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Quality of life instruments used in problem gambling studies: A systematic review and a meta-analysis

Nicolas A. Bonfils[1,3,4,5,*], Henri-Jean Aubin[1,2], Amine Benyamina[1,2], Frédéric Limosin[3,4,5], Amandine Luquiens[1,2]

1. CESP, Univ. Paris-Sud, UVSQ, INSERM, Université Paris-Saclay, Villejuif, France

2. APHP, Hôpitaux Universitaires Paris-Sud, Villejuif, France
Faculté de Médecine Paris Sud, Université Paris XI, Paris, France

3. AP-HP, Hôpitaux Universitaires Paris Ouest, Department of Psychiatry and Addictology, Paris, France

4. Université Paris Descartes, Sorbonne Paris Cité, Faculté de Médecine, Paris, France

5. Inserm, U894, Centre Psychiatrie et Neurosciences, Paris, France

*** Correspondance to:**

Nicolas A. Bonfils

Inserm, U894, Centre Psychiatrie et Neurosciences, Paris, France

nicolas.bonfils@aphp.fr

Phone : +33 6 37 29 40 15

Fax : + 33 1 58 00 47 85

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ABSTRACT

The purpose of this systematic review was to identify the instruments used in original articles to measure quality of life (QOL) or health-related QOL (HRQOL) in gambling-disorder patients and to assess their suitability.

The systematic literature search to identify QOL/HRQOL instruments used among gambling-disorder patients was performed in PubMed, Embase and PsycINFO databases up to November 2018. A meta-analysis was performed to study the effect size of the QOL/HRQOL instruments and gambling outcomes after an intervention.

Thirty-five studies were included. Seven types of instruments aiming at measuring QOL/HRQOL were identified. These instruments explored twenty-six domains. The instruments used were not properly validated in the studies. Most of the clinical trials reported a significant difference in QOL/HRQOL between pre- and post-intervention. These results were concordant with gambling outcomes but had a smaller effect size than gambling outcomes.

The currently used general instruments are efficient to measure a significant change after an intervention but might not evaluate specific areas of health related QOL impacted by gambling disorders

Keywords: review; meta-analysis; gambling; quality of life; harm.

1. INTRODUCTION

Problem gambling is characterized by a persistent and recurrent problematic gambling behavior leading to clinically significant impairment or distress (Browne et al., 2016). However treatment outcomes in this field remain poorly defined and are measured inconsistently across studies (Pickering et al., 2017). This is probably due to no consensual definition of recovery, as remission is only defined by no diagnostic operatory criterion during twelve months (American Psychiatric Association, 2013). Moreover, the course of the disease can vary deeply from one subject to another, as attests DSM-5 specification of the diagnosis “episodic” or “persistent”. Gambling disorder does not follow a linear course over time (Bruneau et al., 2016; LaPlante et al., 2008; Slutske et al., 2003). A wide range of outcome measures is used in gambling disorder research (Walker et al., 2006). A recent systematic review identified sixty-three different outcome measures in gambling disorder studies (Pickering et al., 2017). Their authors recommend developing a multidimensional scale that could assess the efficacy of an intervention in various domains of functioning (Pickering et al., 2017). Earlier, the Banff Consensus provided a framework with the minimum features of reporting efficacy of intervention and came to support the relevance of quality of life assessment in gambling disorder, in complement with the reduction of gambling behavior and the reduction of problems caused by gambling (Walker et al., 2006).

In 1993, the World Health Organization defined quality of life (QOL) “as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, and their relationship to salient features of

their environment" (Szabo and WHOQOL Group, 1996). Two types of QOL instruments are usually used: (i) general QOL instruments exploring overall QOL regardless of any health condition and (ii) health-related QOL (HRQOL) classically involving four areas: physical, physical well-being, psychological state and social relations (Leplège, 1999). On one hand, "quality of life" describes a subjective feeling of satisfaction with life in domains of importance to the subjects. On the other hand, "health-related quality of life" reports a subjective perception of the impact of the disease and its treatment(s) on daily life, physical, psychological and social functioning and well-being (Leidy et al., 1999).

QOL has been discussed in the medical literature since the 1960s (Elkinton, 1966). It became increasingly important in heath care to measure outcomes beyond morbidity and biological functioning (Karimi and Brazier, 2016). The practice of medicine is often based on the identification and management of symptoms, while patients' expectations go beyond management of symptoms: they are looking for optimal well-being (Luquiens and Aubin, 2014). In addiction, QOL assessment matches with the treatment goal of enhanced client functioning and predict treatment adherence (Laudet, 2011). Moreover, participants with addiction at all stages of recovery expressed concerns about multiple areas of functioning (Laudet et al., 2009). QOL is often included as a secondary endpoint in clinical trials, reflecting patients' feelings and functioning and the impact of their health condition beyond simple symptom assessment (Carr et al., 2001). In 2006, Walker et al. stressed that there was a lack of evaluated or validated psychometric instruments assessing QOL in gambling disorder (Walker et al., 2006) whereas evaluated or validated psychometric instruments assessing QOL do exist in substance use disorders (Luquiens et al., 2016; Neale et al., 2016).

