as virtual simulations is still a matter
412 of debate,⁵⁸ we remained inclusive in our definition of SGs. To address potential ambiguities regarding the
413 nature of study interventions, we screened all references independently and in pairs, and all disagreements

414 were resolved through discussion with a third author. Still, we recognize our inclusive definition of SGs as
415 a potential limit to our work.

416 Compared with other educational interventions, SGs **led to neither** statistically better behavioral
417 engagement, knowledge acquisition, cognitive and procedural skills development, attitude change, nor
418 behavior change. Only a statistically significant but small SMD was found in favor of SGs to improve
419 confidence in skills. Additionally, heterogeneous results were found regarding the efficacy of SGs to
420 support any of the identified aspects of experiential engagement. Our findings are impeded by high or
421 unclear risk of bias across studies, inconsistencies in the directions of effect, and imprecisions of study
422 results. As such, our confidence ranges from very low to low regarding the results of almost all meta-
423 analyses that were conducted. We recommend that authors base their SG design choices on a theoretical
424 framework and that they report their results according to the CONSORT statement. Moreover, future
425 research should focus on assessing if healthcare professionals' clinical practice changes occur in post SG
426 training, clinical outcomes in patients under the care of healthcare professionals that used SGs, and long-
427 term retention of learning outcomes.

428 **FINANCIAL DISCLOSURE SUMMARY**

429 We have no potential conflict of interest to disclose and this work received no specific funding.

430 **REFERENCES**

- 431 1. Akl EA, Pretorius RW, Sackett K, et al. The effect of educational games on medical
432 students' learning outcomes: a systematic review: BEME Guide No 14. *Med Teach*.
433 2010;32(1):16-27.
- 434 2. Baranowski T, Buday R, Thompson DI, Baranowski J. Playing for real: video games and
435 stories for health-related behavior change. *Am J Prev Med*. 2008;34(1):74-82.
- 436 3. Knowles MS. *L'apprenant adulte: vers un nouvel art de la formation*. Paris, France:
437 Editions d'Organisation; 1995.
- 438 4. Yoder SL, Terhorst R, 2nd. "Beam me up, scotty": designing the future of nursing
439 professional development. *J Contin Educ Nurs*. 2012;43(10):456-462.
- 440 5. Wynter L, Burgess A, Kalman E, Heron JE, Bleasel J. Medical students: what educational
441 resources are they using? *BMC Med Educ*. 2019;19(1):36.
- 442 6. Kiili K. Digital game-based learning: Towards an experiential gaming model. *Internet
443 High Educ*. 2005;8(1):13-24.
- 444 7. Tettegah S, McCreery M, Blumberg F. Toward a framework for learning and digital
445 games research. *Educ Psychol*. 2016;50(4):253-257.
- 446 8. De Freitas S. *Learning in immersive worlds: a review of game-based learning*. Bristol,
447 Royaume-Uni: Joint Information Systems Committee;2006.
- 448 9. Perski O, Blandford A, West R, Michie S. Conceptualising engagement with digital
449 behaviour change interventions: a systematic review using principles from critical
450 interpretive synthesis. *Transl Behav Med*. 2017;7(2):254-267.
- 451 10. Nevin CR, Westfall AO, Rodriguez JM, et al. Gamification as a tool for enhancing
452 graduate medical education. *Postgraduate medical journal*. 2014:postgradmedj-2013-
453 132486.

- 454 11. Gorbanev I, Agudelo-Londono S, Gonzalez RA, et al. A systematic review of serious
455 games in medical education: quality of evidence and pedagogical strategy. *Med Educ*
456 *Online*. 2018;23(1):1438718.
- 457 12. Ricciardi F, De Paolis LT. A comprehensive review of serious games in health
458 professions. *IJCGT*. 2014;2014:1-11.
- 459 13. Wang R, DeMaria S, Jr., Goldberg A, Katz D. A systematic review of serious games in
460 training health care professionals. *Simul Healthc*. 2016;11(1):41-51.
- 461 14. Boyle EA, Hainey T, Connolly TM, et al. An update to the systematic literature review of
462 empirical evidence of the impacts and outcomes of computer games and serious games.
463 *Comput Educ*. 2016;94:178-192.
- 464 15. Gentry S, Gauthier A, L'Estrade Ehrstrom B, et al. Serious gaming and gamification
465 education in health professions: a systematic review by the Digital Health Education
466 collaboration. *J Med Internet Res*. 2019;21(3):e12994.
- 467 16. Higgins JPT, Green S. *Cochrane Handbook for Systematic Reviews of Interventions*
468 *Version 5.1.0.*: The Cochrane Collaboration; 2011.
- 469 17. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for
470 systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*.
471 2009;6(7):e1000097.
- 472 18. Maheu-Cadotte MA, Cossette S, Dube V, et al. Effectiveness of serious games and impact
473 of design elements on engagement and educational outcomes in healthcare professionals
474 and students: a systematic review and meta-analysis protocol. *BMJ Open*.
475 2018;8(3):e019871.
- 476 19. Hamari J, Shernoff DJ, Rowe E, Coller B, Asbell-Clarke J, Edwards T. Challenging
477 games help students learn: an empirical study on engagement, flow and immersion in
478 game-based learning. *Computers in Human Behavior*. 2016;54:170-179.
- 479 20. Salen K, Zimmerman E. *Rules of play: Game design fundamentals*. MIT press; 2004.

- 480 21. Bergeron B. *Developing serious games*. 1 ed. Newton Centre, Massachusetts: Charles
481 River Media; 2006.
- 482 22. Stokes BG. Videogames have changed: Time to consider serious games? *Development*
483 *Education Journal*. 2005;11(3):12.
- 484 23. Kirkpatrick DL. Luminary perspective: evaluating training programs. In: Biech E, ed.
485 *ASTD Handbook for Workplace Learning Professionals* Alexandria, Virginia: ASTD
486 Press; 2008:485-491.
- 487 24. Vlachopoulos D, Makri A. The effect of games and simulations on higher education: a
488 systematic literature review. *International Journal of Educational Technology in Higher*
489 *Education*. 2017;14(1):22.
- 490 25. Cochrane Effective Practice and Organisation of Care Review Group (EPOC). *Data*
491 *collection checklist*. Ottawa, Canada: Institute of Population Health, University of
492 Ottawa;2002.
- 493 26. Cochrane Effective Practice and Organisation of Care (EPOC). Suggested risk of bias
494 criteria for EPOC reviews. EPOC Resources for review authors Web site.
495 <http://epoc.cochrane.org/resources/epoc-resources-review-authors>. Published 2017.
496 Accessed May 23, 2019.
- 497 27. Savovic J, Turner RM, Mawdsley D, et al. Association Between Risk-of-Bias
498 Assessments and Results of Randomized Trials in Cochrane Reviews: The ROBES Meta-
499 Epidemiologic Study. *Am J Epidemiol*. 2018;187(5):1113-1122.
- 500 28. Higgins JP, Green S. *Cochrane handbook for systematic reviews of interventions*. Vol 4:
501 John Wiley & Sons; 2011.
- 502 29. Johnson L, Adams Becker S, Estrada V, Freeman A. *NMC Horizon Report: 2014 Higher*
503 *Education Edition*. Austin, Texas: The New Media Consortium;2014.

- 504 30. Turner RM, Bird SM, Higgins JPT. The impact of study size on meta-analyses:
505 examination of underpowered studies in Cochrane reviews. *PloS one*. 2013;8(3):e59202-
506 e59202.
- 507 31. Schwarzer G, Carpenter JR, Rücker G. Small-Study Effects in Meta-Analysis. In: *Meta-*
508 *Analysis with R*. Cham: Springer International Publishing; 2015:107-141.
- 509 32. Dijkers M. Introducing GRADE: a systematic approach to rating evidence in systematic
510 reviews and to guideline development. *KT Update*. 2013;1(5):1-9.
- 511 33. Buijs-Spanjers KR, Hegge HHM, Cnossen F, Hoogendoorn E, Jaarsma D, de Rooij SE.
512 Dark play of serious games: effectiveness and features (G4HE2018). *Games Health J*.
513 2019;8(4):1-6.
- 514 34. Kerfoot BP, Baker H. An online spaced-education game for global continuing medical
515 education: a randomized trial. *Ann Surg*. 2012;256(1):33-38.
- 516 35. Haubruck P, Nickel F, Ober J, et al. Evaluation of App-Based Serious Gaming as a
517 Training Method in Teaching Chest Tube Insertion to Medical Students: Randomized
518 Controlled Trial. *J Med Internet Res*. 2018;20(5):e195.
- 519 36. Courtier J, Webb EM, Phelps AS, Naeger DM. Assessing the learning potential of an
520 interactive digital game versus an interactive-style didactic lecture: the continued
521 importance of didactic teaching in medical student education. *Pediatr Radiol*.
522 2016;46(13):1787-1796.
- 523 37. Dankbaar ME, Alsma J, Jansen EE, van Merriënboer JJ, van Saase JL, Schuit SC. An
524 experimental study on the effects of a simulation game on students' clinical cognitive
525 skills and motivation. *Adv Health Sci Educ Theory Pract*. 2016;21(3):505-521.
- 526 38. Harrington CM, Chaitanya V, Dicker P, Traynor O, Kavanagh DO. Playing to your skills:
527 a randomised controlled trial evaluating a dedicated video game for minimally invasive
528 surgery. *Surg Endosc*. 2018;32(9):3813-3821.

- 529 39. Mohan D, Farris C, Fischhoff B, et al. Efficacy of educational video game versus
530 traditional educational apps at improving physician decision making in trauma triage:
531 randomized controlled trial. *BMJ*. 2017;359.
- 532 40. Mohan D, Fischhoff B, Angus DC, et al. Serious games may improve physician heuristics
533 in trauma triage. *Proc Natl Acad Sci U S A*. 2018;115(37):9204-9209.
- 534 41. Rondon S, Sassi FC, de Andrade CRF. Computer game-based and traditional learning
535 method: a comparison regarding students' knowledge retention. *BMC Medical Education*.
536 2013;13(1):30.
- 537 42. Sward KA, Richardson S, Kendrick J, Maloney C. Use of a Web-based game to teach
538 pediatric content to medical students. *Academic Pediatrics*. 2008;8(6):354-359.
- 539 43. Diehl LA, Souza RM, Gordan PA, Esteves RZ, Coelho IC. InsuOnline, an electronic
540 game for medical education on insulin therapy: a randomized controlled trial with primary
541 care physicians. *Journal of Medical Internet Research*. 2017;19(3):e72.
- 542 44. Mohan D, Farris C, Fischhoff B, et al. Efficacy of educational video game versus
543 traditional educational apps at improving physician decision making in trauma triage:
544 randomized controlled trial. *BMJ*. 2017;359:j5416.
- 545 45. Drummond D, Delval P, Abdenouri S, et al. Serious game versus online course for
546 pretraining medical students before a simulation-based mastery learning course on
547 cardiopulmonary resuscitation: a randomised controlled study. *European Journal of*
548 *Anaesthesiology*. 2017;34(12):836-844.
- 549 46. Kerfoot BP, Turchin A, Breydo E, Gagnon D, Conlin PR. An online spaced-education
550 game among clinicians improves their patients' time to blood pressure control: a
551 randomized controlled trial. *Circ Cardiovasc Qual Outcomes*. 2014;7(3):468-474.
- 552 47. Graafland M, Bemelman WA, Schijven MP. Game-based training improves the surgeon's
553 situational awareness in the operation room: a randomized controlled trial. *Surg Endosc*.
554 2017.

- 555 48. Diehl LA, Souza RM, Gordan PA, Esteves RZ, Coelho IC. InsuOnline, an Electronic
556 Game for Medical Education on Insulin Therapy: A Randomized Controlled Trial With
557 Primary Care Physicians. *J Med Internet Res*. 2017;19(3):e72.
- 558 49. Dankbaar ME, Richters O, Kalkman CJ, et al. Comparative effectiveness of a serious
559 game and an e-module to support patient safety knowledge and awareness. *BMC Med*
560 *Educ*. 2017;17(1):30.
- 561 50. Zaharias P, Poylymenakou A. Developing a usability evaluation method for e-learning
562 applications: Beyond functional usability. *Intl Journal of Human-Computer Interaction*.
563 2009;25(1):75-98.
- 564 51. Tan AJQ, Lee CCS, Lin PY, et al. Designing and evaluating the effectiveness of a serious
565 game for safe administration of blood transfusion: A randomized controlled trial. *Nurse*
566 *Educ Today*. 2017;55:38-44.
- 567 52. Wu WH, Hsiao HC, Wu PL, Lin CH, Huang SH. Investigating the learning-theory
568 foundations of game-based learning: a meta-analysis. *J Comput Assist Learn*.
569 2012;28(3):265-279.
- 570 53. Brull S, Finlayson S, Kostelec T, MacDonald R, Krenzischek D. Using Gamification to
571 Improve Productivity and Increase Knowledge Retention During Orientation. *J Nurs*
572 *Adm*. 2017;47(9):448-453.
- 573 54. Cook DA. The research we still are not doing: an agenda for the study of computer-based
574 learning. *Acad Med*. 2005;80(6):541-548.
- 575 55. Sim I, Chan A-W, Gülmezoglu AM, Evans T, Pang T. Clinical trial registration:
576 transparency is the watchword. *The Lancet*. 2006;367(9523):1631-1633.
- 577 56. Schulz KF, Altman DG, Moher D. CONSORT 2010 statement: updated guidelines for
578 reporting parallel group randomised trials. *BMC medicine*. 2010;8(1):18.
- 579 57. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review
580 and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev*. 2015;4(1):1.

581 58. Panzoli D, Lelardeux CP, Galaup M, Lagarrigue P, Minville V, Lubrano V. Interaction
582 and communication in an immersive learning game: the challenges of modelling real-time
583 collaboration in a virtual operating room. In: Ma M, Oikonomou A, Jain LC, eds. *Serious*
584 *Games and Edutainment Applications*. Gewerbestrasse, Suisse: Springer; 2017:147-186.

