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Delay Discounting as a Biomarker for the Treatment of Gambling Disorder: a systematic review

João Correia Martins

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Eu, João Correia Martins, abaixo assinado, nº mecanográfico 201706970, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro ter actuado com absoluta integridade na elaboração do meu trabalho de Dissertação ou Monografia.

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DESIGNAÇÃO DA ÁREA DO PROJECTO

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TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Delay Discounting as a Biomarker for the Treatment of Gambling Disorder: a systematic review

ORIENTADOR

Professor Doutor Jacinto Nuno Costa Azevedo

COORIENTADOR (se aplicável)

ASSINALE APENAS UMA DAS OPÇÕES:

É AUTORIZADA A REPRODUÇÃO INTEGRAL DESTE TRABALHO APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	X
É AUTORIZADA A REPRODUÇÃO PARCIAL DESTE TRABALHO (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) APENAS PARA EFEITOS DE INVESTIGAÇÃO, MEDIANTE DECLARAÇÃO ESCRITA DO INTERESSADO, QUE A TAL SE COMPROMETE.	☐
DE ACORDO COM A LEGISLAÇÃO EM VIGOR, (INDICAR, CASO TAL SEJA NECESSÁRIO, Nº MÁXIMO DE PÁGINAS, ILUSTRAÇÕES, GRÁFICOS, ETC.) NÃO É PERMITIDA A REPRODUÇÃO DE QUALQUER PARTE DESTE TRABALHO.	☐

Faculdade de Medicina da Universidade do Porto, 20/03/2025

Assinatura conforme cartão de identificação: João Correia Martins

UC Dissertação - DECLARAÇÃO DE TRANSPARÊNCIA RELATIVAMENTE À UTILIZAÇÃO DE FERRAMENTAS DE CHATBOT GENERATIVO BASEADAS EM LARGE LANGUAGE MODELS

Eu, João Correia Martins, abaixo assinado, nº mecanográfico 201706970, estudante do 6º ano do Ciclo de Estudos Integrado em Medicina, na Faculdade de Medicina da Universidade do Porto, declaro que:

☒ Não procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* para nenhuma das tarefas no contexto do meu trabalho de Dissertação ou Monografia

☐ Procedi à utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia, encontrando-se todas as interacções (*prompts* e respostas) transcritas em anexo bem como a indicação das aplicações utilizadas.

Neste sentido, confirmo que a eventual utilização de ferramentas de *chatbox* generativo baseadas em *large language models* no contexto do meu trabalho de Dissertação ou Monografia foi exclusivamente descrita na sequência de *prompts* e respostas transcritos em anexo e nas aplicações indicadas.

Faculdade de Medicina da Universidade do Porto, 20/03/2025

Assinatura conforme cartão de identificação:

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Delay Discounting as a Biomarker for the Treatment of Gambling Disorder: a systematic review

Delay Discounting in Gambling Disorder

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WORD COUNT 2985

DECLARATION OF INTERESTS The authors declare no conflicts of interest

PRIMARY FUNDING This research did not receive any funding.

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ABSTRACT

Aims This systematic review aimed to assess whether delay discounting (DD) can be considered a dynamic biomarker in Gambling Disorder (GD) treatment by analyzing its potential changes in response to therapeutic interventions. **Methods** A systematic review was conducted following PRISMA guidelines. Four databases (EBSCO, PubMed, Scopus, and Web of Science) were searched using predefined keywords related to DD, GD, and treatment outcomes. Eligibility criteria included observational and experimental studies that measured DD in individuals diagnosed with GD undergoing treatment or post-treatment. **Results** The search yielded 241 articles, of which five met the inclusion criteria. These included four observational case-control studies and one randomized controlled trial (RCT). Observational studies consistently reported that DD remained elevated in Pathological Gamblers (PGs) undergoing treatment, with no significant differences across treatment stages. The RCT, assessing the effects of transcranial magnetic stimulation (TMS) on PG, found no significant changes in DD values compared to the sham group, despite some effects on gambling behavior. Comparisons with other addictive disorders showed that, unlike substance use disorders, where abstinence and treatment were associated with reduced DD, no such pattern was observed in GD. **Conclusions** The findings suggest that while Delay Discounting is strongly associated with Gambling Disorder, it does not appear to be significantly influenced by treatment, unlike in substance use disorders. Longitudinal studies are needed to better understand possible changes in Delay Discounting in individuals with Gambling Disorder undergoing treatment.