The purpose of this review was (i) to identify the instruments used in original articles to measure QOL/HRQOL in subjects with a gambling disorder in all original articles and then (ii)

to assess the suitability of these instruments (reliability, content validity, effect size) in the gambling disorder field.

2. MATERIAL AND METHODS

The systematic review was conducted independently using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines for systematic reviews (Liberati et al., 2009) . Our review project was registered in PROSPERO database. Our project began in 2016. Since then, we have updated our review and implemented it with a meta-analysis. So we have updated our record in PROSPERO database (https://www.crd.york.ac.uk/PROSPERO/#recordDetails).

2.1. Selection criteria

Articles were included if they were (i) original articles aiming at assessing QOL/HRQOL in problem or pathological gambling/gambling disorder subjects and using an instrument designated to measure QOL/HRQOL by the authors as an outcome and (ii) if subjects were over 18 years old. We excluded (i) articles with subjects that did not fulfill problem or pathological gambling/gambling disorder criteria and (ii) articles with Parkinson disease subjects.

2.2. Data sources

The systematic literature searched to identify original studies using QOL instruments in problem gambling was performed in the following electronic databases: PsycInfo (Ovid), MEDLINE (using PubMed platform), and Embase (Ovid).

2.3. Literature search strategy

A systematic literature search was conducted among peer-reviewed journals from 1950 to November 2018 in these three electronic databases. The search strategy included a combination of the following relevant keywords: “quality of life”, “pathological gambling”, “gambling disorder” and “problem gambling”. The search was conducted to identify original studies that reported the use of QOL/HRQOL instruments in gambling in any country. Electronic database searches were limited to English-language publications.

2.4. Study selection

The study selection process was comprised of the following two phases. First, titles and abstracts of all potentially relevant publications were carefully screened and reviewed for eligibility according to inclusion and exclusion criteria by two authors (AL and NB). Secondly, the full texts of studies selected at the first step were obtained and reviewed for eligibility, using the same inclusion and exclusion criteria as in Level 1, by the same researchers. When necessary, we contacted authors of relevant studies to obtain additional information, article texts, and resolve questions about eligibility. If there were disagreements between the two authors in terms of selection of articles at the abstract level/ article level, discrepancies were resolved by consensus. Finally, with the same method, we systematically conducted any search of the reference list of the included studies

95 **2.5. Data extraction**

96 Data were extracted from the full text of articles by both the two investigators working
97 independently. Data extracted included the following items: aim, research question, design
98 and setting, sample characteristics, intervention, instrument used to assess QOL/HRQOL and
99 result(s) on QOL/HRQOL. For epidemiological studies, the main outcome measure nature
100 and results were extracted. For trials, we extracted whether QOL/HRQOL was a primary or
101 secondary endpoint and the other endpoint nature and results. The data were summarized
102 in ***Tables 2*** (see in results section).

103 Psychometric properties of the instrument (reliability, content validity, effect size) in
104 gambling population were also extracted. The QOL/HRQOL instruments are generally tested
105 for two types of reliability: (i) the internal consistency measured by Cronbach's alpha and (ii)
106 the test-retest reliability estimated by Pearson correlation coefficient. The content validity
107 refers to the degree to which an instrument measures the concept it has to measure. We
108 also studied the effect size of these instruments compared with the effect size of gambling
109 behavioral measures (See below: *Meta-analysis*).

110 Finally, we analyzed currently used QOL/HRQOL concepts in gambling-disorder subjects. For
111 this purpose, we identified the life domains of these instruments by extracting and
112 examining item concepts, after reviewing all relevant instruments. We have included as
113 many domains as possible but some may overlap.

114

115 **2.6. Meta-analysis**

116 To assess the ability to detect the change of QOL/HRQOL instruments, we also performed a
117 meta-analysis from selected trials. Three trials were excluded due to a lack of data with
118 which to perform the meta-analysis (no sample size or lack of documentation on outcome).

Each of the gambling and QOL/HRQOL pre/post intervention outcomes were analyzed by calculating the Cohen's d effect-size for each trial with the uncertainty of each result being expressed by their 95% confidence intervals (CI). An effect-size of 0.2 to 0.3 is considered to be a "small" effect, around 0.5 a "medium" effect, and above 0.8, a "large" effect (Cohen, 1988). Consistent with convention, a conservative estimate of r = 0.70 was imputed as the pre-post correlation in the calculation if it was not reported (Rosenthal, 1991; Wu et al., 2015).

Then we calculated the summarized effect-size of gambling outcomes and QOL/HRQOL ones using a random-effects model. Heterogeneity was assessed by calculating the I^2 value. The random-effects model was chosen because of the between trial heterogeneity. The underlying assumption of a random-effects model is that the true effect could vary between studies based on characteristics of the study population or intervention. Indeed, a wide range of gambling and QOL/HRQOL outcomes were used throughout the different included studies. A random-effect model is more conservative because it produces wider confidence intervals for the effect estimates than a fixed-effects model.