585

586

587 **Figure legends**

588 **Figure 1. PRISMA flow diagram**

589 **Figure 2. Risk of bias graph**

590 **Figure 3. Meta-analysis of the efficacy of serious games on supporting behavioral engagement**

591 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

592 **Figure 4. Meta-analysis of the efficacy of serious games on knowledge acquisition**

593 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

594 **Figure 5. Meta-analysis of the efficacy of serious games on improving confidence in skills**

595 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

596 **Figure 6. Meta-analysis of the efficacy of serious games on improving cognitive skills**

597 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

598 **Figure 7. Meta-analysis of the efficacy of serious games on improving procedural skills**

599 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

600 **Figure 8. Meta-analysis of the efficacy of serious games on attitude change**

601 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

602 **Figure 9. Meta-analysis of the efficacy of serious games on behavior change**

603 Note. CI: confidence interval; IV: inverse of the variance; SD: standard deviation

604

605 **Supplementary Digital Content**

606 **Supplementary Digital Content 1.** pdf, All search strategies

607 **Supplementary Digital Content 2.** pdf, Meta-analyses of studies evaluating the efficacy of SGs versus
608 passive comparators

609 **Supplementary Digital Content 3.** pdf, List of included studies

610 **Supplementary Digital Content 4.** pdf, List of excluded studies at full-text assessment stage

611 **Supplementary Digital Content 5.** pdf, Risk of bias summary

612 **Supplementary Digital Content 6.** pdf, Funnel Plot

613 **Supplementary Digital Content 7.** pdf, Key information of the serious games assessed

614 **Supplementary Digital Content 8.** pdf, Subgroup and sensitivity analyses

Table 1. Key information of included studies

First author-year, Country	Study design	Study participants	Outcomes [†]
Compared to classroom learning			
Courtier-2016 United States	Two-group cluster randomized controlled trial	48 fourth-year medical students	Experiential engagement Knowledge
Diehl-2017 Brazil	Two-group randomized controlled trial	170 primary care physicians	Attitudes [§] Behaviors [§] Cognitive skills ^{§*} Experiential engagement
Hannig-2013 Germany	Two-group randomized controlled trial	55 second-year dental students	Confidence
Knight-2010 United Kingdoms	Two-group randomized controlled trial	91 various healthcare professionals (e.g., medical doctors, nurses, paramedic)	Cognitive skills* Procedural skills
Compared to written material			
Boeker-2013 Germany	Two-group randomized controlled trial	145 third-year medical students	Experiential engagement Knowledge*
Polivka-2019 USA	Two-group randomized controlled trial	74 various healthcare professionals and students	Cognitive skills
Rondon-2013 Brazil	Two-group randomized controlled trial	29 second-year speech-language and hearing science students	Knowledge [§]
Compared to e-learning			
Adjedj-2017 France	Two-group randomized crossover trial	68 medical students	Experiential engagement*

First author-year, Country	Study design	Study participants	Outcomes [†]
Berger-2018 Switzerland	Two-group randomized controlled trial	117 second-year pharmacy students	Attitude Confidence Experiential engagement Knowledge
Buijs-Spanjers-2018 Netherlands	Three-group randomized controlled trial	176 third-year medical students	Attitude Cognitive skills* Experiential engagement*
Dankbaar-2017 Netherlands	Two-group randomized controlled trial	90 fourth-year medical students	Behavioral engagement* Behaviors Confidence Experiential engagement Knowledge
de Sena-2019 Brazil	Two-group randomized controlled trial	45 first-year medical students	Behavioral engagement* Knowledge Procedural skills
Drummond-2017 France	Two-group randomized controlled trial	82 second-year medical students	Procedural skills [§]
Gauthier-2015 Canada	Two-group randomized controlled trial	46 first-year medical anatomy students	Behavioral engagement Knowledge
Kerfoot-2014 USA	Two-group randomized controlled trial	111 physicians, nurse practitioners, and physician assistants	Behavioral engagement Clinical outcome in patients* Knowledge*
Mohan-2017 USA	Four-group randomized controlled trial	368 emergency medicine physicians	Behavioral engagement Cognitive skills ^{§*} Experiential engagement
Scales-2016 USA	Two-group randomized controlled trial	422 resident physicians from various training specialties	Knowledge

First author-year, Country	Study design	Study participants	Outcomes[†]
Sward-2008 USA	Two-group randomized controlled trial	100 third-year medical students	Experiential engagement Knowledge [§]
Compared to another serious game			
Buijs-Spanjers-2019 Netherlands	Two-group randomized controlled trial	159 third-year medical students	Attitudes Cognitive skills Experiential engagement
Haubruck-2018 Germany	Two-group randomized controlled trial	95 third-to-six-year medical students	Experiential engagement* Procedural skills*
Kerfoot-2012 USA	Two-group randomized controlled trial	1470 urologists from various countries	Knowledge*
Compared to simulation or virtual simulation			
Chee-2019 Singapore	Two-group randomized controlled trial	46 registered nurses	Confidence* Procedural skills*
Chien-2013 United States	Two-group randomized controlled trial	14 medical students	Procedural skills
Katz-2017 USA	Two-group randomized controlled trial	44 residents on liver transplant rotation	Procedural skills*
Compared to multiple interventions			
Brull-2017 United States	Three-group randomized controlled trial	115 newly graduated nurses at an urban community teaching hospital	Knowledge*
		Compared to classroom learning and e-learning	
Dankbaar-2016 Netherlands	Three-group randomized controlled trial	79 fourth-year medical students	Behavioral engagement Cognitive skills Experiential engagement

First author-year, Country	Study design	Study participants	Outcomes[†]
		Compared to e-learning and to no intervention	
Mohan-2018 USA	Four-group randomized controlled trial	320 emergency medicine physicians Compared to e-learning, serious game, and no intervention	Behavioral engagement Cognitive skills* Experiential engagement
Compared to no intervention			
Boada-2015 Spain	Two-group randomized controlled trial	109 second-year nursing students	Procedural skills*
Cook-2012 United Kingdoms	Two-group randomized controlled trial	34 third-year nursing students	Procedural skills
Del Blanco-2017 Spain	Two-group randomized controlled trial	132 second- and third-year nursing and medicine students	Behaviors* Confidence
Foss-2014 Norway	Two-group randomized controlled trial	201 first- and second-year undergraduate nursing students	Cognitive skills
Graafland-2017 Netherlands	Two-group randomized controlled trial	31 first- or second-year residents in general surgical training	Cognitive skills
Harrington-2018 Ireland	Two-group randomized controlled trial	20 first-to-third-year medical students	Procedural skills*
Lagro-2014 Netherlands	Two-group randomized controlled trial	145 fifth-year medical students	Attitude Knowledge
Li-2015 China	Two-group randomized controlled trial	97 freshman medical students	Procedural skills*

First author-year, Country	Study design	Study participants	Outcomes[†]
Tan-2017 Singapore	Two-group cluster randomized controlled trial	111 second-year nursing students	Confidence* Knowledge* Procedural skills
Van Nuland- 2014 Canada	Three-group crossover randomized controlled trial	67 kinesiology students	Knowledge*

Note. ‡ Comparator refers to an intervention solely received by the control group (i.e., an intervention that is not shared with the experimental group). § An outcome that was also measured at a follow-up period. * An outcome for which there was a statistically significant difference favoring the experimental group.

Table 2. Summary of our certainty in the quantitative evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

Outcomes	Standardized mean differences (SMDs)/ mean differences (MDs) with 95% confidence interval (CI)	N ^o of participants (studies)	Certainty of the evidence (GRADE)	Justification
Learning time with the intervention (in minutes)	MD 23.21 (95%CI -1.25, 47.66)	377 (4 RCTs)	⊕○○○ Very low	Serious risk of bias and very serious imprecision. However, mostly consistent results
Knowledge	SMD 0.16 (95%CI -0.20, 0.52)	1047 (11 RCTs)	⊕○○○ Very low	Serious risk of bias and inconsistency, and very serious imprecision of results
Confidence in skills	SMD 0.27 (95%CI 0.01, 0.53)	235 (4 RCTs)	⊕⊕⊕○ Moderate	Serious risk of bias. However, consistent and precise results
Cognitive skills	SMD 0.08 (95%CI -0.73, 0.89)	634 (5 RCTs)	⊕○○○ Very low	Serious risk of bias and inconsistency, and very serious imprecision of results
Procedural skills	SMD 0.05 (95%CI -0.78, 0.87)	210 (4 RCTs)	⊕○○○ Very low	Serious risk of bias and inconsistency, and very serious imprecision of results
Attitudes	SMD -0.09 (95%CI -0.38, 0.20)	352 (3 RCTs)	⊕⊕○○ Low	Serious risk of bias and imprecision of results, and very serious inconsistency
Behaviors	SMD 0.2 (95%CI -0.11, 0.51)	164 (2 RCTs)	⊕⊕○○ Low	Serious risk of bias and inconsistency. However, precise results

Note. CI : Confidence interval; RCT : Randomized controlled trial; SMD : Standardized mean difference

Satisfaction The intervention fulfills learners' overall expectations and needs.	- -	+*	+* -	+
Stress The intervention is perceived as excessively demanding by learners.			-	
Usability The intervention is perceived as easy to use by learners.			+ -* +	-* -*

Note. +: The serious game was rated as superior to the comparator intervention; ○: No difference was reported; -: The serious game was rated as inferior to the comparator intervention; *: This difference reached statistical significance.

Figure 1 - PRISMA Flow diagram

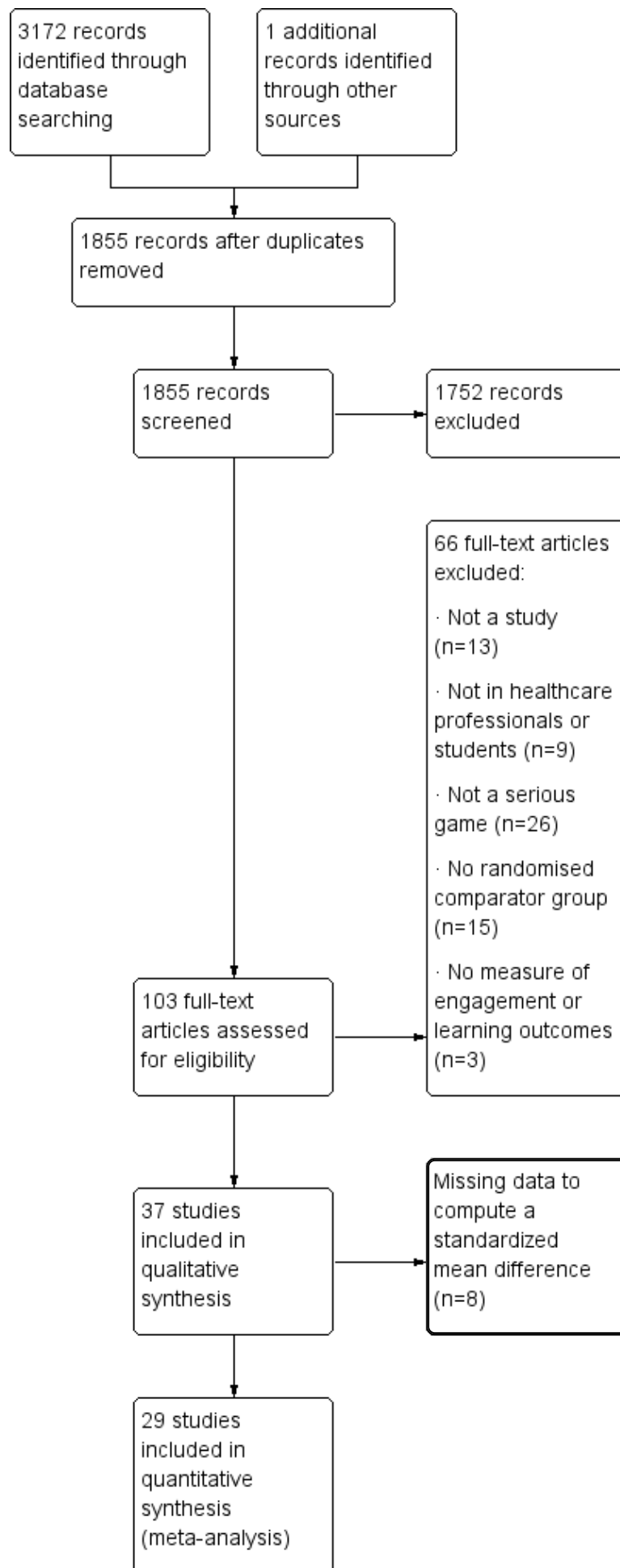


Figure 2 -
Risk of bias graph

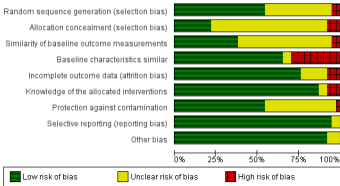
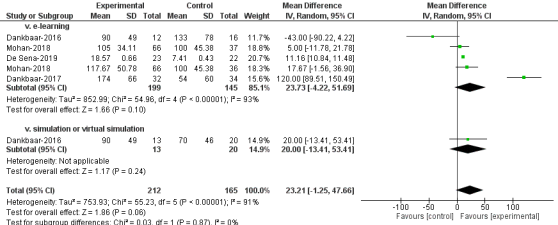
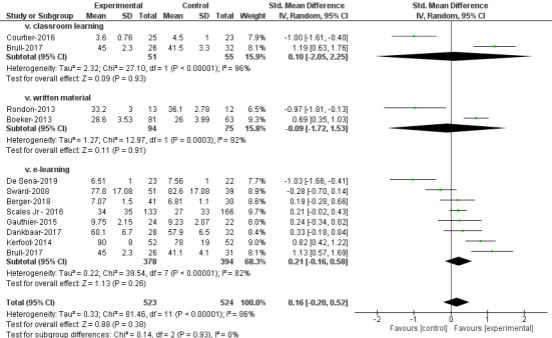


Figure 3 -
Meta-analysis on
time spent with
the intervention



**Figure 4 -
Meta-analysis on
knowledge
acquisition**



**Figure 4 -
Meta-analysis on
confidence
improvement**

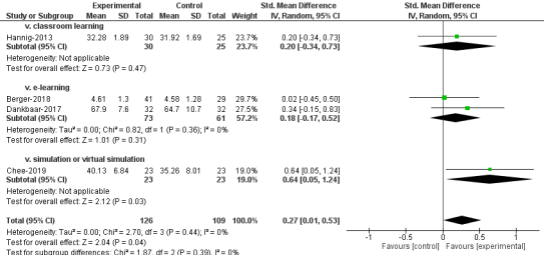
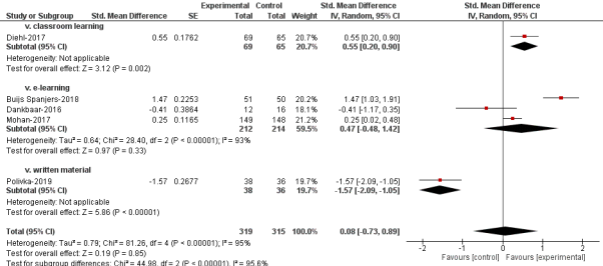
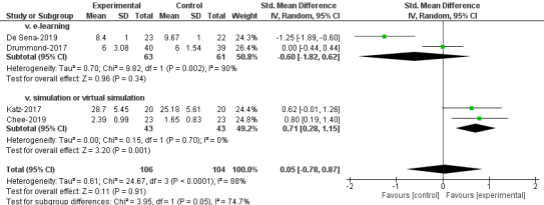


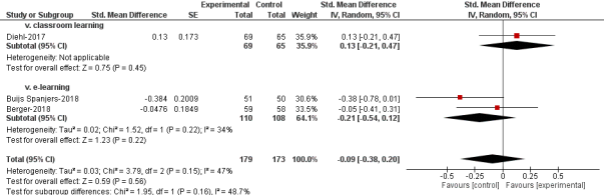
Figure 4 -
Meta-analysis on
cognitive skill
development



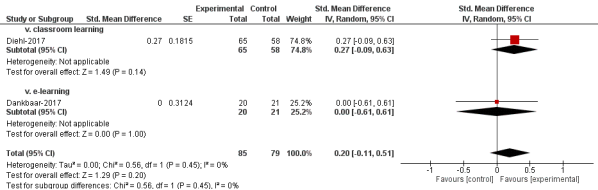
**Figure 5 -
Meta-analysis on
procedural skill
development**



**Figure 6 -
Meta-analysis on
attitude change**



**Figure 7 -
Meta-analysis on
behavior change**



Supplementary
content 1 -
Search strategy

CINAHL

1. TI ("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "overthecounter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*")))) OR AB ("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "over-the-counter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*"))))

2. (MH "Video Games+")