Keywords: Addiction, Biomarker, Delay Discounting, Gambling Disorder, systematic review, Treatment

INTRODUCTION

Delay Discounting (DD) can be defined as the tendency to devalue rewards based on the time required to receive them. Thus, individuals with high DD rates tend to choose smaller and immediate rewards over larger and delayed rewards (1). A term that is often associated with DD is impulsive choice, which refers to the concrete act of choosing a small immediate reward instead of a larger one later. That being said, it is important to understand that high discounting rates do not cause impulsive choice, rather, they are the result of several impulsive choices. Therefore, the two terms should not be regarded as synonyms (2). To assess those rates, Delay Discounting Tasks (DDTs) are often used which consist of asking individuals to choose between an immediate, smaller reward (such as money, cigarettes, or food) and a larger reward with a certain delay. The value of the immediate and/or delayed reward and the amount of the delay are systematically adjusted on each question. DDTs can be conducted using questionnaires previously established by other authors or adapted to each study. The methods for analyzing the data include measures such as the K parameter, which reflects the degree of discounting, and the Area Under the Curve (AUC) - smaller areas equals higher discounting. Despite the different ways to measure DD, discounting rates tend to be higher in various types of addictions (3), obesity, and risky sexual behaviors (4, 5). Specifically in Gambling Disorder (GD), several studies have shown that individuals with this disorder show higher K values (6–10).

In the latest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), Pathological Gambling was moved to the Substance-Related and Addiction Disorders chapter, and the term was changed to GD (11, 12). This change reflects the similarities between these addictions, as reported by multiple studies over the years (13–15), besides often occurring simultaneously (16–18).

The prevalence of gambling has increased substantially in recent years (19). One factor contributing to this increase is the ease of access and the growth of online gambling (20). In a world increasing digitally, we can deduce that accessibility tends to increase. Additionally, the COVID-19 pandemic could have been a factor, which helps to

explain this phenomenon. Because a large number of people were confined, and everything was closed, anxiety and depression increased, creating a perfect environment for an online gambling rise — a trend that was indeed observed (21). Gambling brings severe problems in various domains, such as physical and mental health, relationships with family members, partners, and friends. It also impacts financial stability, creating unemployment and debts, and even leading to criminal behavior. These domains are not isolated, they overlap and affect each other, with general economic and social repercussions (22).

Regarding treatment, studies mainly focused on Substance Use Disorder (SUD) suggest that increased DD values are associated with worse therapeutic outcomes, such as therapy dropout and relapse (23–27). Considering that high DD values are strongly correlated with addictions, it is legitimate to question whether reducing DD levels could lead to behavioral improvements and better outcomes as well as if there is variation in DD in response to treatment. With SUD, there is evidence that discounting rates decrease with abstinence and treatment (28–30), and even former smokers show no significant differences compared to Healthy Controls (HC) (31), suggesting that DD values may align more closely with those of the general population over time.

Considering this, it would be of the utmost interest to determine whether DD could serve as a biomarker for the GD treatment — a value that changes as a result of treatment and could potentially be used to monitor the progress of individuals with GD or explore new therapeutic approaches. However, while there is more research on this topic in the context of SUD, the relationship between DD and GD treatment remains unclear. Therefore, this study aims to address this question.

Regarding terminology, the term we chose to use follows DSM-V terminology, which is currently "Gambling Disorder." On the other hand, we will use the term "Pathological Gamblers" (PGs) to refer to individuals with this condition.

METHODS

A systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.

Search Strategy

To begin the research, four databases were used: EBSCO, PubMed, Scopus, and Web of Science. To identify all relevant studies, the query was constructed using the following terms: (“Delay Discounting” OR “Temporal Discounting” OR “Intertemporal*” OR “impulsive choice”) AND (“Gambling Disorder” OR “Pathological Gambling”) AND (“Treatment” OR “Therap*” OR “Intervention” OR “Outcome”). No restrictions were applied regarding language or publication date. The search was completed on February 21, 2025. The respective reference lists were also reviewed to identify additional relevant studies.

Eligibility Criteria

Studies were selected based on the PICOS question (Population, Intervention, Comparison, Outcome, Study Design) (Table 1), applying the following inclusion criteria: (1) Observational studies assessing DD in individuals diagnosed with GD who were in treatment or post-treatment. Studies comparing different treatment stages (e.g., beginning and end of treatment), abstinent and non-abstinent individuals in post-treatment, or with HC were included. (2) Experimental studies measuring DD before and after a therapeutic intervention, allowing the comparison of DD values based on the success or failure of GD therapy. (3) Experimental studies comparing a therapeutic intervention for GD with a placebo group, assessing DD values of both groups in relation to therapeutic success or failure. Exclusion criteria included: (1) Studies conducted on animals; (2) Studies focusing on other psychiatric disorders without a primary focus on GD; (3) Observational studies assessing PGs exclusively in an early treatment stage without comparisons to more advanced stages or post-treatment periods.

Study Selection

All search results were imported into EndNote, with duplicates being removed. The eligibility screening process consisted of two phases. In phase one, all article titles and abstracts were reviewed by one researcher (JM) according to the previously mentioned criteria. In phase two, full texts of pre-selected articles were analyzed comprehensively, resulting in the final set of included articles. The selection process was

reviewed by a second researcher. Disagreements were discussed and resolved by consensus. In case of no consensus, a third researcher would had to be consulted, which was not deemed necessary.

