UNIVERSITAT DE BARCELONA

# Perfiles clínicos en las adicciones comportamentales en mujeres y pacientes con patología dual

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Memoria de tesis doctoral presentada por


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Para optar al grado de Doctora por la Universitat de Barcelona


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Que **MILAGROS LIZBETH LARA HUALLIPE** ha realizado la Tesis Doctoral que lleva por título *"**PERFILES CLÍNICOS EN LAS ADICCIONES COMPORTAMENTALES EN MUJERES Y PACIENTES CON PATOLOGÍA DUAL"*** que está en condiciones para ser defendida para la obtención del Grado de Doctora por la Universidad de Barcelona frente al correspondiente Tribunal.

Que se han cumplido los códigos étidos y de buenas prácticas.

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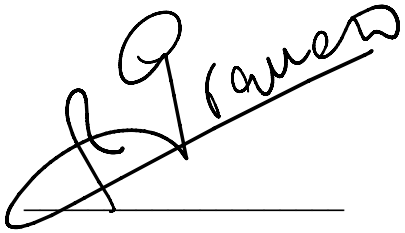

*Firma Directoras:* Susana Jiménez Murcia Roser Granero Pérez

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*A Dios, mis padres y hermana, que son lo más importante en mi vida.*

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# Índice

**Abreviaturas:**

| | |
|---|---|
| APA | "American Psychiatric Association" |
| CC | Compra compulsiva |
| DSM | "Diagnostic and Statistic Manual of Mental Disorders" |
| TCC | Terapia cognitivo conductual |
| TJ | Trastorno de juego |

# Enumeración de los artículos

Tesis en formato de compendio de artículos.

La tesis consta de siete objetivos y cuatro artículos publicados.

Los cuatro artículos están publicados en revistas indexadas en el *Journal Citation Reports (JCR),* y ocupan posiciones dentro del rango Q1 y Q2.

A continuación, se citan los artículos, junto al orden en el cual serán referidos a lo largo de este documento:

Artículo 1: **Lara-Huallipe ML,** Granero R, Fernández-Aranda F, Gómez-Peña M, Moragas L, del Pino-Gutierrez A, Valenciano-Mendoza E, Mora-Maltas B, Baenas I, Etxandi M, Menchón JM, Jiménez-Murcia S. Clustering treatment outcomes in women with gambling disorder, J. Gambl. Stud. 2022; 38(4): 1469-91. doi: 10.1007/s10899-021-10092-5.
*Factor Impacto (JCR 2022, Social Sciences): 2.40*
*Q2 en área de Psicología Multidisciplinar (posición de la revista 72/147)*

Artículo 2: Granero R, Fernández-Aranda F, **Lara-Huallipe ML**, Gómez-Peña M, Moragas L, Baenas I, Müller A, Brand M, Sisquellas C, Jiménez-Murcia S. Latent classes for the treatment outcomes in women with gambling disorder and buying/shopping disorder. J. Clin. Med. 2022; 11, e-3917, doi: 10.3390/jcm11133917.
*Factor Impacto (JCR 2022, Sciences): 3.90*
*Q2 en área de Medicina-General/Interna (posición de la revista 58/167)*

Artículo 3: Granero R, Fernández-Aranda F, del Pino-Gutierrez A, Etxandi M, Baenas I, Gómez-Peña M, Moragas L, Valenciano-Mendoza E, Mora-Maltas B, Valero-Solís S, Codina E, Guillén-Guzmán E, **Lara-Huallipe ML**, Caravaca E, Mestre-Bach G, Menchón JM, Jiménez-Murcia S. The prevalence and features of schizophrenia among individuals with gambling disorder. J. Psychiatr. Res. 2021; 136, 374-83. doi: 10.1016/j.jpsychires.2021.02.025.
*Clave: Artículo. Factor Impacto (JCR 2021, Social Sciences): 5.250*
*Q2 en área de Psiquiatría (posición de la revista 54/155)*