Publication bias was assessed using a funnel plot. In case of asymmetry, Duval and Tweedie's Trim and Fill method was used to impute missing studies. A significance level of $p<.05$ (two-tailed) was used for all analyses (Duval and Tweedie, 2000).

Finally, we performed a quality analysis of the included randomized controlled trials following the "Cochrane Collaboration's tool for assessing risk of bias" (Higgins et al., 2011), which includes five risks of bias: 1- selection bias, assessing random sequence generation and allocation concealment; 2- performance bias, assessing blinding of participants and personnel; 3- detection bias, assessing blinding of outcome assessment; 4- attrition bias,

142 exploring for incomplete outcome data; and 5- reporting bias, searching for selective
143 reporting.
144 All analyses were conducted using the Comprehensive Meta-Analysis statistical program,
145 version 3.0 (Englewood, NJ). HJA and NB extracted the data and performed this meta-
146 analysis.
147
148
149 **3. RESULTS**
150
151 The search yielded 423 citations, published between 1997 and 2018. Of these, 221 were
152 ineligible after review of the title and abstract. Thirty-five studies were included in this
153 review. The PRISMA flow diagram of the study selection process (***Figure 1***) shows the
154 reasons for excluding articles. The thirty-five included articles were published between 2002
155 and 2017. We identified six types of instruments aiming at measure QOL or HRQOL - all
156 instruments self-administered:
157 • The Medical Outcomes Study Item Short-Form Health Survey (SF) with some different
158 length options for the SF: SF-36 (McHorney et al., 1993; Ware, 2000), SF-12 (Ware et
159 al., 1996), SF-8 (Ware and GlaxoSmithKline, 2001) and SF-6D (Brazier et al., 2002,
160 1998),
161 • The European Quality of Life Questionnaire (EQ-5D) and the EQ-Visual analogue scale
162 (EQ-VAS) (EuroQol Group, 1990; Scott and Huskisson, 1976),
163 • The World Health Organization Quality of Life Assessment Instrument (Szabo and
164 WHOQOL Group, 1996) with some length options for the WHO-QOL-BREF and the
165 EUROHIS-QOL 8 item index (Schmidt et al., 2006),

166 • The Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) (Endicott et
167 al., 1993),
168 • The Quality of Life Inventory (QOLI) (Frisch et al., 1992),
169 • The Personal Well Being Index – Adult (PWI-A) (Cummins et al., 2003).
170 The instruments used most frequently were the SF (n=11), followed by the QOLI (n=10) and
171 WHOQOL (n=6) (Table 1). In the last three years of the search (i.e. 2016, 2017, 2018), the
172 four following instruments were used: the QOLI (n=4), the SF (n=3), the WHOQOL-BREF (n=1)
173 and the Q-LES-Q (n=1) (Table 1). These instruments were initially designed for various
174 purposes and referred to different concepts. The SF instruments were constructed to
175 measure HRQOL. The EQ-5D is a standardized measure of health status, commonly used as a
176 HRQOL instrument. The other instruments were developed to measure QOL. None of these
177 instruments were specifically designed to gambling disorder.
178 The methods and the results of the thirty-five articles are presented in ***Tables 2***.
179
180 **3.1. Description of the instruments and their psychometric properties**
181 The instruments differed widely in number of domains and items, scaling, scoring and
182 psychometric properties. The complete description of these instruments is provided in ***Table***
183 ***3*.**
184 The psychometric properties of the included scales have been poorly studied in the gambling
185 population. We report those given in the included articles. The SF-12, SF-8 and SF-6D derive
186 from the SF-36. In a sample of 77 pathological gamblers, internal consistency (Cronbach's
187 alpha) of the SF-12 domains ranged from 0.76 to 0.77, indicating rather good reliability
188 (McIntosh et al., 2016). No more psychometric properties have been reported in the
189 gambling population for SF scales. In a sample of 139 individuals diagnosed with gambling

190 disordered, internal consistency of the WHOQOL-BREF domains measured ranged from 0.66
191 to 0.84, indicating rather good reliability (Oei and Raylu, 2015). In a sample of 260 alcohol-
192 dependent, 282 drug-dependent, and 132 pathological gambling outpatients, internal
193 consistency of the PWI was 0.87 (Manning et al., 2012). To the best of our knowledge,
194 psychometric properties of EQ-5D, QOLI and Q-LES-Q have not been reported in the
195 gambling-disordered population.
196
197 **3.2. Analysis of the current concept of quality of life in gambling-disordered subjects**
198 The twenty-six domains investigated by the QOL/HRQOL instruments of the included articles
199 are presented in ***Table 4***. We categorized these domains into the following broader
200 categories: *relationships with others, activities, physical state, psychological state, financial*
201 *concerns, medical care and satisfaction with life*. Some disparities can be noticed between
202 the different instruments on the assessed areas. Most of the instruments assessed social
203 relationships (8/9) whereas EQ-5D did not. Moreover, only QOLI assessed "problems with
204 children" and only WHOQOL-BREF did not assess family relationships. Social activities form
205 the most explored domain across the instruments. Finally, only 3 instruments out of 6 assess
206 the financial concerns (QOLI, WHOQOL-BREF and Q-LES-Q).
207
208 **3.3. Meta-analysis: effect size of QOL instruments**
209 We studied the effect size of the QOL/HRQOL instruments and gambling outcomes after an
210 intervention. To this end, we only selected trials and performed a meta-analysis on gambling
211 outcomes and QOL outcomes. Three trials were excluded because of a lack of
212 documentation on QOL or outcome results. When combining the seven trials, our meta-
213 analysis showed these results: the global effect size for QOL/HRQOL was 0.54 (95%CI 0.34-