Quality Assessment

Given the inclusion criteria, this systematic review includes observational and experimental studies. Therefore, to assess the quality of the studies, two scales were used: The Newcastle-Ottawa Scale (NOS) (32) and the Revised Cochrane risk of bias tool for randomized trials (RoB 2 for Crossover Trials) (33).

Data Extraction

Data were extracted by one researcher (JM) and entered into two tables. One table focused on observational studies, detailing: Author, year of publication and study design, Participants, Type of treatment, DD measure (DDT and reported values), and Main results (comparission of DD among participants). The second table covered experimental studies, including: Author, year of publication and study design, Participants, Type of treatment, DD measure (DDT and reported values), GD outcome (changes in gambling behavior), and DD outcome (comparission of DD among participants). The collected data were presented qualitatively, describing whether DD values changed or remained stable and whether there were differences between comparison groups, without presenting specific quantitative values. The data extraction process were analyzed and discussed with a second researcher, leading to a consensus.

RESULTS

A total of 241 articles were found through database searches: 40 from PubMed, 84 from Scopus, 64 from Web of Science, and 53 from EBSCO. Despite hand-search of the studies reference list, no additional relevant articles were identified. After removing 118 duplicates, 123 articles remained for title/abstract screening. Following the initial selection, 14 articles were selected for full-text review, and 5 met the eligibility criteria, being included for analysis. The study selection diagram is shown in Figure 1.

The publication dates for the included studies ranged from 2009 and 2017. All PGs recruited were diagnosed according to DSM criteria, confirming the absence of other mental health issues. Four were observational case-control studies (34-37), among these, only one specified the type of treatment applied (35) — Cognitive Behavioral Therapy (CBT). Only one was a randomized controlled trial (RCT) (39). Further information can be found in Tables 2 and Table 3, accordingly.

Quality of the Included Studies

The 5 included studies did not present a risk of bias according to the scales used. In the NOS, only one study had a score of 7 (36), while the others had a score of 8 (34, 35, 37), with the maximum score being 9, which corresponds to the highest quality. Regarding the RoB 2 for crossover trials, the study (39) presented an overall low risk. More detailed information can be found in Table 4 and Table 5, respectively.

Observational studies

Among the observational studies with a case-control design, two used treatment-seeking and non-treatment-seeking PGs and compared DD values between them as well as with HC. Ledgerwood, D.M. (34), et al. recruited 27 treatment-seeking PGs, 34 community-based PGs, and 41 HCs. In all three groups, the preference for smaller short-term rewards over larger long-term ones was analyzed using the Delayed Discounting of Monetary Rewards (9) to obtain the AUC (area under the curve). The statistical analysis of this study showed that PGs had higher DD compared to the control group (despite 44% of them being in treatment), and the comparison between treatment-seeking and non-treatment-seeking PGs revealed no statistically significant differences. In Michalczuk, R., et al. (35), 30 PGs (15 prior treatment; 7 receiving treatment; 8 completed a 10-session treatment) and 30 HCs participated. DD was measured using the Kirby Monetary Choice Questionnaire (38), and the results were presented as K value and AUC. Similar to the previous study, the PGs group showed higher DD values compared to the control group. Regarding the comparison between different treatment stages, there were no statistically significant differences in DD values. Grecucci, A. (36), et al. used a sample of 23 treatment-seeking PGs and 23 HCs. All participants completed

a Monetary Delay Discounting Task (k value), and the results showed that despite being in treatment, the DD values of PGs remained higher than those of the control group. Similar results were found in the study by Navas, J.F. (37), et al., where 71 treatment-seeking PGs and 74 non-problematic community gamblers completed the Kirby Monetary Choice Questionnaire (38) (logarithm of k). Once again, the treatment-seeking PGs group exhibited higher DD values.

RCT Study

Crossover RCT, Zack et al. (39), aimed at assessing the effects of repeated Transcranial Magnetic Stimulation (rTMS) of the medial prefrontal cortex (PFC) and continuous theta burst stimulation (cTBS) of the right dorsolateral PFC on impulsive choice in men with GD. The study included 9 PGs randomly assigned to three groups: rTMS, cTBS, and sham. Participants switched groups each week. The procedure was as follows: participants underwent stimulation (active or sham), played a slot machine for 15 minutes, and completed a Monetary DDT. Assessments were also carried out to understand the effect of the intervention on gambling, that is, its potential as a treatment. Results showed that, compared to the sham group, the rTMS group reduced increases in Desire to Gamble after slot machine stimulation, while the cTBS group reduced subjective psychostimulant-like effects and diastolic blood pressure. However, DD values did not differ significantly between the intervention and sham groups, indicating no decrease in discounting rates, contrary to what the authors expected.

DISCUSSION

This systematic review included observational studies comparing treatment-seeking PGs with other PGs in different treatment stages or HCs (34-37), as well as an experimental study (39) comparing DD values when receiving active intervention with sham values. The goal of this selection was to find studies that could help draw conclusions about whether DD can be interpreted as a dynamic biomarker, meaning if it changes in response to therapeutic interventions. Therefore, studies that allowed analysis of the impact of treatment on discounting rates were gathered. In the analyzed case-control studies, DD values in treatment-seeking PGs were compared to control

groups, revealing consistent results: DD remained elevated regardless of treatment (34-37). It is important to note that in two of these studies, not all PGs were undergoing treatment, but internal analyses showed no statistically significant differences between the different treatment stages (before, during, and after treatment), indicating that DD values remained stable throughout the process.