Artículo 4: Granero R, Fernández-Aranda F, Demetrovics Z, **Lara-Huallipe M**, Morón-Fernández A, Jiménez-Murcia S. Network analysis of the structure of the core symptoms and clinical correlates in comorbid schizophrenia and gambling disorder. 2022; Int. J. Ment. Health Addict. doi: 10.1007/s11469-022-00983-y.
*Factor Impacto (JCR 2022, Sciences and Social Sciences): 8.00*
*Q1 en área Psychiatry (posición de la revista 12/144 Social Sciences)*

# Resumen


**Introducción**

El término adicción hace referencia a alteraciones en los procesos relacionados con la toma de decisiones y el control inhibitorio, que conllevan que los sujetos realicen determinadas conductas de forma recurrente y generan dependencia, a pesar de las graves consecuencias que pueden representar para sí mismo y/o para los demás. Las adicciones a sustancias son las más conocidas por la población general, pero existen otras situaciones en las que el sujeto es incapaz de detener-controlar la realización de ciertas conductas en ausencia de sustancias químicas. Son las denominadas adicciones comportamentales.

Existen diferentes formas de adicción comportamental, como el juego de azar (o apuesta), las compras, el sexo, los videojuegos, y las nuevas tecnologías. De todas ellas, el DSM-5 ha incluido al Trastorno de Juego (TJ) como una condición clínica en la categoría denominada "Trastornos relacionados con sustancias y trastornos adictivos", y esto ha supuesto un cambio relevante respecto a las versiones previas de este manual, que lo consideraba como un trastorno relacionado con la falta de control de impulsos. La justificación para esta reubicación son los numerosos estudios empíricos que evidencian las similitudes entre el TJ y las adicciones a sustancias en la psiconeurológía del sistema de recompensa y refuerzo, así como también en las semejanzas en los endofenotipos y los aspectos relacionados con la respuesta terapéutica.

Existen numerosas variables que se relacionan con el inicio y la progresión de las adicciones comportamentales. Por ejemplo, el género, que se asocia con aspectos tan relevantes como el tipo de adicción. Así, el TJ es más prevalente en los hombres, quienes también suelen iniciar este trastorno a edades más tempranas. Las mujeres presentan una mayor prevalencia de trastornos como la compra compulsiva (CC), suelen iniciar estos problemas a edades más tardías, pero requieren menos tiempo entre el inicio de los comportamientos adictivos y el desarrollo de los síntomas a nivel clínico (esto es lo que se denomina efecto telescópico). Por todo ello, las mujeres se consideran actualmente un grupo de alta vulnerabilidad para la presencia de las adicciones comportamentales y, sin embargo, son un colectivo escasamente estudiado.

La comorbilidad es también un factor estrechamente vinculado a las adicciones, ya que se considera tanto un factor predisponente como una consecuencia grave del curso de estas complejas condiciones clínicas (muchos pacientes con adicción comportamental presentan síntomas de depresión, ansiedad, poli-consumo de sustancias, trastornos de personalidad, y otras formas de patología dual). Asimismo, los trastornos mentales severos (TMS) y, más concretamente, la psicosis es uno de los trastornos que se asocia a las adicciones comportamentales, y en concreto al TJ. La concurrencia de esquizofrenia y TJ se considera una patología dual grave, y los pacientes que la presentan forman también un grupo de alta vulnerabilidad.

Esta tesis se plantea como un proyecto empírico para el estudio de los mecanismos implicados en las adicciones comportamentales en mujeres (en concreto con problemas asociados al TJ y la CC), y en pacientes con patología dual (TJ con esquizofrenia). Se analizan aspectos del perfil clínico de sujetos que solicitan ayuda terapéutica debido a los problemas relacionados con las conductas de juego, y también los resultados que se obtienen con terapia cognitivo-conductual (TCC). El proyecto de tesis se presenta como compendio de cuatro trabajos empíricos publicados en revistas indexadas en el Journal Citation Reports.