214 0.73); concerning gambling outcome, the global effect size was 1,550 (95%CI 1.20-1.90)
215 (Figure 2). Thus the measurement of QOL with non-gambling specific instruments showed a
216 significant medium-range effect size, significantly smaller than the large-range gambling
217 outcome effect size. The heterogeneity was quite high, rather similar for both outcomes: I^2=
218 87,82 for gambling outcome and I2= 83,20 for QOL/HRQOL. A visual inspection of the funnel
219 plot for open-label studies revealed asymmetry, indicating possible publication bias (Figure
220 3). Using Trim and Fill the imputed point estimate is barely modified: 0.54 (95%CI 0.34-0.73)
221 for the QOL/HRQOL outcome and 1.53 (95%CI 1.17-1.89) for the gambling outcome.
222
223 **4. DISCUSSION**
224
225 To our knowledge, this is the first review that inventories and assesses the suitability of
226 QOL/HRQOL instruments in the gambling problem. We reviewed randomized controlled
227 trials, non-comparative trials and epidemiological studies in order to be as comprehensive as
228 possible. We explored the suitability of these instruments through their psychometric
229 properties and their content. In addition, we performed a meta-analysis to analyze their
230 global effect size compared to the effect size of gambling behavioral outcomes.
231
232 First, this review found that a high degree of heterogeneity in QOL/HROL used
233 instruments in the gambling studies: six different types of instruments were used in thirty-
234 five included articles. Among these thirty-five included articles, only three articles were
235 randomized clinical trials and seven were non-comparative trials. We found twenty-five
236 epidemiologic studies that completed the inventory. Among trials, QOL/HRQOL was a
237 secondary outcome for eight (Carlbring and Smit, 2008; Garcia-Caballero et al., 2018; Grant

238 and Potenza, 2006; Kim et al., 2016; Lahti et al., 2010; McIntosh et al., 2016; Oei et al., 2018;
239 Zimmerman et al., 2002) and among epidemiological articles, only eight assessed
240 QOL/HRQOL as a primary endpoint (Black et al., 2003; Ekholm et al., 2018; Grant and Kim,
241 2005; Kohler, 2014; Loo et al., 2016; Manning et al., 2012; Mythily et al., 2011; Scherrer JF et
242 al., 2005). This finding shows that the relevance of QOL/HRQOL is not fully recognized in
243 gambling studies. The addiction field has come late to the chronic disease perspective. These
244 models address the impact of disease and services on the patient's overall well-being. That is
245 why the concept of QOL/HRQOL in addiction is relatively undeveloped whereas it is highly
246 relevant (Laudet, 2011). If we consider observational studies, only one study was
247 longitudinal; the others were cross-sectional with no possibility of exploring a change over
248 time. Most often, QOL/HRQOL has been studied according to whether one is a pathological
249 gambler, a problem gambler or a non-gambler. Despite the use of heterogeneous and
250 generalist QOL/HRQOL measurement instruments, observational studies found that
251 pathological and problem gamblers were more impacted than controls in QOL (Black et al.,
252 2013; Chamberlain et al., 2016; Ekholm et al., 2018; Grant and Kim, 2005; Kohler, 2014;
253 Medeiros et al., 2016; Mythily et al., 2011; Scherrer JF et al., 2005). The duration of illness
254 was also correlated with QOL (Medeiros et al., 2017). Some sub-scores on the scales,
255 particularly SF scale, were not significant: physical subscale, bodily pain and even social
256 functioning for example (Mason and Arnold, 2007; Morasco and Petry, 2006; Najavits et al.,
257 2010; Scherrer JF et al., 2005). This could be explained by the fact that these sub-dimensions
258 seem to be poorly adapted to problem gambling. The instruments used were not completely
259 or not at all validated in this population regarding the psychometric properties. It is an
260 important limit regarding the use of these instruments. Moreover, we performed a meta-
261 analysis that revealed a smaller effect size of QOL/HRQOL instruments than gambling