3. 1 OR 2

4. TI ("Health Personnel" OR "Health professional*" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student*" OR "Medical assistant*" OR "health worker*" OR Audiologist* OR Chiropractor* OR Dentist* OR Dietitian* OR Dermatolog* OR Endocrinologist* OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife* OR neurologi* OR nutritionist* OR Nurse* OR nursing OR Optometrist* OR "Occupational Therapist*" OR Patholog* OR Paramedic* OR Paediatric* OR pediatrician* OR Paediatrician* OR pediatric* OR Pharmacist* OR Pharmaconomist* OR Pharmacologist* OR "Pharmacy technician*" OR Phlebotomist* OR Physician* OR Podiatrist* OR Psychologist* OR Psychotherapist* OR psychiatrist* OR "Physical therapist*" OR physiotherapist* OR "Respiratory therapist*" OR Surgeon* OR surgical OR Clinician* OR Cardiologist* OR "medical technician*" OR "emergency doctor*" OR emergentologist* OR "clinical officer*" OR "Community health worker*" OR Radiographer* OR technologist* OR Radiotherapist* OR Anesthetist* OR Resident* OR trainee* OR intern*) OR AB ("Health Personnel" OR "Health professional*" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student*" OR "Medical assistant*" OR "health worker*" OR Audiologist* OR Chiropractor* OR Dentist* OR Dietitian* OR Dermatolog* OR endocrinologist* OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife* OR neurologi* OR nutritionist* OR Nurse* OR nursing OR Optometrist* OR "Occupational Therapist*" OR Patholog* OR Paramedic* OR Paediatric* OR pediatrician* OR Paediatrician* OR pediatric* OR Pharmacist* OR Pharmaconomist* OR Pharmacologist* OR "Pharmacy technician*" OR Phlebotomist* OR Physician* OR Podiatrist* OR Psychologist* OR Psychotherapist* OR psychiatrist* OR "Physical therapist*" OR physiotherapist* OR "Respiratory therapist*" OR Surgeon* OR surgical OR Clinician* OR Cardiologist* OR "medical technician*" OR "emergency doctor*" OR emergentologist* OR "clinical officer*" OR "Community health worker*" OR Radiographer* OR technologist* OR Radiotherapist* OR Anesthetist* OR Resident* OR trainee* OR intern*)

5. (MH "Health Personnel+") OR (MH "Students, Medical") OR (MH "Students, Nursing+")

6. (MH "Education, Premedical") OR (MH "Education, Medical+") OR (MH "Education, Nursing+") OR (MH "Education, Pharmacy")

7. 4 OR 5 OR 6

8. TI (Knowledge* OR Aptitude* OR accuracy OR abilit* OR capacity* OR confidence OR competenc* OR impact* OR skill* OR performance* OR "Learning outcome*" OR "training outcome*" OR effectiveness OR efficacy OR improvement* OR innovat* OR retention OR "randomi?ed controlled trial") OR AB (Knowledge* OR Aptitude* OR accuracy OR abilit* OR capacity* OR confidence OR competenc* OR impact* OR skill* OR performance* OR "Learning outcome*" OR "training outcome*" OR effectiveness OR efficacy OR improvement* OR innovat* OR retention OR "randomi?ed controlled trial")

9. (MH "Knowledge+") OR (MH "Clinical Competence+") OR (MH "Quality Improvement+") OR (MH "Learning+") OR (MH "Educational Measurement+") OR (PT "randomized controlled trial")

10. 8 OR 9

11. 3 AND 7 AND 10

12. 11 AND LA ((english OR french)) AND DT 20000101-20171231 AND PT Journal Article

EMBASE (OVID)

1. ("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "overthecounter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*")))).ti,ab.
2. exp video game/
3. 1 OR 2
4. ("Health Personnel" OR "Health professional\$1" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student\$1" OR "Medical assistant\$1" OR "health worker\$1" OR Audiologist\$1 OR Chiropractor\$1 OR Dentist\$1 OR Dietitian\$1 OR Dermatolog* OR endocrinologist\$1 OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife\$1 OR neurologi*OR nutritionist\$1 OR Nurse\$1 OR nursing OR Optometrist\$1 OR "Occupational Therapist\$1" OR Patholog* OR Paramedic\$1 OR Paediatric\$1 OR pediatrician\$1 OR Paediatrician\$1 OR podiatrist\$1 OR pediatric\$1 OR Pharmacist\$1 OR Pharmaconomist\$1 OR Pharmacologist\$1 OR "Pharmacy technician\$1" OR Phlebotomist\$1 OR Physician\$1 OR Podiatrist\$1 OR Psychologist\$1 OR Psychotherapist\$1 OR psychiatrist\$1 OR "Physical therapist\$1" OR physiotherapist\$1 OR "Respiratory therapist\$1" OR Surgeon\$1 OR Surgical OR Clinician\$1 OR Cardiologist\$1 OR "medical technician\$1" OR "emergency doctor\$1" OR emergentologist\$1 OR "clinical officer\$1" OR "Community health worker\$1" OR Radiographer\$1 OR technologist\$1 OR Radiotherapist\$1 OR Anesthetist\$1 OR Resident\$1 OR trainee\$1 OR intern\$1).ti,ab.
5. exp health care personnel/ OR exp premedical student/ OR exp medical student/ OR exp nursing student/
6. exp medical education/ OR exp nursing education/ OR exp clinical education/
7. 4 OR 5 OR 6
8. (Knowledge\$1 OR Aptitude\$1 OR accuracy OR abilit* OR capacity* OR confidence OR competenc*OR impact\$1 OR skill\$1 OR performance\$1 OR "Learning outcome\$1" OR "training outcome*" OR effectiveness OR efficacy OR improvement\$1 OR innovat* OR retention OR "randomi?ed controlled trial").ti,ab.
9. exp clinical competence/ OR *total quality management/ OR exp learning curve/ OR exp knowledge/ OR exp Randomized Controlled Trials as Topic/
10. 8 OR 9
11. 3 AND 7 AND 10
12. 2000:2017.dp. AND (english OR french).la. AND Journal: Article.pt.
13. 11 AND 12

ERIC (ProQuest)

1. TI,AB("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "over-the-counter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*"))))
2. SU.EXACT("Video Games")
3. 1 OR 2
4. TI,AB("Health Personnel" OR "Health professional\$1" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student\$1" OR "Medical assistant\$1" OR "health worker\$1" OR Audiologist\$1 OR Chiropractor\$1 OR Dentist\$1 OR Dietitian\$1 OR Dermatolog* OR endocrinologist\$1 OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife\$1 OR neurologi*OR nutritionist\$1 OR Nurse\$1 OR nursing OR Optometrist\$1 OR "Occupational Therapist\$1" OR Patholog* OR Paramedic\$1 OR Paediatric\$1 OR pediatrician\$1 OR Paediatrician\$1 OR podiatrist\$1 OR pediatric\$1 OR Pharmacist\$1 OR Pharmaconomist\$1 OR Pharmacologist\$1 OR "Pharmacy technician\$1" OR Phlebotomist\$1 OR Physician\$1 OR Podiatrist\$1 OR Psychologist\$1 OR Psychotherapist\$1 OR psychiatrist\$1 OR "Physical therapist\$1" OR physiotherapist\$1 OR "Respiratory therapist\$1" OR Surgeon\$1 OR Surgical OR Clinician\$1 OR Cardiologist\$1 OR "medical technician\$1" OR "emergency doctor\$1" OR emergentologist\$1 OR "clinical officer\$1" OR "Community health worker\$1" OR Radiographer\$1 OR technologist\$1 OR Radiotherapist\$1 OR Anesthetist\$1 OR Resident\$1 OR OR trainee\$1 OR intern\$1)
5. SU.EXACT.EXPLODE("Health Personnel") OR SU.EXACT("Premedical Students")OR SU.EXACT.EXPLODE("Medical Students") OR SU.EXACT.EXPLODE("Nursing Students")
6. SU.EXACT.EXPLODE("Pharmaceutical Education") OR SU.EXACT.EXPLODE("Medical Education") OR SU.EXACT.EXPLODE("Nursing Education") OR SU.EXACT.EXPLODE("Clinical Experience")
7. 4 OR 5 OR 6
8. TI,AB(Knowledge\$1 OR Aptitude\$1 OR accuracy OR abilit* OR capacity* OR confidence OR competenc*OR impact\$1 OR skill\$1 OR performance\$1 OR "Learning outcome\$1" OR "training outcome*" OR effectiveness OR efficacy OR improvement\$1 OR innovat* OR retention OR "randomi?ed controlled trial")
9. SU.EXACT.EXPLODE("Learning Processes") OR SU.EXACT.EXPLODE("Knowledge Level") OR SU.EXACT.EXPLODE("Skill Development") OR SU.EXACT.EXPLODE("Outcomes of Education")
10. 8 OR 9
11. 3 AND 7 AND 10
12. PD(2000-2017) AND LA(english OR french) AND DTYPE(journal articles)
13. 11 AND 12

PsychINFO (APA PsychNet)

1. **Title** : ("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "over-the-counter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*")))) *OR Abstract* : ("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "over-the-counter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*")))) *OR Index terms*: {Computer Games}

2. **Title** : ("Health Personnel" OR "Health professional*" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student*" OR "Medical assistant*" OR "health worker*" OR Audiologist* OR Chiropractor* OR Dentist* OR Dietitian* OR Dermatolog* OR endocrinologist* OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife* OR neurologi* OR nutritionist* OR Nurse* OR nursing OR Optometrist* OR "Occupational Therapist*" OR Patholog* OR Paramedic* OR Paediatric* OR pediatrician* OR Paediatrician* OR pediatric* OR Pharmacist* OR Pharmaconomist* OR Pharmacologist* OR "Pharmacy technician*" OR Phlebotomist* OR Physician* OR Podiatrist* OR Psychologist* OR Psychotherapist* OR psychiatrist* OR "Physical therapist*" OR physiotherapist* OR "Respiratory therapist*" OR Surgeon* OR surgical OR Clinician* OR Cardiologist* OR "medical technician*" OR "emergency doctor*" OR emergentologist* OR "clinical officer*" OR "Community health worker*" OR Radiographer* OR technologist* OR Radiotherapist* OR Anesthetist* OR Resident* OR trainee* OR intern*) *OR Abstract*: ("Health Personnel" OR "Health professional*" OR "Health care profession*" OR "Healthcare profession*" OR "Medical student*" OR "Medical assistant*" OR "health worker*" OR Audiologist* OR Chiropractor* OR Dentist* OR Dietitian* OR Dermatolog* OR endocrinologist* OR Gastroenterolog* OR Gynecolog* OR Radiolog* OR "Medical Staff" OR Midwife* OR neurologi* OR nutritionist* OR Nurse* OR nursing OR Optometrist* OR "Occupational Therapist*" OR Patholog* OR Paramedic* OR Paediatric* OR pediatrician* OR Paediatrician* OR pediatric* OR Pharmacist* OR Pharmaconomist* OR Pharmacologist* OR "Pharmacy technician*" OR Phlebotomist* OR Physician* OR Podiatrist* OR Psychologist* OR Psychotherapist* OR psychiatrist* OR "Physical therapist*" OR physiotherapist* OR "Respiratory therapist*" OR Surgeon* OR surgical OR Clinician* OR Cardiologist* OR "medical technician*" OR "emergency doctor*" OR emergentologist* OR "clinical officer*" OR "Community health worker*" OR Radiographer* OR technologist* OR Radiotherapist* OR Anesthetist* OR Resident* OR trainee* OR intern*) *OR Index terms*: {Allied Health Personne} OR {Health Personne} OR {Medical Personnel} OR {Mental Health Personnel} OR {Medical Students} OR {Nursing Students} *OR Index terms*: {Medical Education} OR {Nursing Education} OR {Medical Internship} OR {Medical Residency} OR {Psychiatric Training}

3. **Title** : (Knowledge* OR Aptitude* OR accuracy OR abilit* OR capacity* OR confidence OR competenc* OR impact* OR skill* OR performance* OR "Learning outcome*" OR "training outcome*" OR effectiveness OR efficacy OR improvement* OR innovat* OR retention OR "randomi?ed controlled trial") *OR Abstract* : (Knowledge* OR Aptitude* OR accuracy OR abilit* OR capacity* OR confidence OR competenc* OR impact* OR skill* OR performance* OR "Learning outcome*" OR "training outcome*" OR effectiveness OR efficacy OR

improvement* OR innovat* OR retention OR "randomized controlled trial") OR **Index Terms:**
{Declarative Knowledge} OR {Health Knowledge} OR {Job Knowledge} OR {Knowledge
(General)} OR {Learning} OR {Procedural Knowledge} OR {Professional Competence} OR
{Skill Learning} OR {Educational Measurement}

4. 1 AND 2 AND 3

5. **Language:**(english OR french) AND **Document type:** Journal Article AND **Year:** 2000 to
2017

6. 4 AND 5

PubMed

1. serious gam*[TIAB] OR applied gam*[TIAB] OR ((simulation[TIAB] OR training [TIAB] OR teaching[TIAB] OR educational[TIAB] OR education[TIAB] OR learning[TIAB] OR interactive[TIAB]) AND (((online[TIAB] OR electronic[TIAB] OR digital[TIAB] OR "over-the-counter"[TIAB] OR commercial[TIAB] OR computer[TIAB] OR virtual[TIAB] OR mobile application*[TIAB] OR mobile app[TIAB]) AND (game[TIAB] OR games[TIAB] OR gamification[TIAB] OR gaming[TIAB] OR game-based[TIAB]))) OR (videogame*[TIAB] OR video game*[TIAB]))
2. "Video Games"[MH]
3. #1 OR #2
4. Health Personnel*[TIAB] OR Health professional*[TIAB] OR Health care profession*[TIAB] OR Healthcare profession*[TIAB] OR Medical student*[TIAB] OR Medical assistant*[TIAB] OR health worker*[TIAB] OR Audiologist*[TIAB] OR Chiropractor*[TIAB] OR Dentist[TIAB] OR Dentists[TIAB] OR Dietitian*[TIAB] OR Dermatolog*[TIAB] OR endocrinologist*[TIAB] OR Gastroenterolog*[TIAB]OR Gynecolog*[TIAB]OR Radiolog*[TIAB] OR Medical Staff[TIAB] OR Midwife*[TIAB] OR neurologi*[TIAB] OR nutritionist*[TIAB] OR Nurse[TIAB] OR Nurses[TIAB] OR nursing[TIAB] OR Optometrist*[TIAB] OR Occupational Therapist*[TIAB] OR Patholog*[TIAB] OR Paramedic[TIAB] OR Paediatric[TIAB] OR pediatrician*[TIAB] OR Paediatrician*[TIAB] OR pediatricist*[TIAB] OR pediatric[TIAB] OR Pharmacist*[TIAB] OR Pharmaconomist*[TIAB] OR Pharmacologist*[TIAB] OR Pharmacy technician*[TIAB] OR Phlebotomist*[TIAB] OR Physician OR Podiatrist*[TIAB] OR Psychologist*[TIAB] OR Psychotherapist*[TIAB] OR psychiatrist*[TIAB] OR Physical therapist*[TIAB] OR physiotherapist*[TIAB] OR Respiratory therapist*[TIAB] OR Surgeon*[TIAB] OR surgical [TIAB] OR Clinician*[TIAB] OR Cardiologist*[TIAB] OR medical technician*[TIAB] OR emergency doctor*[TIAB] OR emergentologist*[TIAB] OR clinical officer*[TIAB] OR Community health worker*[TIAB] OR Radiographer*[TIAB] OR Radiotherapist*[TIAB] OR technologist[TIAB] Anesthetist*[TIAB] OR Resident[TIAB] OR residents[TIAB] OR trainee[TIAB] OR trainees[TIAB] OR intern[TIAB] OR interns[TIAB]
5. "Health Personnel"[MH] OR "Students, Premedical"[MH] OR "Students, Medical"[MH] OR "Students, Nursing"[Mesh]
6. "Education, Premedical"[MH] OR "Education, Medical"[MH] OR "Education, Nursing"[MH] OR "Education, Pharmacy"[MH] OR "Education, Public Health Professional"[MH] OR "Clinical Clerkship"[MH]
7. #4 OR #5 OR 6
8. knowledge*[TIAB] OR aptitude*[TIAB] OR accuracy[TIAB] OR ability[TIAB] OR abilities[TIAB] OR capacity [TIAB] OR capacities[TIAB] OR confidence[TIAB] OR competency[TIAB] OR competencies[TIAB] OR impact*[TIAB] OR skill*[TIAB] OR performance*[TIAB] OR learning outcome*[TIAB] OR training outcome*[TIAB] OR effectiveness[TIAB] OR efficacy[TIAB] OR improvement*[TIAB] OR innovative*[TIAB] OR innovation*[TIAB] OR retention[TIAB] OR randomised controlled trial[TIAB] OR randomized controlled trial[TIAB]
9. "Clinical Competence"[MH] "Quality Improvement"[MH] OR "Learning Curve"[MH] OR Knowledge [MH] OR "Educational Measurement"[MH] OR "randomized controlled trial"[PT]