In the analyzed RCT (39), DD did not change in the intervention group compared to the sham group, despite the intervention group showing beneficial effects on gambling reinforcement. These results contrast with similar studies (40, 41) in which DD values decreased in healthy volunteers following the same TMS (transcranial magnetic stimulation) protocols.

Considering similar studies related to other types of addiction, active drug users and those in abstinence showed lower DD values, suggesting that drug misuse increases discounting and that it decreases with the cessation of the stimulus, implying that DD is not fixed and can be altered (28). Other studies also found lower rates for opioid dependents in abstinence (29) and under treatment (30), although this was not the case for cocaine and alcohol abusers (29). Regarding treatment, smokers in therapy showed lower DD values than active smokers (42). In another comparison (43) between active smokers, ex-smokers, and never-smokers, DD values of ex-smokers and never-smokers did not differ, while active smokers showed increased values. This study shows similarities with two included in this review for GD, though with opposite results. Additionally, a study found that individuals participating in a 50-minute workshop about mindful eating experienced decreased DD values in a hypothetical food task, unlike the control group (44). However, this decrease was not observed in a monetary DD task, similar to another study involving gambling cravings in a sample of university students, where a brief meditation failed to lower DD values in a monetary task (45).

Given these findings, it seems there is several studies to show that other fields of research have shown that DD has changed with treatment, whereas in the case of GD, this is not as commonly observed. The results of the included studies and the comparison of abstinent PGs (despite lacking treatment information) with active PGs (46) also showed no changes in DD values. The authors even suggested that impulsive

choice may play a more significant role in triggering GD than perpetuating it after its onset. It is also known that SUD and GD share similarities, both being associated with reward response dysfunction (13-15) and often co-occurring (16-18). It is suggested that SUD may involve a reversible process, that is not present in GD (46), as there are no neurotoxic effects of external substances in GD that could confound addiction research. This implies that in GD, the differences observed in PGs may reflect intrinsic characteristics of these individuals, considering that they are individuals who present changes in neurocognitive function (39, 47). To counter this perspective, a study analyzing the effect of tolcapone (48), an inhibitor of the dopamine-degrading enzyme catechol-O-methyltransferase (COMT), managed to reduce DD values in PGs with this intervention, something previously done with healthy individuals (49). However, this study did not provide data on therapeutic outcomes, meaning whether the intervention impacted gambling itself or just the gamblers discounting rates. This has been observed in smoking cessation treatments where DD values changed, but cigarette consumption remained the same (50). Another study on tolcapone (51) suggested a correlation between the intervention and GD, reducing the score on the Yale-Brown Obsessive Compulsive Scale Modified for Pathological Gambling (PG-YBOCS). Together, these two studies (48, 51) open the door to better explore the dynamics of DD in GD treatment, though longitudinal studies are needed to better understand the process (48).

Strengths and Limitations

Despite the systematic search across multiple platforms, there is a slight possibility that some studies may not have been found. However, several authors mention that this is an area with limited research. Nevertheless, the main limitation of this systematic review is the small number of included articles, as larger sample sizes are better for drawing conclusions. Among the observational studies, only one provided detailed information on the treatment and its stage (35). The remaining studies mentioned treatment in qualified clinics, indicating credibility. Furthermore, it was indicated that, as the participants were receiving treatment, the results should be interpreted considering the possible influence of the treatment (36, 37). In light of this, we can conclude that individuals in the early stages of therapy were not recruited.

Regarding the RCT (39), it had a small sample size, and despite showing potential as an intervention to mitigate GD in men, TMS is not yet a regular treatment for GD, so the reason why DD was not altered may indeed be the lack of effectiveness of TMS as a treatment for GD. However, it has been shown that TMS altered DD in HC (40, 41), so there is still the possibility that it did not change in that study precisely because it involved PGs. Therefore, further research on this treatment is needed to draw better conclusions.

The protocol for this study was not registered on any platform.

CONCLUSION

To conclude, Delay Discounting values have a strong correlation with Gambling Disorder, but they do not seem to present the same correlation with treatment, unlike what happens with smokers, and drug, and alcohol abusers. This can be explained by the fact that, in the case of Gambling Disorder, there is no external aggressor, meaning there is no chemical substance being administered (which can be halted), to directly cause behavioral changes, but rather a factor much more deeply rooted in individuals that leads to neurocognitive function alterations compared to individuals with no involvement in gambling. However, the study conducted with Tolcapone showed that it was possible to reduce the discounting rates in Pathological Gamblers, though it did not report on the implications this had on the gambling behavior itself. Ideally, longitudinal studies with large-scale samples, not only with Tolcapone but also with other treatments, would be needed, where Delay Discounting values are measured before, during, and after treatment, also interpreting the results based on therapeutic outcomes.