262 outcomes. It was not surprising that QOL/HRQOL showed a smaller effect size than gambling
263 specific outcomes, as it was a more general construct, and could be affected by factors
264 unrelated to gambling. However, this difference seemed huge. We have two explanations
265 for this result. The first is that current therapeutic interventions would improve the
266 behavioral symptoms of addiction but would not consequently improve QOL/HRQOL. It
267 would then be important to consider interventions that improve QOL/HRQOL beyond
268 behavioral change, without excluding each other. The other explanation would be that
269 change in QOL/HRQOL is not fully captured by the QOL/HRQOL instruments used. This could
270 be explained by the fact that these instruments are not gambling specific and are less able to
271 measure a change than the other specific gambling behavioral measures. It would be
272 interesting to develop an instrument to measure QOL specific to gambling.
273
274 Secondly, a content analysis of the QOL/HRQOL instruments revealed that they explored
275 twenty-six domains that we have categorized in seven broader categories: relationships with
276 others, activities, physical state, psychological state, financial concerns, medical care and
277 satisfaction with life. Nevertheless, these instruments are general (i.e. unspecific)
278 QOL/HRQOL instruments, and might not evaluate the whole range of impacted QOL/HRQOL
279 caused by gambling disorders. Only a few studies revealed the results of the scale sub-
280 scores, while others gave an overall result. When we looked at the studies giving the results
281 of the sub scores, only one study found a significant result on all the sub-scores including
282 mental health, physical functioning, bodily pain, and general health (Black et al., 2003). The
283 other studies found mental sub-score significantly associated with gambling but no
284 significant results regarding physical, bodily pain, vitality or general health sub-scores (Black
285 et al., 2013; Mason and Arnold, 2007; McIntosh et al., 2016; Morasco and Petry, 2006;

286 Najavits et al., 2010; Scherrer JF et al., 2005). Previous studies focused on harms caused by
287 gambling (Commission, 2010; Langham et al., 2015) or on HRQOL areas impacted by
288 gambling (Bonfils et al., 2019). Bonfils et al. (2019) aimed to describe HRQOL impacted by
289 problem gambling from a patients' perspective, through a qualitative study. Financial
290 pressure, relationships deterioration, negative emotions, loneliness, feeling of
291 incomprehension, preoccupation with gambling and avoidance of helping relationship were
292 found to be HRQOL domains impacted by gambling (Bonfils et al., 2019). Loneliness, feeling
293 of incomprehension, preoccupation with gambling and avoidance of helping relationship
294 were not mentioned in HRQOL instruments previously used in problem gambling (Bonfils et
295 al., 2019). Moreover, Luquiens et al. (Luquiens et al., 2015) studied the impact of alcohol use
296 disorder on HRQOL through a qualitative analysis. To this end, they conducted focus groups
297 with 38 alcohol use disorder subjects and found seven areas of impact: relationships,
298 emotional impact, living conditions, control, activities, looking after self and sleep. Only the
299 first three areas were common for both addictive disorders. Although substance use
300 disorder and gambling disorder share common characteristics, people with gambling
301 disorders also have specific characteristics (Grant and Chamberlain, 2015). It seems that
302 general QOL/HRQOL instruments do not capture gambling specificities. It was for this reason
303 that recent Burden of Disease assessments of gambling in New Zealand and Australia utilized
304 time trade off and visual analogic scale elicitation methods to direct assess community and
305 expert opinions, rather inferring QOL from generic instruments (Browne et al., 2017). The six
306 different instruments listed in the included articles are very heterogeneous regarding the
307 QOL/HRQOL domains they assess (***Table 3***). It would be interesting to standardize
308 QOL/HRQOL instruments in this population in order to allow comparisons across different
309 studies. However, there is currently no specific instrument to assess a change in QOL/HRQOL

310 in subjects with a gambling disorder while there are instruments for specific diseases in
311 many specialties (such as oncology (Macquart-Moulin et al., 2000) or neurology (Fujishima-
312 Hachiya and Inoue, 2012; Tan et al., 2005) or gastroenterology (Zingone et al., 2013)), and in
313 the addiction field in particular (as alcoholism (Luquiens et al., 2016, 2015; Neale et al.,
314 2016)).
315
316 However, it seems interesting to look at which general instruments of QOL/HRQOL seem
317 most appropriate to use in this field of research, taking into account psychometric properties
318 and content. SF, WHOQOL, PWI are the only instruments that are partially psychometrically
319 validated with a correct internal consistency in gambling population. Only SF scales are
320 HRQOL instruments; WHOQOL and PWI are QOL instruments. Nevertheless, SF scales fail to
321 capture functioning in domains—especially financial concerns or self-esteem —that are
322 important to gambling disorder-affected populations. The same is true for PWI, which also
323 does not explore these domains or psychological well-being. The scale with both
324 psychometric qualities and the most appropriate content for gambling is probably WHOQOL
325 which offers a very promising alternative, yielding scores in psychological and social
326 functioning; living environment; and an overall satisfaction score (Laudet, 2011).
327
328 Finally, QOL instruments should be designed to reflect the impact of diseases and
329 interventions in daily life from the subject's perspective (Leplège, 1999). However, most
330 items of these instruments have been defined by experts to answer their own questions.
331 Therefore a tension may appear between the objective of the experts and the impact of the
332 or treatment as perceived by subjects. Despite being self-administered and requesting
333 subjects' subjective answers, the instruments are not necessarily a good reflection of