10. #8 OR 9

11. #3 AND #7 AND #10

12. (english[LA] OR french[LA]) AND 2000:2017[DP]

13. #11 AND #12

Web of Sciences

Science Citation Index Expanded (SCI-EXPANDED) --1945-present

Social Sciences Citation Index (SSCI) --1956-present

1. TS=("serious gam*" OR "applied gam*" OR ((simulation OR training OR teaching OR educational OR education OR learning OR interactive) AND (((online OR electronic OR digital OR "over-the-counter" OR commercial OR computer OR virtual OR "mobile application*" OR "mobile app") AND (game OR games OR gamification OR gaming)) OR (videogame* OR "video game*"))))

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3. TS=("Clinical Clerkship" OR ((Clinical OR medical OR premedical OR pharma* OR nurse\$) NEAR/3 (education OR training))

4. 2 OR 3

5. TS=(Knowledge\$ OR Aptitude\$ OR accuracy OR abilit* OR capacity* OR confidence OR competenc* OR impact\$ OR skill\$ OR performance\$ OR "Learning outcome\$" OR "training outcome*" OR effectiveness OR efficacy OR improvement\$ OR innovat* OR retention OR "randomi?ed controlled trial")

6. 1 AND 2 AND 4

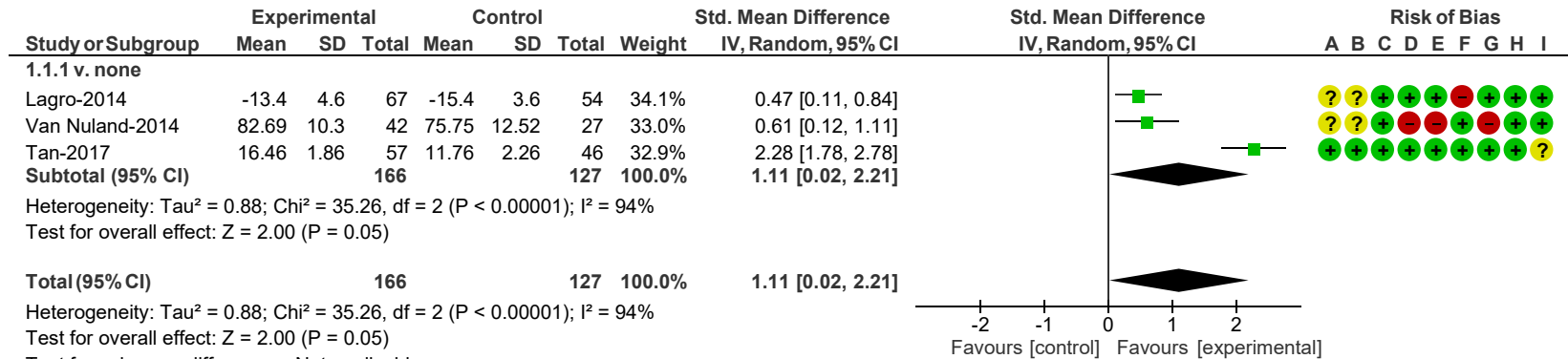
7. (PY=(2000-2017)) AND LANGUAGE: (English OR French) AND DOCUMENT TYPES: (Article OR Review)

8. 6 AND 7

Supplementary
content 2 -
Meta-analyses
on the efficacy
of serious
games versus
passive
comparators

1 Serious games v. passive comparators

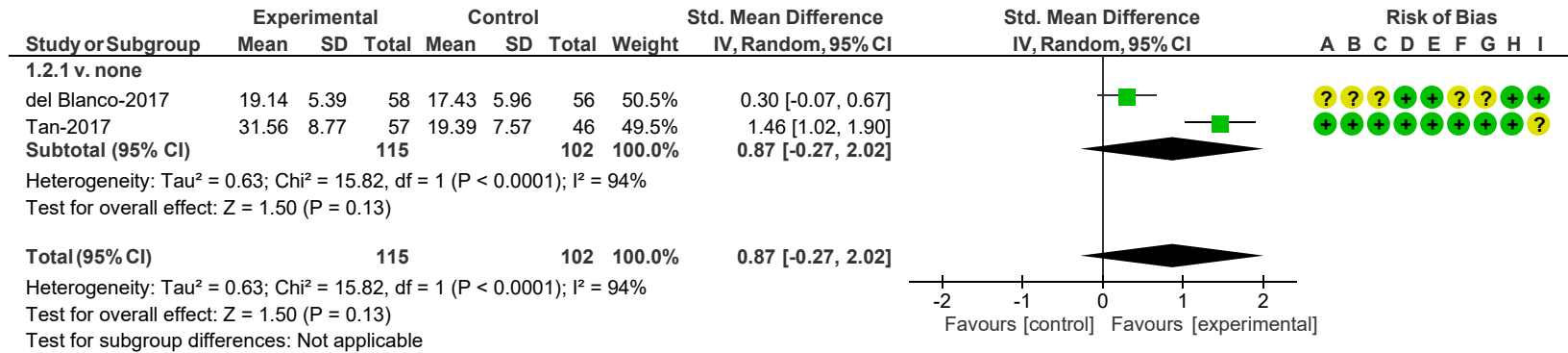
1.1 Knowledge



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

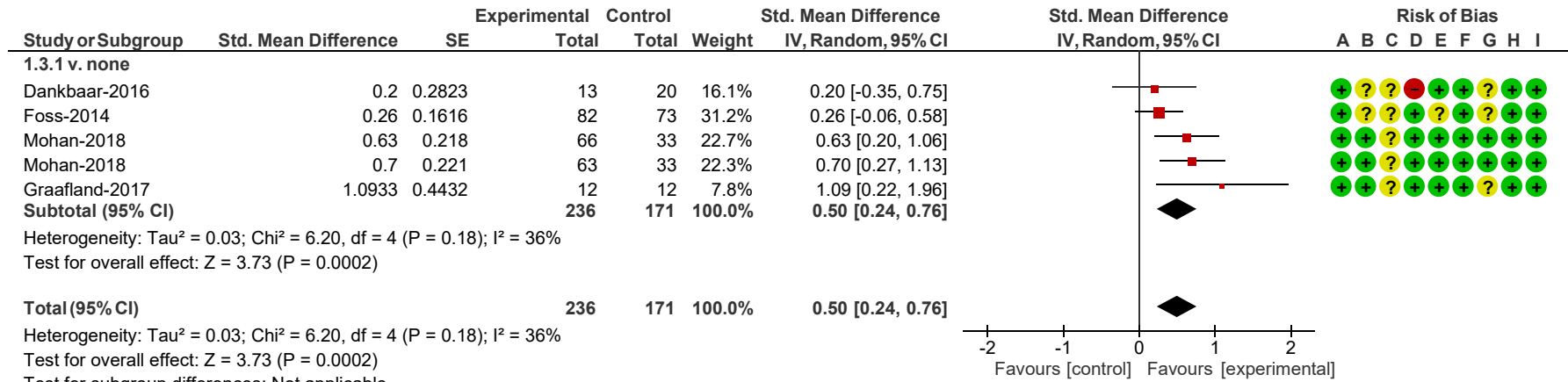
1.2 Confidence in skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

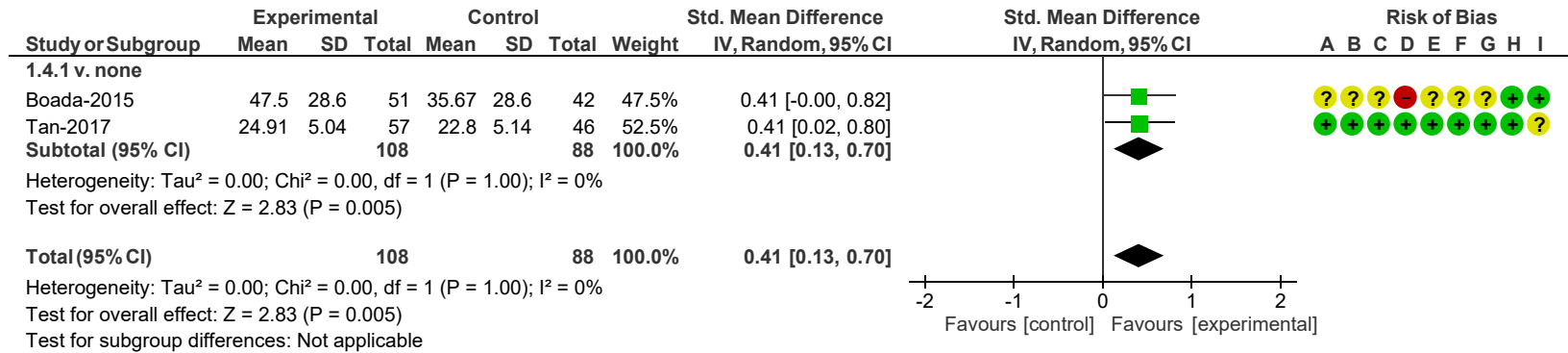
1.3 Cognitive skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

1.4 Procedural skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

Supplementary content 3 -
List of included studies

List of included studies

1. Adjedj J, Ducrocq G, Bouleti C, et al. Medical student evaluation with a serious game compared to multiple choice questions assessment. *JMIR serious games*. 2017;5(2):e11.
2. Berger J, Bawab N, De Mooij J, et al. An open randomized controlled study comparing an online text-based scenario and a serious game by Belgian and Swiss pharmacy students. *Currents in pharmacy teaching & learning*. 2018;10(3):267-276.
3. Boada I, Rodriguez-Benitez A, Garcia-Gonzalez JM, Olivet J, Carreras V, Sbert M. Using a serious game to complement CPR instruction in a nurse faculty. *Computer methods and programs in biomedicine*. 2015;122(2):282-291.
4. Boeker M, Andel P, Vach W, Frankenschmidt A. Game-based e-learning is more effective than a conventional instructional method: a randomized controlled trial with third-year medical students. *PloS one*. 2013;8(12):e82328.
5. Brull S, Finlayson S, Kostelec T, MacDonald R, Krenzischek D. Using gamification to improve productivity and increase knowledge retention during orientation. *J Nurs Adm*. 2017;47(9):448-453.
6. Buijs-Spanjers KR, Hegge HH, Jansen CJ, Hoogendoorn E, de Rooij SE. A Web-Based Serious Game on Delirium as an Educational Intervention for Medical Students: Randomized Controlled Trial. *JMIR serious games*. 2018;6(4):e17.
7. Buijs-Spanjers KR, Hegge HHM, Cnossen F, Hoogendoorn E, Jaarsma D, de Rooij SE. Dark play of serious games: effectiveness and features (G4HE2018). *Games Health J*. 2019;8(4):1-6.

Efficacy of serious games in healthcare professions education

8. Chee EJM, Prabhakaran L, Neo LP, et al. Play and Learn with Patients-Designing and Evaluating a Serious Game to Enhance Nurses' Inhaler Teaching Techniques: A Randomized Controlled Trial. *Games Health J.* 2019.
9. Chien JH, Suh IH, Park SH, Mukherjee M, Oleynikov D, Siu KC. Enhancing fundamental robot-assisted surgical proficiency by using a portable virtual simulator. *Surgical innovation.* 2013;20(2):198-203.
10. Cook NF, McAloon T, O'Neill P, Beggs R. Impact of a web based interactive simulation game (PULSE) on nursing students' experience and performance in life support training-- a pilot study. *Nurse Educ Today.* 2012;32(6):714-720.
11. Courtier J, Webb EM, Phelps AS, Naeger DM. Assessing the learning potential of an interactive digital game versus an interactive-style didactic lecture: the continued importance of didactic teaching in medical student education. *Pediatric radiology.* 2016;46(13):1787-1796.
12. Dankbaar ME, Alsma J, Jansen EE, van Merriënboer JJ, van Saase JL, Schuit SC. An experimental study on the effects of a simulation game on students' clinical cognitive skills and motivation. *Advances in health sciences education : theory and practice.* 2016;21(3):505-521.
13. Dankbaar ME, Richters O, Kalkman CJ, et al. Comparative effectiveness of a serious game and an e-module to support patient safety knowledge and awareness. *BMC medical education.* 2017;17(1):30.

Efficacy of serious games in healthcare professions education

14. de Sena DP, Fabricio DD, da Silva VD, Bodanese LC, Franco AR. Comparative evaluation of video-based on-line course versus serious game for training medical students in cardiopulmonary resuscitation: A randomised trial. *PloS one*. 2019;14(4):e0214722.
15. Del Blanco A, Torrente J, Fernandez-Manjon B, Ruiz P, Giner M. Using a videogame to facilitate nursing and medical students' first visit to the operating theatre. A randomized controlled trial. *Nurse Educ Today*. 2017;55:45-53.
16. Diehl LA, Souza RM, Gordan PA, Esteves RZ, Coelho IC. InsuOnline, an electronic game for medical education on insulin therapy: a randomized controlled trial with primary care physicians. *J Med Internet Res*. 2017;19(3):e72.
17. Drummond D, Delval P, Abdenouri S, et al. Serious game versus online course for pretraining medical students before a simulation-based mastery learning course on cardiopulmonary resuscitation: A randomised controlled study. *Eur J Anaesthesiol*. 2017;34(12):836-844.
18. Foss B, Lokken A, Leland A, Stordalen J, Mordt P, Oftedal BF. Digital Game-Based Learning: A Supplement for Medication Calculation Drills in Nurse Education. *E-Learning and Digital Media*. 2014;11(4):342-349.
19. Gauthier A, Corrin M, Jenkinson J. Exploring the influence of game design on learning and voluntary use in an online vascular anatomy study aid. *Comput Educ*. 2015;87:24-34.