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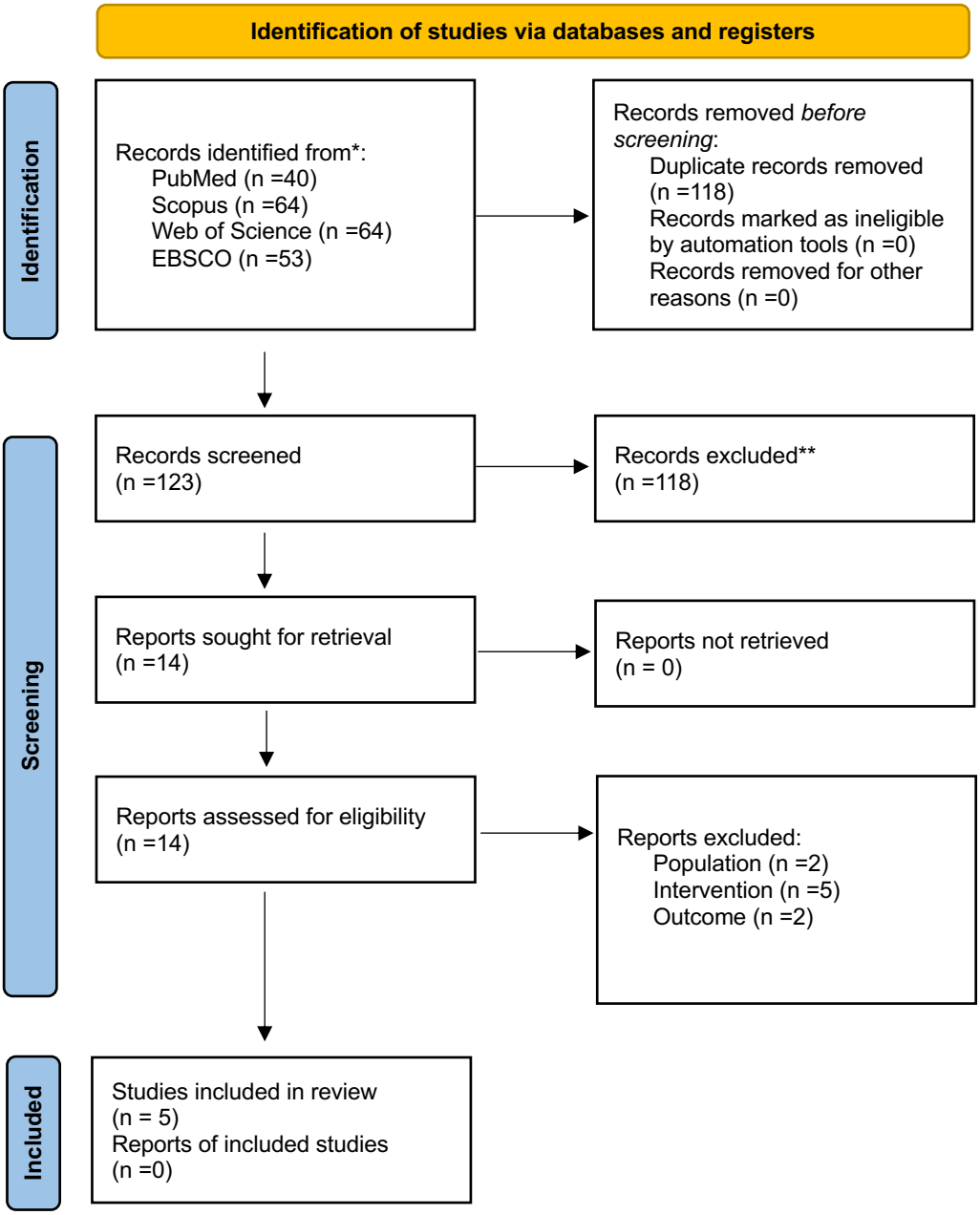

Figure 1 - Overview of RCT included study

Population	Individuals diagnosed with GD (gambling disorder – DSM-5) undergoing or who have undergone treatment
Intervention/Exposure	Assessment of delay discounting
Comparison	PGs receiving treatment at different stages or post-treatment, or healthy controls
Outcome	Variation in delay discounting
Study Designs	Primary, observational, and experimental studies