334 subjects concerns. Moreover, if these general instruments can partially explore the
335 occurrence of adverse consequences related to gambling disorder, it is important to
336 evaluate the subjective value of these consequences for each subject. It is clear that two
337 subjects can assign different weights to a single negative consequence related to his
338 gambling addiction. While many studied areas are common across the six instruments, the
339 wording of the question and thus the answers can differ widely. For instance, the wording of
340 the question on the financial aspect varies between two questionnaires. The Q-LES-Q is
341 interested in the satisfaction with the economic status during the past week. The WHOQOL-
342 BREF asks if the subject had enough money to meet his (her) needs in the last two weeks.
343 The different wordings and the different periods explored could induce dissimilar answers.
344
345 The Food and Drug Administration (FDA) encourages specific Patients Reported Outcomes
346 (PROs) instrument to support labeling claims of medical products (FDA, 2009). PRO
347 instruments insure the subjectivity of the outcome, but not its clinical pertinence. A
348 pertinent PRO instrument should be patient-focused. One way to reach this goal would be to
349 develop the instrument from the subjects themselves, via qualitative analysis of interviews
350 with gambling-disorder subjects. This methodology would allow identification of the most
351 impacted domains of life in this particular population and those aspects that are most
352 sensitive to change, thereby promising real usefulness in assessing the efficacy of
353 interventions among gambling disorder subjects. The development of a patient-focused
354 rigorous PRO QOL instrument specific to subjects with gambling disorders would allow
355 clinicians to have a relevant instrument to administer to their patients (Arpinelli and Bamfi,
356 2006).
357

There are several limitations to our literature review. First of all, we did not conduct an in-depth search of the grey literature. However, we looked at the grey literature with the same keywords on the database OpenSIGLE, recommended by Cochrane, and did not find any results. Secondly, our review was limited to English-language articles. Some studies may not have been included due to this. With regard to meta-analysis, we can also highlight some limitations. First of all, the included articles had a great heterogeneity of judgment criteria. Finally, we did not take into account the biases of the trials for inclusion in the meta-analysis.

5. Conclusion

A successful intervention can be indirectly measured by consequent increases in the QOL. The currently used general instruments are efficient to measure a significant change after an intervention but might not evaluate specific areas of health related QOL impacted by gambling disorders. Moreover, they are not totally validated in the problem gambling population and are probably less sensitive than gambling behavioral criteria. Despite being self-administered and requesting subjective answers, these instruments do not necessarily explore the entire spectrum of patients' concerns on the impact on QOL of gambling disorder and do not take into account the patient's subjectivity. Patients should contribute to define the content of impact on QoL of gambling disorder. Such an approach could serve as the basis for the future development of a tool specifically designed for gambling disorders in order to assess health-related QoL.

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Figure and Tables

Figure 1. PRISMA flow diagram of the study selection process

Legend: 'Wrong populations' designed subject without gambling disorder or, in other term, without gambling problem/pathological gambling