Efficacy of serious games in healthcare professions education

20. Graafland M, Bemelman WA, Schijven MP. Game-based training improves the surgeon's situational awareness in the operation room: a randomized controlled trial. *Surgical endoscopy*. 2017;31(10):4093-4101.
21. Hannig A, Lemos M, Spreckelsen C, Ohnesorge-Radtke U, Rafai N. Skills-O-Mat: Computer Supported Interactive Motion- and Game-Based Training in Mixing Alginate in Dental Education. *J Educ Comput Res*. 2013;48(3):315-343.
22. Harrington CM, Chaitanya V, Dicker P, Traynor O, Kavanagh DO. Playing to your skills: a randomised controlled trial evaluating a dedicated video game for minimally invasive surgery. *Surgical endoscopy*. 2018;32(9):3813-3821.
23. Haubruck P, Nickel F, Ober J, et al. Evaluation of app-based serious gaming as a training method in teaching chest tube insertion to medical students: randomized controlled trial. *J Med Internet Res*. 2018;20(5):e195.
24. Katz D, Zerillo J, Kim S, et al. Serious gaming for orthotopic liver transplant anesthesiology: A randomized control trial. *Liver transplantation : official publication of the American Association for the Study of Liver Diseases and the International Liver Transplantation Society*. 2017;23(4):430-439.
25. Kerfoot BP, Baker H. An online spaced-education game for global continuing medical education: a randomized trial. *Annals of surgery*. 2012;256(1):33-38.
26. Kerfoot BP, Turchin A, Breydo E, Gagnon D, Conlin PR. An online spaced-education game among clinicians improves their patients' time to blood pressure control: a

Efficacy of serious games in healthcare professions education

- randomized controlled trial. *Circulation Cardiovascular quality and outcomes*. 2014;7(3):468-474.
27. Knight JF, Carley S, Tregunna B, et al. Serious gaming technology in major incident triage training: a pragmatic controlled trial. *Resuscitation*. 2010;81(9):1175-1179.
 28. Lagro J, van de Pol MH, Laan A, Huijbregts-Verheyden FJ, Fluit LC, Olde Rikkert MG. A randomized controlled trial on teaching geriatric medical decision making and cost consciousness with the serious game GeriatriX. *Journal of the American Medical Directors Association*. 2014;15(12):957 e951-956.
 29. Li J, Xu Y, Xu Y, et al. 3D CPR Game Can Improve CPR Skill Retention. *Studies in health technology and informatics*. 2015;216:974.
 30. Mohan D, Farris C, Fischhoff B, et al. Efficacy of educational video game versus traditional educational apps at improving physician decision making in trauma triage: randomized controlled trial. *BMJ*. 2017;359:j5416.
 31. Mohan D, Fischhoff B, Angus DC, et al. Serious games may improve physician heuristics in trauma triage. *Proceedings of the National Academy of Sciences of the United States of America*. 2018;115(37):9204-9209.
 32. Polivka BJ, Anderson S, Lavender SA, et al. Efficacy and Usability of a Virtual Simulation Training System for Health and Safety Hazards Encountered by Healthcare Workers. *Games Health J*. 2019;8(2):121-128.

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33. Rondon S, Sassi FC, Furquim de Andrade CR. Computer game-based and traditional learning method: a comparison regarding students' knowledge retention. *BMC medical education*. 2013;13:30.
34. Scales CD, Jr., Moin T, Fink A, et al. A randomized, controlled trial of team-based competition to increase learner participation in quality-improvement education. *International journal for quality in health care : journal of the International Society for Quality in Health Care*. 2016;28(2):227-232.
35. Sward KA, Richardson S, Kendrick J, Maloney C. Use of a Web-based game to teach pediatric content to medical students. *Ambulatory pediatrics : the official journal of the Ambulatory Pediatric Association*. 2008;8(6):354-359.
36. Tan AJQ, Lee CCS, Lin PY, et al. Designing and evaluating the effectiveness of a serious game for safe administration of blood transfusion: A randomized controlled trial. *Nurse Educ Today*. 2017;55:38-44.
37. Van Nuland SE, Roach VA, Wilson TD, Belliveau DJ. Head to head: The role of academic competition in undergraduate anatomical education. *Anat Sci Educ*. 2015;8(5):404-412.

Supplementary content 4 -
List of excluded studies at the full text assessment stage

List of excluded studies at the full-text assessment stage

Not a study

1. Borro-Escribano B, Martinez-Alpuente I, Blanco AD, Torrente J, Fernandez-Manjon B, Matesanz R. Application of game-like simulations in the Spanish Transplant National Organization. *Transplantation proceedings*. 2013;45(10):3564-3565.
2. Cowan B, Sabri H, Kapralos B, Moussa F, Cristancho S, Dubrowski A. A serious game for off-pump coronary artery bypass surgery procedure training. *Studies in health technology and informatics*. 2011;163:147-149.
3. del Blanco A, Fernandez-Manjon B, Ruiz P, Giner M. Using videogames facilitates the first visit to the operating theatre. *Med Educ*. 2013;47(5):519-520.
4. Gallagher AG, Traynor O. Simulation in surgery: opportunity or threat? *Ir J Med Sci*. 2008;177(4):283-287.
5. Haldal I, Backlund P, Johannesson M, Lebram M, Lundberg L. Connecting the Links: Narratives, Simulations and Serious Games in Prehospital Training. *Studies in health technology and informatics*. 2017;235:343-347.
6. Johnston CL, Whatley D. Pulse!!--A virtual learning space project. *Studies in health technology and informatics*. 2006;119:240-242.
7. Kerfoot BP, Kissane N. The use of gamification to boost residents' engagement in simulation training. *JAMA surgery*. 2014;149(11):1208-1209.

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8. Magro A, Swarz J, Ousley A. CancerSPACE: An Interactive E-learning Tool Aimed to Improve Cancer Screening Rates. *Journal of Computer-Mediated Communication*. 2010;15(3):482-499.
9. Semeraro F, Frisoli A, Ristagno G, et al. Relive: a serious game to learn how to save lives. *Resuscitation*. 2014;85(7):e109-110.
10. Shewaga R, Knox A, Ng G, Kapralos B, Dubrowski A. Z-DOC: a serious game for Z-plasty procedure training. *Studies in health technology and informatics*. 2013;184:404-406.
11. Smith-Stoner M, Willer A. Innovative use of the Internet and intranets to provide education by adding games. *Computers, informatics, nursing : CIN*. 2005;23(5):237-241.
12. Truchot-Cardot D. ["Games, to nurse? Is this legitimate?"]. *Krankenpfl Soins Infirm*. 2016;109(2):8-11, 58-61, 82-15.
13. Young J. Using a Role-Play Simulation Game to Promote Systems Thinking. *J Contin Educ Nurs*. 2018;49(1):10-11.

Not with healthcare professionals or students

1. Asadipour A, Debattista K, Chalmers A. Visuohaptic augmented feedback for enhancing motor skills acquisition. *Visual Computer*. 2017;33(4):401-411.
2. Bauer KN, Brusso RC, Orvis KA. Using Adaptive Difficulty to Optimize Videogame-Based Training Performance: The Moderating Role of Personality. *Military Psychology*. 2012;24(2):148-165.

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3. Chan WY, Qin J, Chui YP, Heng PA. A serious game for learning ultrasound-guided needle placement skills. *IEEE Trans Inf Technol Biomed.* 2012;16(6):1032-1042.
4. Olson DK, Scheller A, Larson S, Lindeke L, Edwardson S. Using gaming simulation to evaluate bioterrorism and emergency readiness education. *Public health reports (Washington, DC : 1974).* 2010;125(3):468-477.
5. Simic G, Jevremovic A, Kostic Z, Dordevic D. Assessment based on Serious Gaming Interactive Questions (SGIQ). *Journal of Computer Assisted Learning.* 2015;31(6):623-637.
6. Sotomayor TM. Teaching tactical combat casualty care using the TC3 Sim Game-based simulation: a study to measure training effectiveness. *Studies in Health Technology & Informatics.* 2010;154:176-179.
7. Sterkenburg PS, Vacaru VS. The effectiveness of a serious game to enhance empathy for care workers for people with disabilities: A parallel randomized controlled trial. *Disabil Health J.* 2018;11(4):576-582.
8. van Dijk T, Spil T, van der Burg S, Wenzler I, Dalmolen S. Present or Play. *International Journal of Game-Based Learning.* 2015;5(2):55-69.
9. Yu FY, Han C, Chan TW. Experimental comparisons of face-to-face and anonymous real-time team competition in a networked gaming learning environment. *Cyberpsychol Behav.* 2008;11(4):511-514.

Not a serious game

1. Amer RS, Denehy GE, Cobb DS, Dawson DV, Cunningham-Ford MA, Bergeron C. Development and evaluation of an interactive dental video game to teach dentin bonding. *J Dent Educ.* 2011;75(6):823-831.
2. Ang ET, Chan JM, Gopal V, Li Shia N. Gamifying anatomy education. *Clin Anat.* 2018;31(7):997-1005.
3. Ankay Yilbas A, Canbay O, Akca B, et al. The effect of playing video games on fiberoptic intubation skills. *Anaesthesia, critical care & pain medicine.* 2018.
4. Ankay Yilbas A, Canbay O, Akca B, et al. The effect of playing video games on fiberoptic intubation skills. *Anaesthesia, critical care & pain medicine.* 2018.
5. Blakely G, Skirton H, Cooper S, Allum P, Nelmes P. Use of educational games in the health professions: a mixed-methods study of educators' perspectives in the UK. *Nursing & health sciences.* 2010;12(1):27-32.
6. Chalhoub M, Khazzaka A, Sarkis R, Sleiman Z. The role of smartphone game applications in improving laparoscopic skills. *Advances in medical education and practice.* 2018;9:541-547.
7. Chang TP, Raymond T, Dewan M, et al. The effect of an International competitive leaderboard on self-motivated simulation-based CPR practice among healthcare professionals: A randomized control trial. *Resuscitation.* 2019;138:273-281.
8. Cowan B, Rojas D, Kapralos B, Moussa F, Dubrowski A. Effects of sound on visual realism perception and task performance. *Visual Computer.* 2015;31(9):1207-1216.

Efficacy of serious games in healthcare professions education

9. Creutzfeldt J, Hedman L, Fellander-Tsai L. Effects of pre-training using serious game technology on CPR performance--an exploratory quasi-experimental transfer study. *Scandinavian journal of trauma, resuscitation and emergency medicine*. 2012;20:79.
10. Diehl LA, Gordan PA, Esteves RZ, Coelho IC. Effectiveness of a serious game for medical education on insulin therapy: a pilot study. *Archives of endocrinology and metabolism*. 2015;59(5):470-473.
11. El-Beheiry M, McCreery G, Schlachta CM. A serious game skills competition increases voluntary usage and proficiency of a virtual reality laparoscopic simulator during first-year surgical residents' simulation curriculum. *Surgical endoscopy*. 2017;31(4):1643-1650.
12. Evans DA, Curtis AR. Animosity, antagonism, and avatars: teaching conflict management in second life. *The Journal of nursing education*. 2011;50(11):653-655.
13. Fonseca LM, Aredes ND, Fernandes AM, et al. Computer and laboratory simulation in the teaching of neonatal nursing: innovation and impact on learning. *Revista latino-americana de enfermagem*. 2016;24:e2808.
14. Gunn T, Jones L, Bridge P, Rowntree P, Nissen L. The use of virtual reality simulation to improve technical skill in the undergraduate medical imaging student. *Interactive Learning Environments*. 2017;26(5):613-620.
15. Hashimoto DA, Gomez ED, Beyer-Berjot L, et al. A Randomized Controlled Trial to Assess the Effects of Competition on the Development of Laparoscopic Surgical Skills. *Journal of surgical education*. 2015;72(6):1077-1084.

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16. Hedman L, Schlickum M, Fellander-Tsai L. Surgical novices randomized to train in two video games become more motivated during training in MIST-VR and GI Mentor II than students with no video game training. *Studies in health technology and informatics*. 2013;184:189-194.
17. Jalink MB, Heineman E, Pierie JP, ten Cate Hoedemaker HO. The effect of a preoperative warm-up with a custom-made Nintendo video game on the performance of laparoscopic surgeons. *Surgical endoscopy*. 2015;29(8):2284-2290.
18. Lin CC, Huang SC, Lin HH, Huang WJ, Chen WS, Yang SH. Naked-eye box trainer and training box games have similar training effect as conventional video-based box trainer for novices: A randomized controlled trial. *Am J Surg*. 2018;216(5):1022-1027.
19. Mak WW, Cheng SS, Law RW, Cheng WW, Chan F. Reducing HIV-related stigma among health-care professionals: a game-based experiential approach. *AIDS care*. 2015;27(7):855-859.
20. McGrath J, Kman N, Danforth D, et al. Virtual alternative to the oral examination for emergency medicine residents. *The western journal of emergency medicine*. 2015;16(2):336-343.
21. McMullan M, Jones R, Lea S. The effect of an interactive e-drug calculations package on nursing students' drug calculation ability and self-efficacy. *International journal of medical informatics*. 2011;80(6):421-430.
22. Moglia A, Perrone V, Ferrari V, et al. Influence of videogames and musical instruments on performances at a simulator for robotic surgery. *Minimally invasive therapy & allied*

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- technologies : MITAT : official journal of the Society for Minimally Invasive Therapy.*
2017;26(3):129-134.
23. Orwoll B, Diane S, Henry D, et al. Gamification and Microlearning for Engagement With Quality Improvement (GAMEQI): A Bundled Digital Intervention for the Prevention of Central Line-Associated Bloodstream Infection. *American journal of medical quality : the official journal of the American College of Medical Quality.* 2018;33(1):21-29.
 24. Rosser JC, Jr., Gentile DA, Hanigan K, Danner OK. The effect of video game "warm-up" on performance of laparoscopic surgery tasks. *JSLS : Journal of the Society of Laparoendoscopic Surgeons.* 2012;16(1):3-9.
 25. Sapkaroski D, Baird M, McInerney J, Dimmock MR. The implementation of a haptic feedback virtual reality simulation clinic with dynamic patient interaction and communication for medical imaging students. *Journal of medical radiation sciences.* 2018;65(3):218-225.
 26. Schlickum MK, Hedman L, Enochsson L, Kjellin A, Fellander-Tsai L. Systematic video game training in surgical novices improves performance in virtual reality endoscopic surgical simulators: a prospective randomized study. *World journal of surgery.* 2009;33(11):2360-2367.

No randomized comparator group

1. Albright G, Adam C, Goldman R, Serri D. A Game-Based Simulation Utilizing Virtual Humans to Train Physicians to Screen and Manage the Care of Patients with Mental Health Disorders. *Games Health J.* 2013;2(5):269-273.
2. Butt AL, Kardong-Edgren S, Ellertson A. Using Game-Based Virtual Reality with Haptics for Skill Acquisition. *Clin Simul Nurs.* 2018;16:25-32.
3. Buttussi F, Pellis T, Cabas Vidani A, Pausler D, Carchietti E, Chittaro L. Evaluation of a 3D serious game for advanced life support retraining. *International journal of medical informatics.* 2013;82(9):798-809.
4. Cowan B, Sabri H, Kapralos B, et al. A serious game for total knee arthroplasty procedure, education and training. *Journal of Cyber Therapy and Rehabilitation.* 2010;3(3):285-298.
5. Cutumisu M, Brown MRG, Fray C, Schmolzer GM. Growth Mindset Moderates the Effect of the Neonatal Resuscitation Program on Performance in a Computer-Based Game Training Simulation. *Frontiers in pediatrics.* 2018;6:195.
6. Dankbaar ME, Roozeboom MB, Oprins EA, et al. Preparing Residents Effectively in Emergency Skills Training With a Serious Game. *Simulation in healthcare : journal of the Society for Simulation in Healthcare.* 2017;12(1):9-16.
7. Hannig A, Kuth N, Ozman M, Jonas S, Spreckelsen C. eMedOffice: a web-based collaborative serious game for teaching optimal design of a medical practice. *BMC medical education.* 2012;12:104.

Efficacy of serious games in healthcare professions education

8. Kang J, Suh EE. Development and Evaluation of "Chronic Illness Care Smartphone Apps" on Nursing Students' Knowledge, Self-efficacy, and Learning Experience. *Computers, informatics, nursing : CIN*. 2018;36(11):550-559.
9. Kanthan R, Senger JL. The impact of specially designed digital games-based learning in undergraduate pathology and medical education. *Archives of pathology & laboratory medicine*. 2011;135(1):135-142.
10. McKenzie K. A comparison of the effectiveness of a game informed online learning activity and face to face teaching in increasing knowledge about managing aggression in health settings. *Advances in health sciences education : theory and practice*. 2013;18(5):917-927.
11. Middeke A, Anders S, Schuelper M, Raupach T, Schuelper N. Training of clinical reasoning with a Serious Game versus small-group problem-based learning: A prospective study. *PloS one*. 2018;13(9):e0203851.
12. O'Neill E, Reynolds PA, Hatzipanagos S, Gallagher JE. Graphic (games research applied to public health with innovative collaboration)--designing a serious game pilot for dental public health. *Bull Group Int Rech Sci Stomatol Odontol*. 2013;51(3):e30-31.
13. Qin J, Chui YP, Pang WM, Choi KS, Heng PA. Learning blood management in orthopedic surgery through gameplay. *IEEE computer graphics and applications*. 2010;30(2):45-57.