Table 1 – PICOS Question

Author (Year and study design)	Participants (n)	Type of treatment	DD measure	Main results
Ledgerwood, D.M., et al. (2009) (34) (case-control)	61 PGs (27 treatment-seeking; 34 community-based PGs) 41 HC	Undefined	The Delayed Discounting of Monetary Rewards (Petry and Casarella, 1999) (9) (AUC)	**PGs showed higher DD values than the control group.** **No statistically significant differences were found between the PGs on treatment and those not on treatment.**
Michalczuk, R., et al. (2011) (35) (case-control)	30 PGs (15 prior treatment; 7 receiving treatment; 8 completed a 10-session treatment) 30 HC	Cognitive Behavioural Therapy (CBT)	Kirby Monetary Choice Questionnaire (MCQ ; Kirby et al. 1999) (38) (k value and AUC)	**PG showed higher DD values than the control group.** **No statistically significant differences were found between the different stages of DD treatment.**
Grecucci, A., et al. (36) (2014) (case-control)	23 PGs treatment-seeking 23 HC	Undefined	Monetary Delay Discounting Task (k value)	**PGs showed higher DD values than the control group.**
Navas, J.F., et al. (2017) (37) (case-control)	71 PGs treatment-seeking 74 non-problematic community gamblers	Undefined	Kirby Monetary Choice Questionnaire (MCQ ; Kirby et al. 1999) (38) (logarithm of k)	**PGs showed higher DD values than the control group.**

Table 2 - Overview of the included observational studies

Author (Year and study design)	Participants (n)	Type of treatment	DD measure	PG outcome	DD Outcome
Zack et al. (2016) (39) (Crossover RCT)	9 PG	1. Repeated transcranial magnetic stimulation (rTMS) 2. Continuous theta burst stimulation (cTBS)	Monetary Delay Discounting Task (k value)	1. rTMS reduced post-game increases in Desire to Gamble 2. cTBS reduced subjective psychostimulant-like effects, and diastolic blood pressure (Relative to sham)	No differences were found in relation to the sham group.

Table 3 - Overview of RCT included study

	SELECTION	COMPARABILITY	EXPOSURE	Total
Ledgerwood, D.M., et al. (2009) (34)	***	**	***	8
Michalczuk, R., et al. (2011) (35)	****	**	**	8
Grecucci, A., et al. (2014) (36)	**	**	***	7
Navas, J.F., et al. (2017) (37)	***	**	***	8

Table 4 - The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies

	D1	DS	D2	D3	D4	D5	Overall
Zack et al. (2016) (39)	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Some Concerns	Low Risk

Table 5 - Revised Cochrane RoB 2 tool for crossover trials. D1 - Domain 1a: Risk of bias arising from the randomization process; DS - Domain S: Risk of bias arising from period and carryover effects; D2 – Domain 2: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention); D3 – Domain 3: Risk of bias due to missing outcome data; D4 – Domain 4: Risk of bias in measurement of the outcome; D5 - Domain 5: Risk of bias in selection of the reported result; Overall - Overall risk of bias.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page and paragraph/ table #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both. **- MANDATÓRIO**	Page 1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number. **– SEGUIR RECOMENDAÇÕES DA REVISTA**	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. **– MANDATÓRIO** ***O rationale corresponde à justificação da importância da revisão sistemática***	Page 3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS). **- MANDATÓRIO**	Page 3-4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number. **– FACULTATIVO**	NA
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. **– MANDATÓRIO** ***É altamente recomendado, de acordo com as boas práticas da Cochrane, que não sejam aplicados critérios de exclusão baseados na língua e/ou data de publicação dos estudos.***	Page 5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched. **– MANDATÓRIO** ***Em consonância com as boas práticas da Cochrane, é mandatório que se verifique pesquisa em pelo menos duas bases de pesquisa bibliográfica (idealmente, deverão ser pesquisadas duas bases generalistas e uma específica da área). No caso de revisões sistemáticas de estudos experimentais/ensaios clínicos aleatorizados, é altamente recomendado que uma das bases pesquisadas corresponda à CENTRAL ou a bases de ensaios clínicos como a ClinicalTrials.gov.*** ***Estudos de revisão da literatura em que a pesquisa decorra numa única base de dados não serão classificados como revisões sistemáticas.***	Page 5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated. **– MANDATÓRIO** ***A query de pesquisa deve ser obrigatoriamente disponibilizada. A utilização de filtros de pesquisa da InterTASC é altamente recomendada (https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/home)***	Page 5

PRISMA 2009 Checklist

Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis). **– MANDATÓRIO** ***As fases de selecção dos estudos primários devem ser descritas. Em consonância com as boas práticas da Cochrane, é mandatório que o processo de selecção envolva duas fases (fase de rastreio, em que os registos são seleccionados por título e abstract, e fase de inclusão, na qual se procede à leitura integral dos full texts). Em cada uma destas fases, o processo de selecção deve mandatoriamente envolver dois investigadores actuando de forma independente.***	Page 5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators. **– MANDATÓRIO** ***Trata-se de descrever de que forma se procedeu à extracção de dados dos estudos primários. Em consonância com as boas práticas da Cochrane, tal processo deverá envolver dois investigadores de forma independente.***	Page 6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made. **– MANDATÓRIO** ***Trata-se de descrever as variáveis para as quais foi obtida informação.***	Page 6
Risk of bias in individual studies / Risk of bias across studies	12/ 15	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis. **– MANDATÓRIO** ***Em todas as revisões sistemáticas, deverá existir um processo de avaliação da qualidade dos estudos primários. No caso de revisões sistemáticas de estudos experimentais/ensaios clínicos aleatorizados, a aplicação dos critérios de risco de viés (Risk of Bias) da Cochrane é altamente recomendada. No caso de revisões sistemáticas de estudos observacionais, poderão ser seguidos os critérios ROBINS ou os critérios dos National Institutes of Health (https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools).***	Page 6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). **– FACULTATIVO. APENAS NECESSÁRIO SE FOR FEITA META-ANÁLISE**	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis. **– FACULTATIVO. APENAS NECESSÁRIO SE FOR FEITA META-ANÁLISE**	NA
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified. **– FACULTATIVO. APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE**	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram. **– MANDATÓRIO**	Page 6-7
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations. **– MANDATÓRIO**	Page 6-7
Risk of bias within and across studies	19/ 22	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12). **– MANDATÓRIO**	Page 6-7
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot. **– FACULTATIVO.**	NA