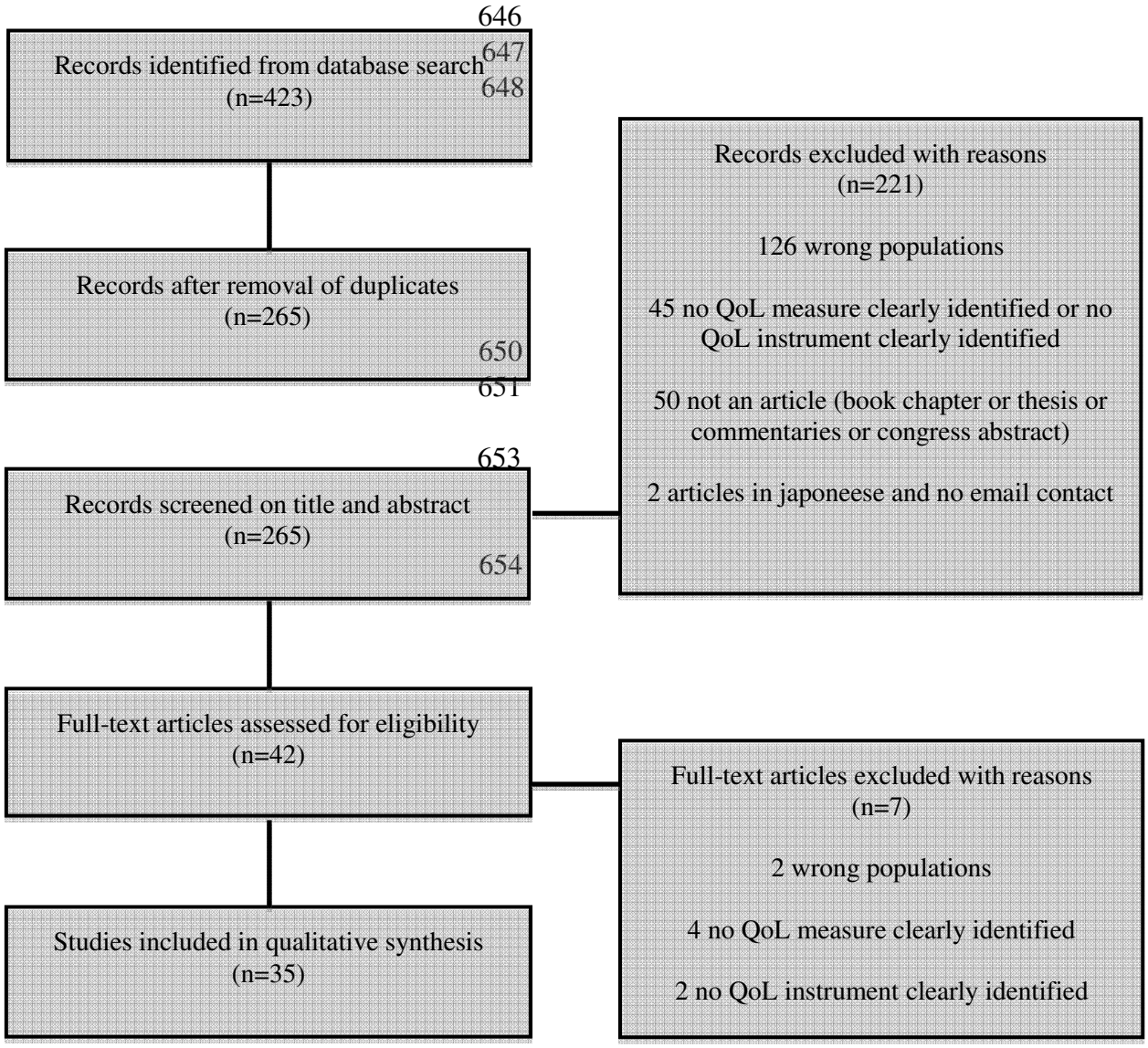


Figure 2. Forest plot

Group by Outcome	Studyname	Subgroup within study	Outcome	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	pValue
Gambling outcome	McIntosh 2016	CBT - first	Gambling outcome	2,400	0,440	0,194	1,538	3,262	5,455	0,000
Gambling outcome	McIntosh 2016	MF - first	Gambling outcome	1,520	0,310	0,096	0,912	2,128	4,903	0,000
Gambling outcome	McIntosh 2016	TAU	Gambling outcome	1,690	0,350	0,123	1,004	2,376	4,829	0,000
Gambling outcome	Calbring 2008	intervention	Gambling outcome	2,172	0,243	0,059	1,695	2,649	8,921	0,000
Gambling outcome	Calbring 2008	Waiting list	Gambling outcome	0,764	0,156	0,024	0,459	1,069	4,911	0,000
Gambling outcome	Manning 2014	Blank	Gambling outcome	1,381	0,083	0,007	1,218	1,544	16,648	0,000
Gambling outcome	Carlbring 2012	Blank	Gambling outcome	1,954	0,078	0,006	1,800	2,107	24,923	0,000
Gambling outcome	Grant 2006	Blank	Gambling outcome	1,093	0,351	0,123	0,406	1,780	3,118	0,002
Gambling outcome	Garcia-Caballero 2018	Blank	Gambling outcome	1,035	0,292	0,085	0,462	1,607	3,543	0,000
Gambling outcome	Oei 2018	intervention	Gambling outcome	6,870	3,020	9,120	0,951	12,789	2,275	0,023
Gambling outcome				1,550	0,180	0,033	1,196	1,903	8,587	0,000
QoL outcome	McIntosh 2016	CBT - first	QoL outcome	0,430	0,155	0,024	0,126	0,734	2,774	0,006
QoL outcome	McIntosh 2016	MF - first	QoL outcome	0,670	0,225	0,051	0,229	1,111	2,978	0,003
QoL outcome	McIntosh 2016	TAU	QoL outcome	0,360	0,177	0,031	0,013	0,707	2,034	0,042
QoL outcome	Calbring 2008	intervention	QoL outcome	0,808	0,153	0,023	0,508	1,107	5,279	0,000
QoL outcome	Calbring 2008	Waiting list	QoL outcome	0,024	0,137	0,019	-0,244	0,293	0,178	0,859
QoL outcome	Manning 2014	Blank	QoL outcome	0,831	0,069	0,005	0,696	0,966	12,071	0,000
QoL outcome	Carlbring 2012	Blank	QoL outcome	0,592	0,050	0,002	0,494	0,689	11,876	0,000
QoL outcome	Grant 2006	Blank	QoL outcome	0,688	0,308	0,095	0,083	1,292	2,230	0,026
QoL outcome	Garcia-Caballero 2018	Blank	QoL outcome	0,451	0,094	0,009	0,267	0,635	4,796	0,000
QoL outcome	Oei 2018	intervention	QoL outcome	71,590	17,180	295,152	37,918	105,262	4,167	0,000
QoL outcome				0,538	0,099	0,010	0,344	0,732	5,432	0,000