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14. Savazzi F, Isernia S, Jonsdottir J, Di Tella S, Pazzi S, Baglio F. Engaged in learning neurorehabilitation: Development and validation of a serious game with user-centered design. *Computers & Education*. 2018;125:53-61.
15. Verkuyl M, Romaniuk D, Mastrilli P. Virtual gaming simulation of a mental health assessment: A usability study. *Nurse Educ Pract*. 2018;31:83-87.

No engagement or learning outcome

1. Hawkins GE, Rae B, Nesbitt KV, Brown SD. Gamelike features might not improve data. *Behav Res Methods*. 2013;45(2):301-318.
2. Kowalewski KF, Hendrie JD, Schmidt MW, et al. Validation of the mobile serious game application Touch Surgery for cognitive training and assessment of laparoscopic cholecystectomy. *Surgical endoscopy*. 2017;31(10):4058-4066.
3. Mohan D, Angus DC, Ricketts D, et al. Assessing the validity of using serious game technology to analyze physician decision making. *PloS one*. 2014;9(8):e105445.

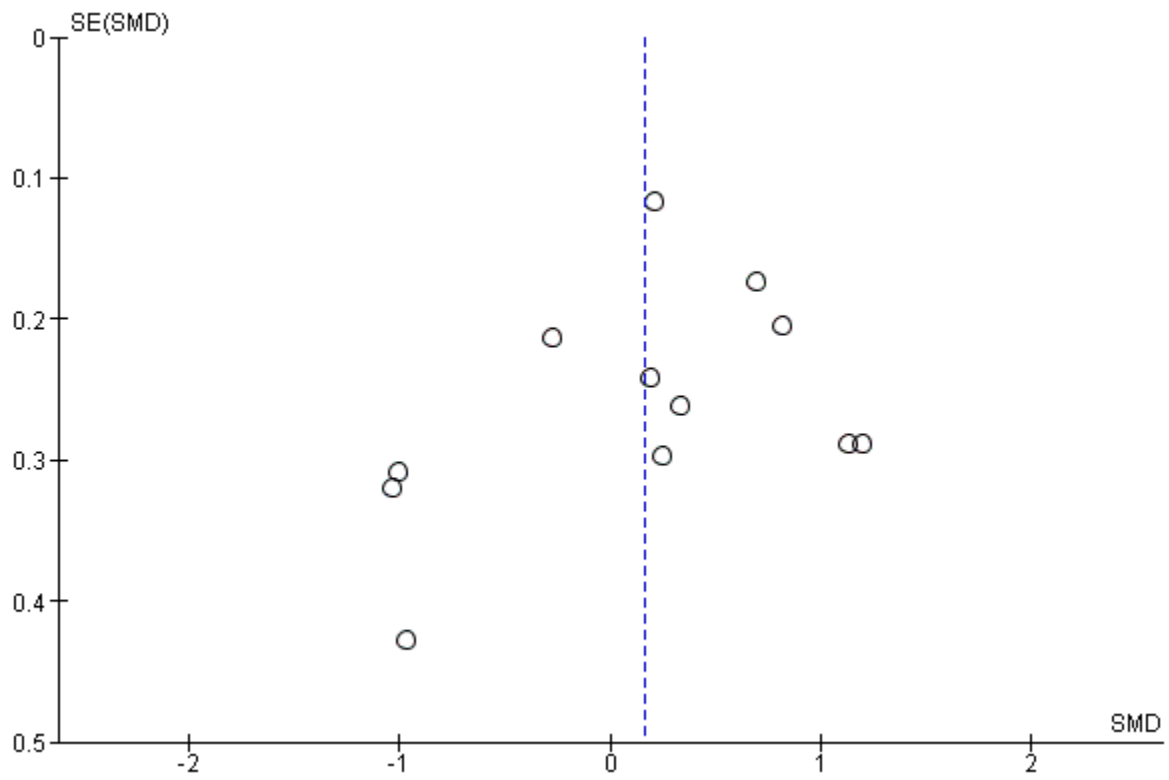
Supplementary content 5 -
Risk of bias summary

Risk of bias summary

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Similarity of baseline outcome measurements	Baseline characteristics similar	Incomplete outcome data (attrition bias)	Knowledge of the allocated interventions	Protection against contamination	Selective reporting (reporting bias)	Other bias
Adjedj-2017	?	?	?	+	+	+	?	+	+
Berger-2018	+	?	+	+	+	+	?	+	+
Boada-2015	?	?	?	+	?	?	+	+	+
Boeker-2013	+	?	?	+	+	+	?	+	+
Brull-2017	+	+	+	+	+	+	+	+	+
Buijs Spanjers-2018	+	?	?	+	+	+	+	+	?
Buijs Spanjers-2019	+	?	?	+	+	+	+	+	+
Chee-2019	+	?	+	+	+	+	?	+	+
Chien-2013	?	?	?	+	+	+	+	+	+
Cook-2012	?	?	?	+	?	+	?	+	+
Courtier-2016	?	?	?	+	+	+	+	+	?
Dankbaar-2016	+	?	?	+	+	+	?	+	+
Dankbaar-2017	+	?	?	+	+	+	?	+	+
del Blanco-2017	?	?	?	+	+	?	?	+	+
De Sena-2019	+	?	?	?	+	+	?	+	+
Diehl-2017	+	+	+	+	+	+	+	+	+
Drummond-2017	+	+	+	+	+	+	+	+	+
Foss-2014	+	?	?	+	?	+	?	+	+
Gauthier-2015	+	?	+	+	+	+	+	+	+
Graafland-2017	+	+	?	+	+	+	?	+	+
Hannig-2013	?	?	+	+	?	+	+	+	+
Harrington-2018	+	+	?	+	+	+	?	+	+
Haubruck-2018	+	+	?	?	+	+	+	+	+
Katz-2017	+	?	+	+	+	+	?	+	+
Kerfoot-2012	?	?	+	+	+	+	+	+	+
Kerfoot-2014	?	?	+	+	+	+	+	+	+
Knight-2010	+	+	?	+	?	+	?	+	+
Lagro-2014	?	?	+	+	+	+	+	+	+
Li-2015	?	+	?	+	?	+	?	+	+
Mohan-2017	+	+	?	+	+	+	?	+	+
Mohan-2018	+	+	?	+	+	+	+	+	+
Polivka-2018	?	?	?	+	+	+	+	+	+
Rondon-2013	?	?	+	+	+	+	+	+	+
Scales Jr - 2016	+	?	+	+	+	+	?	+	+
Sward-2008	?	?	+	+	+	+	+	+	+
Tan-2017	+	+	+	+	+	+	+	+	?
Van Nuland-2014	?	?	+	+	+	+	+	+	+

Supplementary content 6 -
Funnel plot for knowledge
acquisition

Figure. Funnel plot of the knowledge acquisition outcome.



Note. SE: Standard error; SMD: Standardized mean difference.

Supplementary content 7 -
Key information of the
serious games assessed

Table. Key information of the serious games assessed

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Adjedj-2017	Name non-reported, computer and tablets	Atrial fibrillation management	Not reported	A single 30-minute session	To correctly examine various patients and provide them with the correct treatment in a medical office.
Berger-2018	Name non-reported, platform non-reported	Pharmacist triage	Not reported	A single session, duration not reported	To perform an adequate pharmacist triage and to provide a correct intervention in response.
Boada-2015	Life Support Simulation Activities (LISSA), computer	Cardiopulmonary resuscitation	Not reported	Not reported	To save a character from sudden cardiac arrest by performing cardiopulmonary resuscitation.
Boeker-2013	Uro-Island, computer	Phase contrast microscopic urinalysis	Not reported	Not reported	To free a character from an island by formulating clear diagnosis regarding various urine pathologies.
Brull-2017	World of Salus, computer	Pain management, wound management, and fall prevention and management.	Not reported	Frequency not reported, two to four hours of usage	Not reported

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Buijs-Spangers-2019	Delirium Experience, computer	Delirium management	Not reported	Not reported	To provide inadequate management of a patient diagnosed with delirium
Buijs-Spangers-2018	Delirium Experience, computer	Delirium management	Not reported	A single 20-minute session	To take proper care of a patient diagnosed with delirium
Chien-2013	Name non-reported, computer	Bimanual carrying and peg transfer	Not reported	A single 40-minute session	Not reported
Chee-2019	Play-learn inhalation game, computer and iOS	Administration of inhaled medication	Technology, pedagogy, and content knowledge framework	A single 10-minute session	To answer the most questions and to match the most pictures correctly.
Cook-2012	PULSE, computer, PlayStation Portable	Cardiopulmonary resuscitation	Not reported	Unlimited access for two weeks	To solve various clinical scenarios by using clinical equipment.
Courtier-2016	Tic-tac-toe, computer	Imaging study	Not reported	A single one-hour session	To form a tic-tac-toe before the other competing team by answering questions correctly.

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Dankbaar-2016	abcdeSIM, computer	Acutely-ill patients (e.g., bleeding)	Not reported	Frequency not reported, two to four hours of usage	To stabilize within 15 minutes patients presenting to an emergency department.
Dankbaar-2017	Air Medic Sky-1, computer	Patient safety awareness and personal stress management	Not reported	Frequency not reported, three to four hours of usage	To watch videos, to perform breathing exercises, and to diagnose and treat patients in a virtual flying hospital over the globe.
Del Blanco-2017	Operating Theater Game, computer	Functioning of an operating theater	Not reported	Not reported. However, participants had access to the game for a day.	Not reported
de Sena-2019	Name non-reported, iOS	Cardiopulmonary resuscitation	Not reported	A single 20-minute session	To identify a victim of cardiac arrest and to perform cardiopulmonary resuscitation.
Diehl-2017	InsuOnline, computer	Diabetes management	Adult- and problem-based learning	Frequency not reported, four hours of usage	To improve blood sugar management in patients diagnosed with diabetes

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Drummond-2017	<i>Staying Alive</i> , computer, electronic tablet	Sudden cardiac arrest	Not reported	Two sessions, 12 minutes of usage	To save a character from sudden cardiac arrest by performing cardiopulmonary resuscitation
Foss-2014	The Medication Game, computer	Basic mathematical concepts in medication calculation	Multiple intelligence theory	Not reported	To perform various mathematical calculations
Gauthier-2015	Vascular Invaders, computer	Human vascular anatomy	Evidence-centered design framework	Not reported. However, 35 days of free use.	To travel in a nanobot through various vascular vessels to destroy invaders.
Graafland-2017	Dr. Game, Surgeon Trouble, iOS and Android platforms	Equipment problems of the laparoscopic tower	Non-reported	Two 30-minute sessions	To align three similar titles (in a title-matching design) while solving laparoscopic equipment-related issues.
Hannig-2013	Skills-O-Mat, computer	Alginate mixing in dentistry	Peyton's method	Not reported	To mix alginate at the correct speed.
Harrington-2018	Underground, Nintendo WiiU	Laparoscopic technical skills	Not reported	Frequency not reported, 20 hours of usage	To build paths by moving objects in a maze.

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Haubruck-2019	Touch Surgery, iOS	Chest tube insertion	Not reported	A single 120-minute session	To answer the most questions correctly.
Katz-2017	Orthotopic liver transplant Trainer, iOS and Android platforms	Management of orthotopic liver transplant	Not reported	At least once per week for a month, duration of usage non-reported	To properly assess and manage a patient during the peri- and the per-operative periods to gain credits.
Kerfoot-2012	Name non-reported, computer (through e-mails)	Urology clinical practice guidelines	Spaced education	Two to four questions sent per e-mail every two to four days for 34 weeks	To answer the most questions correctly.
Kerfoot-2014	Name non-reported, computer (through e-mails)	Hypertension management	Salen and Zimmerman game design fundamentals Spaced education	One to two questions sent every three days for 52 weeks	To answer the most questions correctly.
Knight-2010	Triage trainer, computer	Basic incident triage sieve skills	Not reported	A single 60-minute session	As a first-respondent at a major incident scene, to assign the right priority to each casualty.

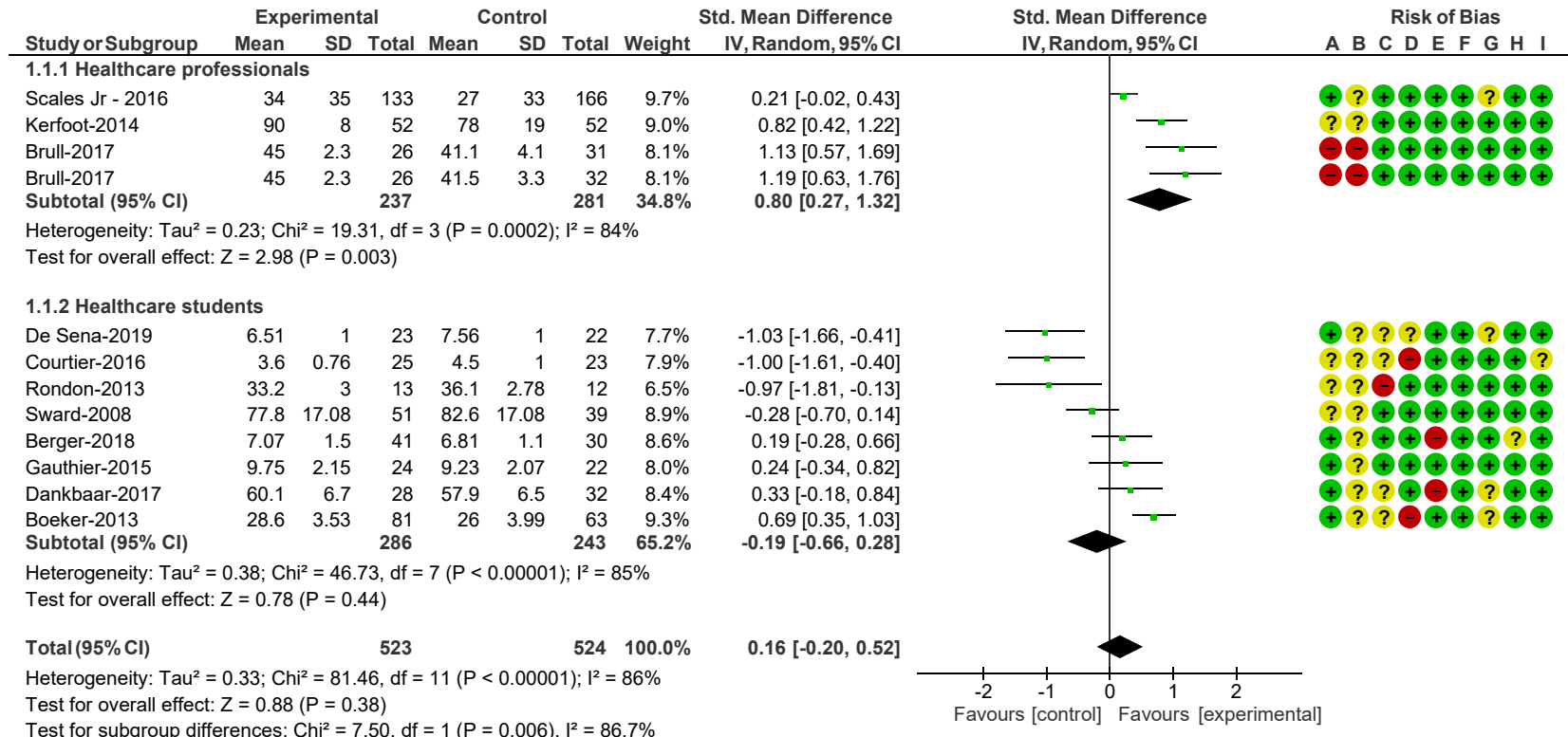
First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Lagro-2014	GeriatricX, computer	Geriatric medical decision-making and cost consciousness	Not reported	Frequency not reported; 60 to 90 minutes of usage	To provide proper assessment and management to elderly patients.
Li-2015	3D CPR game, platform non-reported	Cardiopulmonary resuscitation	Not reported	Not reported	To save a character from sudden cardiac arrest by performing cardiopulmonary resuscitation.
Mohan-2018	Shift: The Next Generation, iOS	Trauma triage	Unspecified behavioral learning theories	Frequency not reported, two hours of usage	To triage a prespecified number of patients in the emergency department under time pressure.
Mohan-2017, 2018	Night Shift, electronic tablet	Trauma triage	Narrative engagement and unspecified behavioral learning theories	Mohan, 2017: A single one-hour session Mohan-2018: Frequency not reported, two hours of usage	To provide proper assessment and management to patients with severe injuries in the emergency department while solving an in-game mystery.