PRISMA 2009 Checklist

		APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE	NA
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency. **– FACULTATIVO. MANDATÓRIO APENAS SE FOR FEITA META-ANÁLISE**	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). **– FACULTATIVO. APLICÁVEL APENAS SE FOR FEITA META-ANÁLISE**	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers). **– MANDATÓRIO**	Page 8-11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). **– MANDATÓRIO**	Page 10-11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research. **– MANDATÓRIO**	Page 10-11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. **– SEGUIR RECOMENDAÇÕES DA REVISTA**	Page 1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

Author Guidelines

Addiction will be published in online-only format effective with the 2023 volume. This is a proactive move towards reducing the environmental impact caused by the production and distribution of printed journal copies and will allow the journal to invest in further innovation, digital development and sustainability measures. Published articles will continue to be disseminated quickly through the journal's broad network of indexing services, including Web of Science, MEDLINE and Scopus. Articles will also continue to be discoverable through popular search engines such as Google.

Sections

*learn more about the journal's "Declaration of Interest" here.

1. Submission and Peer Review Process

Addiction welcomes manuscripts reporting original research on clinical, epidemiological, human experimental, policy-related, and historical aspects of addiction and addictive behaviours including, but not limited to, alcohol, opioids, stimulants, cannabinoids, tobacco, nicotine, and gambling. *Addiction* does not publish single clinical case reports. *Addiction* does not publish animal research — but authors of this research may wish to send their manuscript to *Addiction Biology*.

We strive to give authors a prompt service in terms of the time it takes to complete an initial evaluation of a manuscript, and if taken forward, completion of its peer review. Usually, we complete the former in 1-2 weeks, and the latter within 6-8 weeks. We can also *fast track* manuscripts with highly important findings that will inform practice and policy; here, our aim is to complete the review process within 2-3 weeks. Please contact the Editor-in-Chief if you have a manuscript nearing completion and you would like us to consider expedited review.

Once the submission materials have been prepared in accordance with the Author Guidelines, manuscripts should be submitted online at http://mc.manuscriptcentral.com/addiction.

Addiction requires all authors to provide a declaration of interests statement.

We will not normally publish editorials, reviews, and commentaries that refer to a commercial organization, its affiliates, and any product or device, where the author has a financial connection with the organization or product in any of the following categories of conflict of interest: shares, consultancy, employment, honoraria for providing lectures, and any work on the manuscript that has been funded with support of a commercial organisation.

Artificial Intelligence Generated Content (AIGC) tools—such as ChatGPT and others based on large language models (LLMs)—cannot be considered capable of initiating an original piece of research without direction by human authors. They also cannot be accountable for a published work or for research design, which is a generally held requirement of authorship (as discussed in the previous section), nor do they have legal standing or the ability to hold or assign copyright. Therefore—in accordance with COPE's position statement on AI tools—these tools cannot fulfill the role of, nor be listed as, an author of an article. If an author has used this kind of tool to develop any portion of a manuscript, its use must be described, transparently and in detail, in the Methods or Acknowledgements section. The author is fully responsible for the accuracy of any information provided by the tool and for correctly referencing any supporting work on which that information depends. Tools that are used to improve spelling, grammar, and general editing are not included in the scope of these guidelines. The final decision about whether use of an AIGC tool is appropriate or permissible in the circumstances of a submitted manuscript or a published article lies with the journal's editor or other party responsible for the publication's editorial policy.

2. Article Types Published in *Addiction*

Research Reports

Research reports are expected to contain a quantitative, qualitative, mixed-methods or narrative analysis. When producing a findings manuscript from these studies, we approve of presentation economy and judicious editing. Placing material in an appendix is often a good means of keeping a manuscript within limits; but we recognize that some manuscripts — especially those describing complex methods and findings — need more space.

As a guide on word length (excluding abstract, tables, figures, and references):

- a quantitative short-report should not exceed 2,000 words (with no more than 15 references);
- a quantitative research report from an observational study should generally not exceed 3,500 words unless the authors provide good reason;
- the editors recognise that certain research designs and analyses - including but not limited to randomised controlled trials and other experiments, complex observational follow-up cohort studies, and qualitative and mixed-methods evaluations - need more space to clearly describe their methods and procedures, but authors are nonetheless strongly encouraged to not exceed 4,500 without a clear justification set out in a covering letter;

Authors wishing to submit longer reports should contact the Editor-in-Chief to discuss.