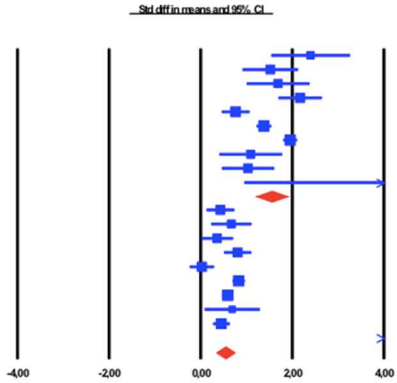
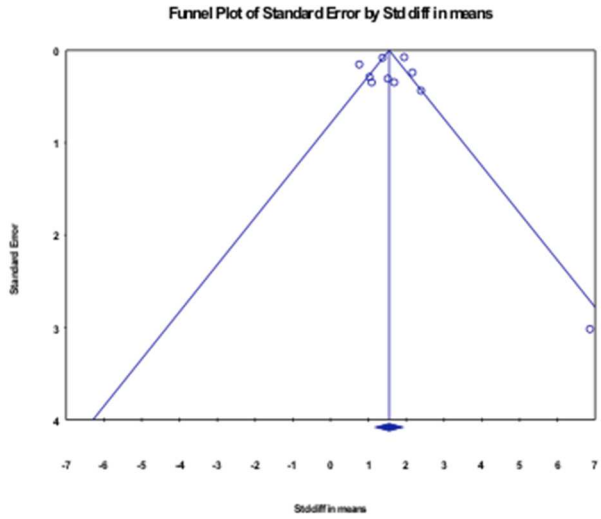
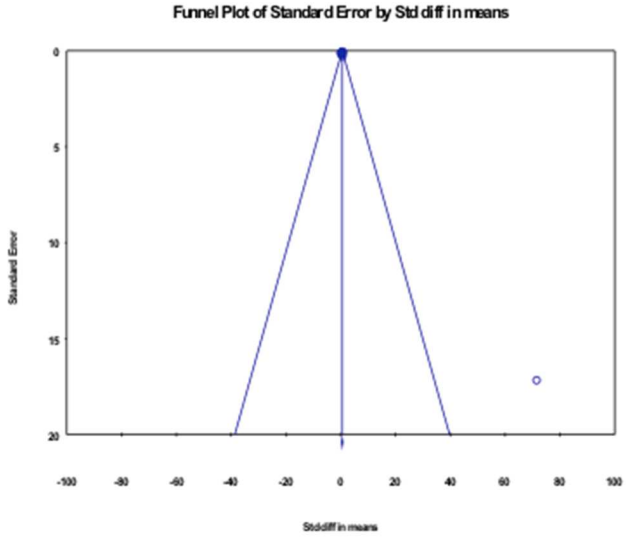


Figure 3. Tunnel plot

a. Funnel plot for gambling outcome



b. Funnel plot for QoL outcome



667 **Table 1. Instruments designated as measuring quality of life in included studies among**
668 **gambling-disorder patients.**
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670

	SF-36/SF-12 SF6 –D/SF-8	QOLI	WHO-QOL-BREF, EUROHIS-QOL 8-item index	Q-LES-Q	EQ-5D EQ-VAS	PWI
Ekholm et al. (2018) (Ekholm et al., 2018)	x					
Harries et al. (2018) (Harries et al., 2018)		x				
Oei et al. (2018) (Oei et al., 2018)			x			
Garcia-Caballero et al. (2018) (Garcia-Caballero et al., 2018)				x		
Black et al. (2017) (Black et al., 2017)	x					
Blum et al. (2017) (Blum et al., 2017)		x				
Chamberlain et al. (2017) (Chamberlain et al., 2017)		x				
Medeiros et al. (2017) (Medeiros et al., 2017)		x				
Chamberlain et al. (2016) (Chamberlain et al., 2016)		x				
Kim et al (2016) (Kim et al., 2016)			x			
Loo et al. (2016) (Loo et al., 2016)			x			
Madeiros et al. (2016) (Medeiros et al., 2016)		x				
McIntosh et al. (2016) (McIntosh et al., 2016)	x					
Manning et al. (2015) (Manning et al., 2015)						x
Oei et al. (2015) (Oei and Raylu, 2015)			×			
Subramanian et al (2015) (Subramaniam et al., 2015)					x	
Kohler (2014) (Kohler, 2014)	×				×	
Manning et al. (2014) (Manning et al., 2014)						×
Suomi et al (2014) (Suomi et al., 2014)			×			
Black et al. (2013) (Black et al., 2013)	×					
Carlbring et al. (2012) (Carlbring et al., 2012)		×				
Manning et al. (2012) (Manning et al., 2012)						×
Chou et al. (2011) (Chou and Afifi, 2011)	×					
Mythily et al. (2011) (Mythily et			×			

al., 2011)						
Kennedy et al. (2010) (Kennedy et al., 2010)				×		
Lahti et al. (2010) (Lahti et al., 2010)					×	
Najavits et al. (2010) (Najavits et al., 2010)	x			x		
Carlbring et al. (2008) (Carlbring and Smit, 2008)		×				
Mason et al. (2007) (Mason and Arnold, 2007)	×					
Grant et al. (2006) (Grant and Potenza, 2006)		×				
Morasco et al. (2006) (Morasco and Petry, 2006)	×					
Grant et al. (2005) (Grant and Kim, 2005)		×				
Scherrer et al. (2005) (Scherrer JF et al., 2005)	×					
Black et al. (2003) (Black et al., 2003)	×					
Zimmerman et al. (2002) (Zimmerman et al., 2002)				×		