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Polivka-2018	HH-VSTS, computer	Health and safety hazards	Not reported	Not reported	To identify potential health and safety hazards in a home.
Rondon-2013	Anatesse 2.0, computer	Anatomy and physiology of the speech, language, hearing, and swallowing mechanisms	Not reported	Nine sessions (once per week), duration of usage not reported	To answer the most questions correctly.
Scales-2016	Name non-reported, computer (through e-mails)	Quality improvement and patient safety	Content retrieval	Two questions twice a week	To answer the most questions correctly.
Sward-2008	Name non-reported, computer	Pediatric	Not reported	Four one-hour sessions	To answer the most questions correctly to progress through an electronic game board.
Tan-2017	Name non-reported, computer	Blood transfusion	Experiential gaming model ⁶	A single 30-minute session	Various challenges related to blood transfusion (e.g., choosing the correct material, checking if the blood product is right)

First author-year	Name of the serious game, platform	Clinical topic	Theoretical framework for the design or the development process of the serious game	Planned frequency (# of session) and duration (# of minutes) of usage	Challenge
Van Nuland-2014	Online Competitive Anatomy Tournament, computer	Functional anatomy	Not reported	A single 20-minute session	To answer the most questions correctly.

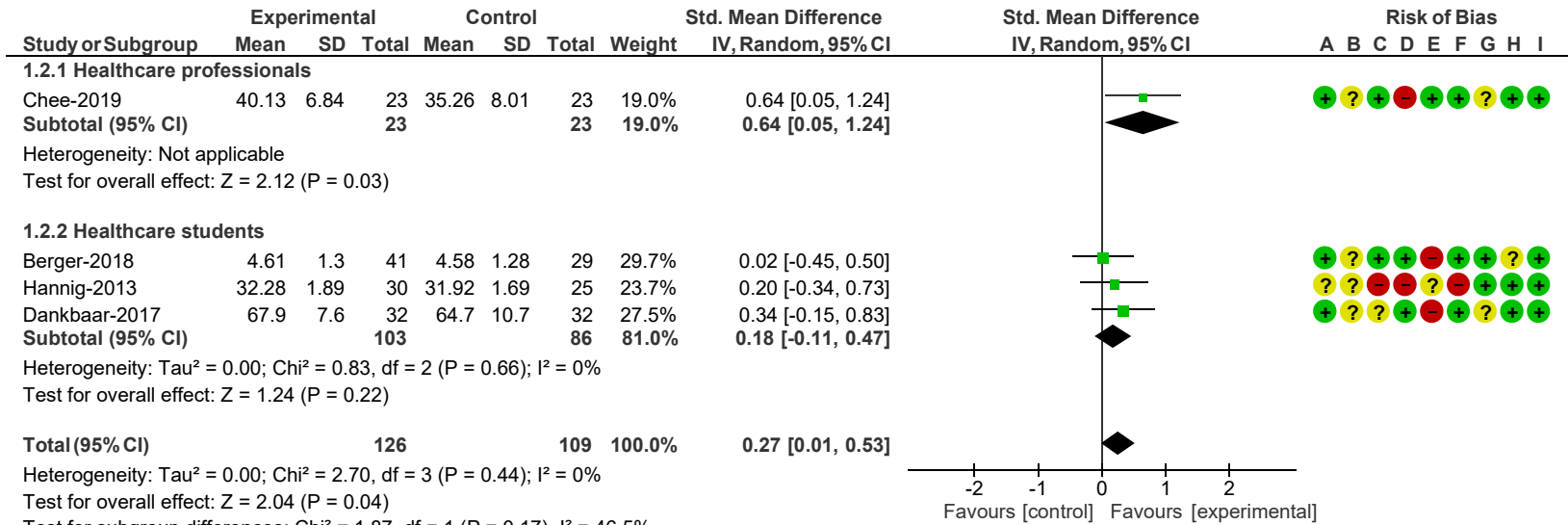
Supplementary content 8 -
Other sensitivity and
subgroup analyses

1.1 Knowledge



- Risk of bias legend
- (A) Random sequence generation (selection bias)
 - (B) Allocation concealment (selection bias)
 - (C) Similarity of baseline outcome measurements
 - (D) Baseline characteristics similar
 - (E) Incomplete outcome data (attrition bias)
 - (F) Knowledge of the allocated interventions
 - (G) Protection against contamination
 - (H) Selective reporting (reporting bias)
 - (I) Other bias

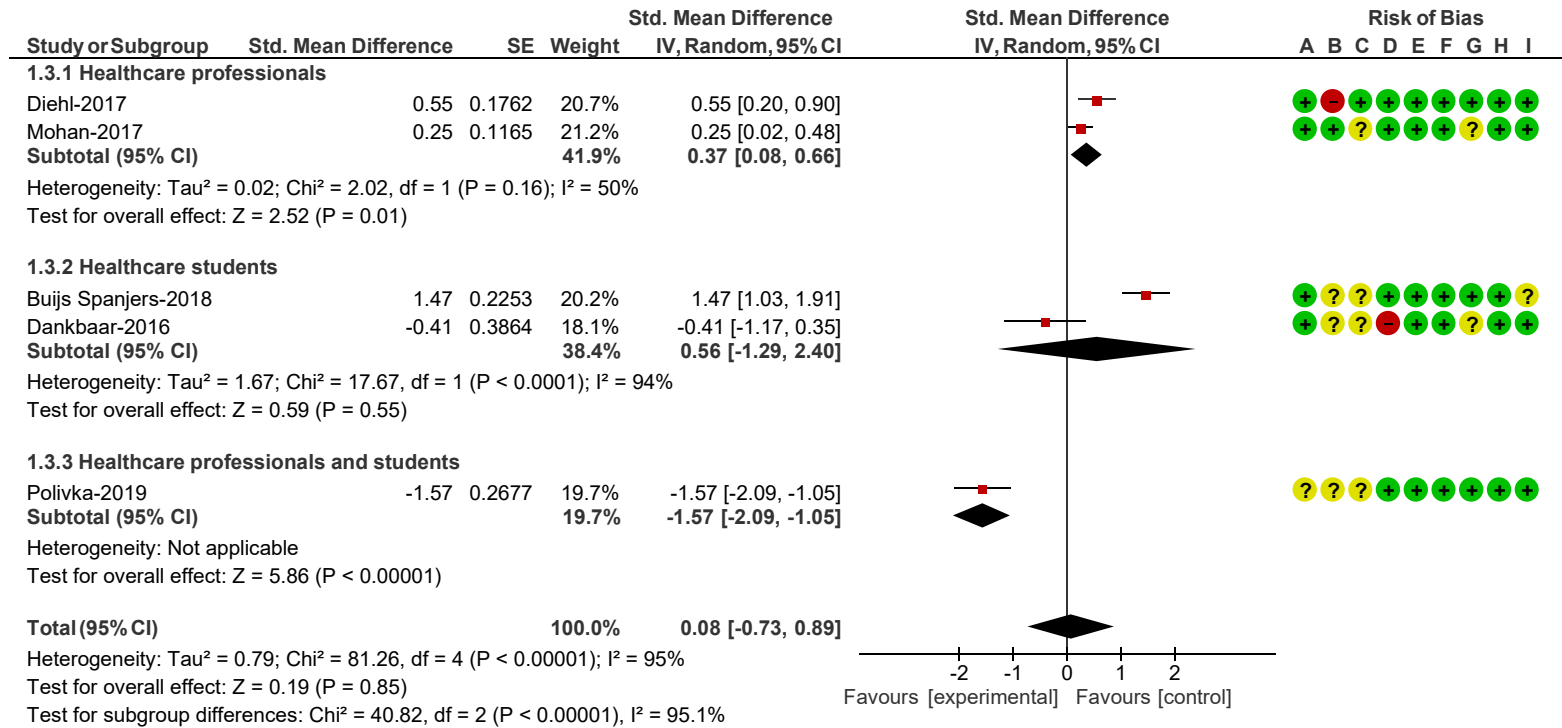
1.2 Confidence in skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

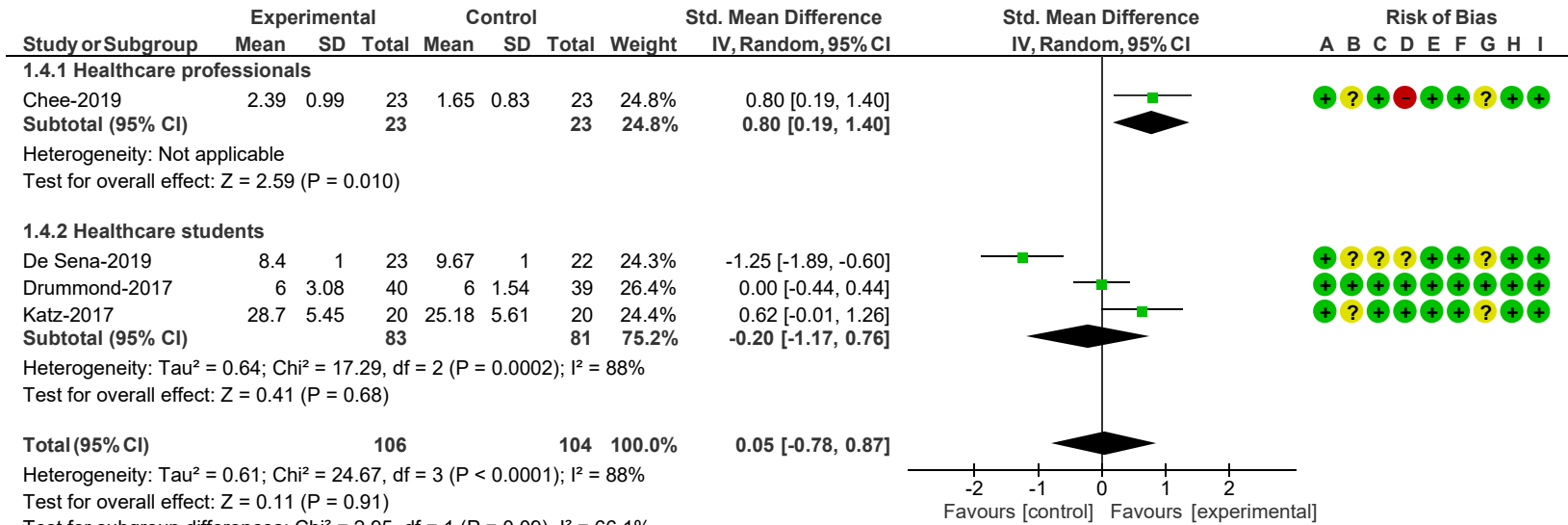
1.3 Cognitive skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

1.4 Procedural skills

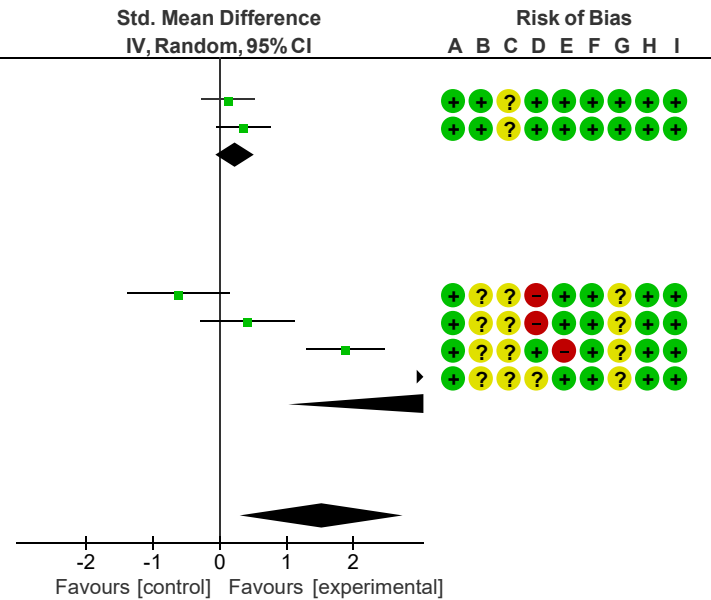


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

1.5 Learning time with the intervention

Study or Subgroup	Experimental			Control			Weight	Std. Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
1.5.1 Healthcare professionals								
Mohan-2018	105	34.11	66	100	45.38	37	19.3%	0.13 [-0.27, 0.53]
Mohan-2018	117.67	50.78	66	100	45.38	36	19.3%	0.36 [-0.05, 0.77]
Subtotal (95% CI)			132			73	38.6%	0.24 [-0.05, 0.53]
Heterogeneity: Tau ² = 0.00; Chi ² = 0.61, df = 1 (P = 0.43); I ² = 0%								
Test for overall effect: Z = 1.65 (P = 0.10)								
1.5.2 Healthcare students								
Dankbaar-2016	90	49	12	133	78	16	18.3%	-0.62 [-1.39, 0.15]
Dankbaar-2016	90	49	13	70	46	20	18.5%	0.41 [-0.29, 1.12]
Dankbaar-2017	174	66	32	54	60	34	18.9%	1.88 [1.30, 2.47]
De Sena-2019	18.57	0.66	23	7.41	0.43	22	5.7%	19.59 [15.31, 23.87]
Subtotal (95% CI)			80			92	61.4%	3.57 [1.03, 6.11]
Heterogeneity: Tau ² = 5.85; Chi ² = 100.97, df = 3 (P < 0.00001); I ² = 97%								
Test for overall effect: Z = 2.76 (P = 0.006)								
Total (95% CI)			212			165	100.0%	1.53 [0.32, 2.75]
Heterogeneity: Tau ² = 1.94; Chi ² = 109.90, df = 5 (P < 0.00001); I ² = 95%								
Test for overall effect: Z = 2.48 (P = 0.01)								
Test for subgroup differences: Chi ² = 6.52, df = 1 (P = 0.01), I ² = 84.7%								