Below is our specific guidance on the various types of research report we publish:

Randomized Studies

Addiction accepts submissions under three categories of randomized controlled trials: **Full RC Trial, RC feasibility/pilot trial, RC experimental study**.

For all 3 categories, the study should have been registered with details available online and a **CONSORT checklist and participant flow diagram** should be included in the submission. Also, the main body of the article should contain a full description of the randomization and sample size calculations. The three types of study are distinguished primarily by the type and number of primary outcomes.

For a **full RCT**, there should be a single primary outcome measured at a single time point or over a single time interval which has a direct harm or benefit implication for the individual. The exception to this CONSORT requirement of a single primary is when the goal of the intervention is to affect clinical outcomes in two distinct and contrasting domains (e.g. drinking behaviour and re-offending), in which case the two primaries should be referred to as "co-primaries". It should be noted that the primary outcome is a statistical comparison variable (e.g. drinks per day, stopped smoking), which comes from, or is derived from, a possibly broader clinical outcome (e.g. drinking or smoking behaviour throughout the course of the study).

In the case of a full RCT, all the requirements of the CONSORT guideline (and its relevant extensions) should be met, as abbreviated in the **CONSORT checklist** (2010/2016) and the detailed guidance notes by Moher et. al. BMJ 2010; 340 : c869 doi: 10.1136/bmj.c869. Reports on full RCTs must concern a registered study, usually with a **published protocol,** including a statistical analysis plan. There are several international and regional registries including gov and ISRCTN. The front page of the manuscript should specify the trial registration number, the date of registration and when this was done. This should also be shown in the method section along with a link to the registry location if possible. Usually, the trial is registered before enrolment of the first participant. All major amendments to the protocol must be described that have a bearing on the analysis.

Descriptions of behavioural interventions should use the **TIDieR** checklist. To assist review and for later reproducibility, reports should include a link to a protocol or other materials, or submit supplementary material for the article's on-line appendix.

For an internal or external **RCT feasibility/pilot trial**, there is no restriction (within reason) on the number of primary outcomes, although at least one of these should be a measure which strongly relates to feasibility (e.g. acceptance of intervention, follow-up rates etc.) independently of the clinical outcomes, and is informs progression to the full trial. At least one of these co-primary outcomes should be based on a clinical measure which has a direct harm implication and is potentially the single primary comparison outcome in a full RCT. A specific pilot/feasibility trials **CONSORT**

checklist should be submitted (2010/2016) following the guidance notes by Eldrige et.al. BMJ 2016; 355: i5239 doi:10.1136/bmj i5239.

For a **RC experimental studies** there is also no restriction (within reason, say 4) on the number of primary outcomes. None of these will have a primary harm implication for the individual, such as substance-taking behaviour. A full **CONSORT checklist** should be submitted (rather than the pilot/feasibility checklist)

The title of the report should reflect which type of randomized study the report falls into (e.g. : A randomized controlled trial, : A randomized feasibility trial, : A randomized experimental study). The journal prefers authors to start their title with the topic under study, followed by ":" and the type of randomized study, as described above. In cases where authors have placed their report in one category, although in the opinion of the journal editors it does not meet the Journal requirements set out above for that category, they will be asked to change the category and/or revise the number or classification (primary/secondary) of the outcomes.

Reports on randomized studies should use the **appropriate CONSORT checklist** (e.g. for pilot and feasibility trials; pragmatic trials; non-pharmacologic treatment interventions; multi-arm parallel group randomized trials; cluster randomized controlled trials, and adaptive designs). All items specified on the CONSORT checklist should be included in the main text of the report, even if they have previously been included in a protocol or registration document. It is not sufficient to simply reference such documents on the CONSORT checklist. The checklist should be submitted with the report to aid reviewers.

Observational studies should be reported following the STROBE or TREND guideline.

Qualitative studies should be reported following an appropriate guideline (e.g. COREQ, SRQR, RATS, and CASP). Our guidance on qualitative studies can be found here and here.

Economic evaluations should use the CHEERS guideline.

Diagnostic accuracy evaluations of instruments and measures should use the STARD

Effect mediation analyses should be reported using the AGReMA Statement.

Please note that authors must complete the appropriate guideline checklist and submit this alongside the manuscript. Reviewers will use this to check compliance.

Pre-registration of analysis plans

Addiction encourages pre-registration of the analysis plans for the analysis of data and requires that all manuscripts report whether or not pre-registration was conducted.

A pre-registered statistical or health economic analysis plan presents a detailed description of the research aims and hypotheses, along with a detailed description of

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Monographs should be structured as research reports or reviews as appropriate.

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References:

1. The SPIRIT statement
2. The CONSORT statement
3. Moher et. al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869 doi: 10.1136/bmj.c869

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