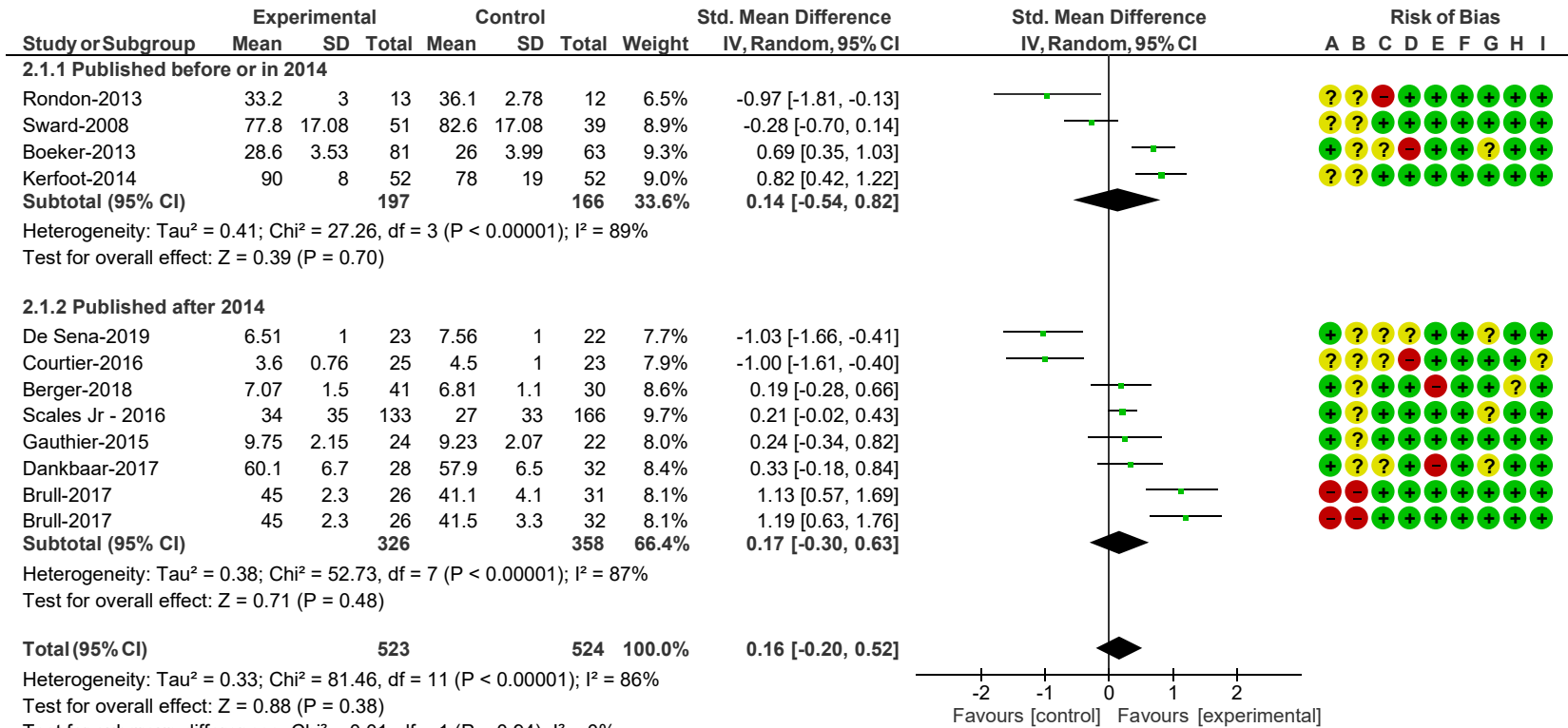


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

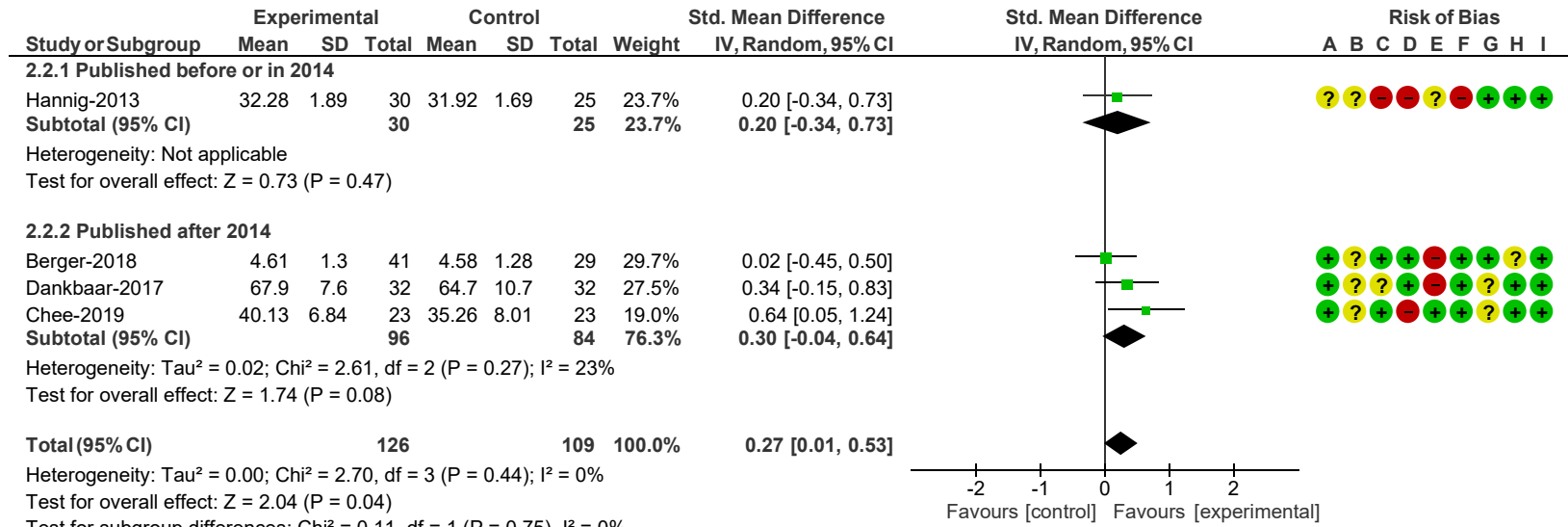
2 Publisher before or in 2014 v. published after 2014

2.1 Knowledge



- Risk of bias legend
- (A) Random sequence generation (selection bias)
 - (B) Allocation concealment (selection bias)
 - (C) Similarity of baseline outcome measurements
 - (D) Baseline characteristics similar
 - (E) Incomplete outcome data (attrition bias)
 - (F) Knowledge of the allocated interventions
 - (G) Protection against contamination
 - (H) Selective reporting (reporting bias)
 - (I) Other bias

2.2 Confidence in skills

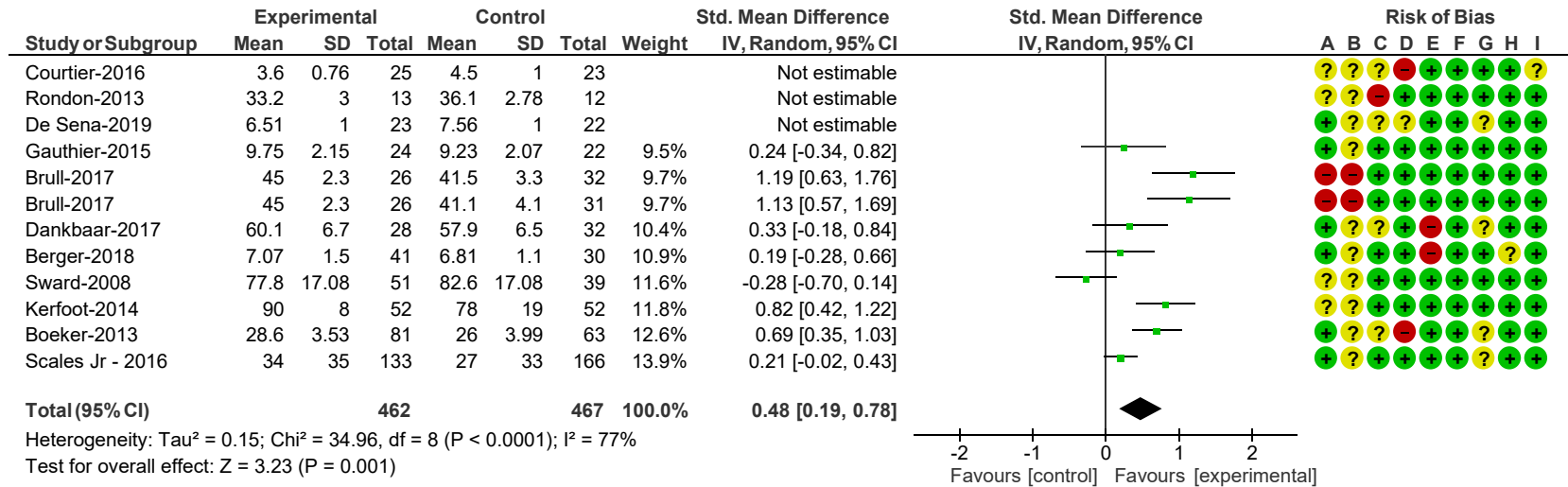


Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

3 Sample size

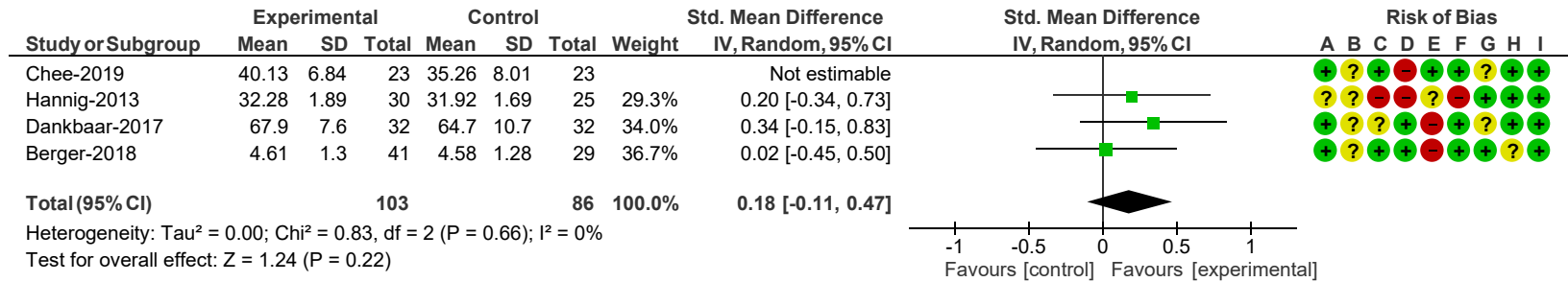
3.1 Knowledge



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

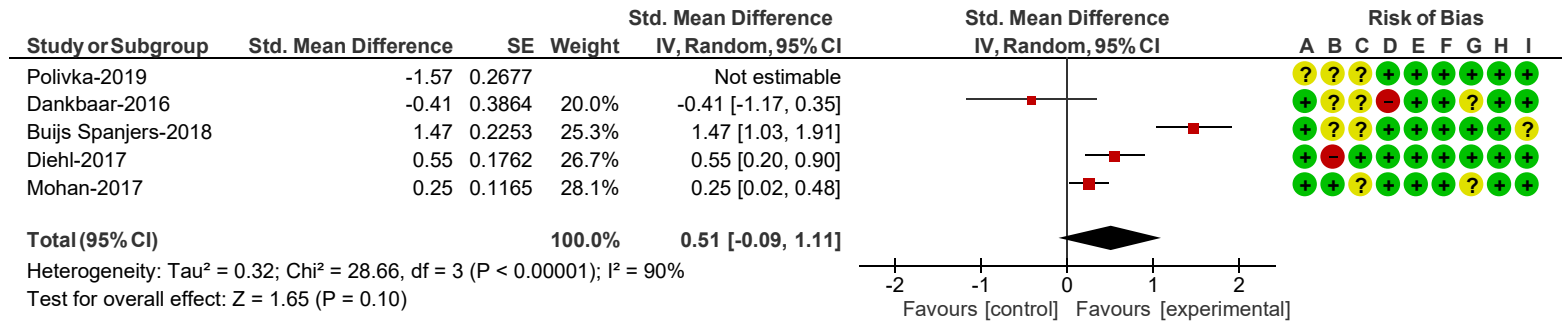
3.2 Confidence in skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

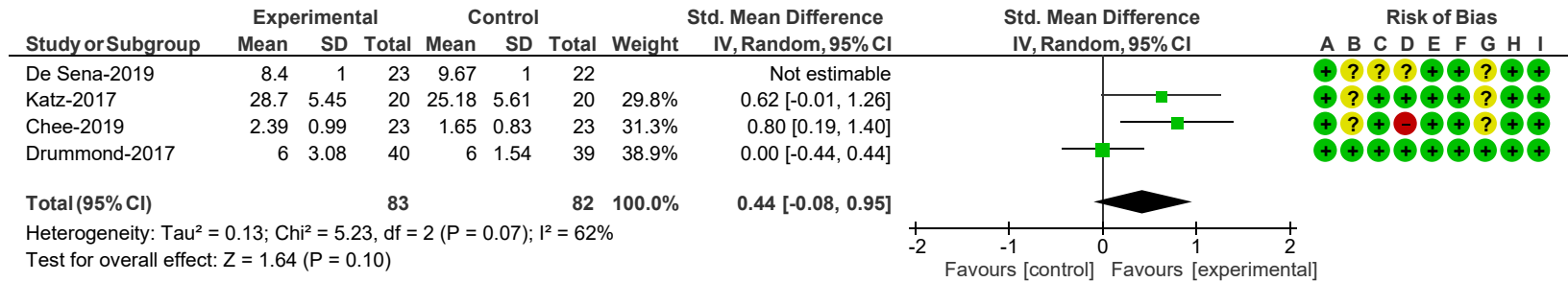
3.3 Cognitive skills



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

3.4 Procedural skills



Risk of bias legend

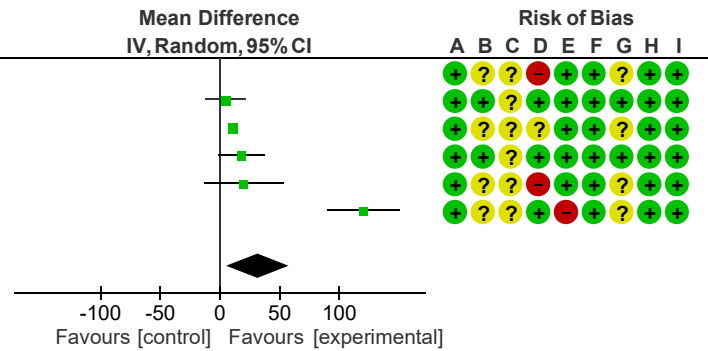
- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias

3.5 Learning time with the intervention

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total		
Dankbaar-2016	90	49	12	133	78	16		Not estimable
Mohan-2018	105	34.11	66	100	45.38	37	21.3%	5.00 [-11.78, 21.78]
De Sena-2019	18.57	0.66	23	7.41	0.43	22	23.5%	11.16 [10.84, 11.48]
Mohan-2018	117.67	50.78	66	100	45.38	36	20.7%	17.67 [-1.56, 36.90]
Dankbaar-2016	90	49	13	70	46	20	16.8%	20.00 [-13.41, 53.41]
Dankbaar-2017	174	66	32	54	60	34	17.6%	120.00 [89.51, 150.49]
Total (95% CI)			200			149	100.0%	31.88 [6.20, 57.55]

Heterogeneity: Tau² = 730.81; Chi² = 50.17, df = 4 (P < 0.00001); I² = 92%

Test for overall effect: Z = 2.43 (P = 0.01)



Risk of bias legend

- (A) Random sequence generation (selection bias)
- (B) Allocation concealment (selection bias)
- (C) Similarity of baseline outcome measurements
- (D) Baseline characteristics similar
- (E) Incomplete outcome data (attrition bias)
- (F) Knowledge of the allocated interventions
- (G) Protection against contamination
- (H) Selective reporting (reporting bias)
- (I) Other bias