**Hipótesis - objetivos**

El primero de los artículos que forma parte de esta tesis explora los perfiles de mujeres que solicitan tratamiento para el TJ, en función de un conjunto de indicadores que incluyen características sociodemográficas, rasgos de personalidad, estado clínico en el momento de la consulta y los resultados de la terapia cognitivo-conductual. El segundo artículo explora la existencia de clases empírcas latentes de mujeres con TJ y CC, en base a su evolución durante la intervención, y también identifica predictores de las diferentes trayectorias evolutivas en función de los perfiles sociodemográficos y clínicos en la línea base. El tercer estudio estima la prevalencia del diagnóstico dual (TJ con esquizofrenia) y las diferencias en los perfiles de pacientes con TJ con y sin concurrencia de esquizofrenia. El cuarto estudio utiliza metodología de redes para identificar los nodos con mayor centralidad en pacientes con patología dual, incluyendo síntomas específicos del TJ (criterios DSM-5), medidas de deterioro relacionadas con el TJ (deudas y actos ilegales), síntomas específicos de psicosis (ideación psicótica y paranoide), malestar psicopatológico global, uso de sustancias y perfil de personalidad.

**Métodos**

Los participantes que se incluyen en los diferentes estudios empíricos de esta tesis son pacientes que han acudido a la Unidad de Juego Patológico y Otras Adicciones Comportamentales del Hospital Universitario de Bellvitge. La elección de los sujetos se ha basado en el cumplimiento de los criterios de inclusión/exclusión de cada estudio/artículo.

**Resultados principales**

Los resultados de los estudios que se incluyen en esta tesis doctoral han evidenciado la existencia de tres perfiles de mujeres con TJ: a) el primero está caracterizado por niveles medios de gravedad de sintomatología del juego de apuesta y mejor funcionamiento psicopatológico; b) el segundo por niveles menores de gravedad de síntomas en el TJ y puntuaciones medias de funcionamiento psicopatológico; y c) el tercero por mayor gravedad y peor estado psicopatológico. Estos resultados evidencian la heterogeneidad que existe en el grupo de mujeres que solicitan tratamiento por TJ.

Cuando se realiza un estudio de clasificación entre mujeres con TJ y problemas de CC, se identifican cuatro perfiles asociados a la progresión de la sintomatología adictiva durante la intervención con TCC. Estas trayectorias se diferencian en función del tipo de respuesta, y más concretamente por la inclusión de pacientes con alta versus baja probabilidad de abandono y/o recaída.

En los estudios con pacientes que presentan patología dual de TJ con esquizofrenia, se observó que esta compleja condición clínica se asocia a género masculino, estado civil soltero, menor nivel educativo, situación laboral inactiva, desventaja económica, menor edad cronológica, inicio más temprano de los problemas de juego, peor estado psicopatológico global y perfil de personalidad más disfuncional. Además, el análisis de redes evidencia que los nodos con mayor impacto en la estructura subyacente fueron dos rasgos de personalidad: búsqueda de novedad y autotrascendencia. Este análisis también permitió identificar cuatro agrupaciones modulares de nodos, cada una de las cuales incluye información relevante sobre diferentes dominios de funcionalidad.

## Conclusiones

Los trabajos que se presentan en esta tesis aportan evidencia que resultará de ayuda a la hora de conocer con mayor precisión los perfiles sociodemográficos y clínicos de grupos, que son considerados de alta vulnerabilidad en el ámbito de las adicciones comportamentales (las mujeres y las patologías duales). También se identifican trayectorias evolutivas de respuesta al tratamiento, así como las variables que mejor discriminan los distintos grupos. En conjunto, los trabajos que se incluyen en esta tesis aportan evidencias empíricas relevantes para diseñar instrumentos de evaluación que resulten más precisos (con mayor sensibilidad y especificidad), tratamientos más individualizados, que den respuesta a las necesidades específicas de cada paciente, así como planes de prevención más eficaces,

## Palabras clave

Trastorno de Juego, compra compulsiva, patología dual, mujeres, esquizofrenia, terapia cognitivo-conductual.

# 1. Introducción

## 1.1 Adicciones comportamentales: conceptualización

Cuando un comportamiento que puede formar parte de nuestro día a día se repite de forma reiterada se convierte en un hábito. Pero cuando dicha conducta domina la vida del individuo y éste es incapaz de controlarla o abandonarla, a pesar de los daños que le genera, la conducta se transforma en una adicción. La cuestión básica que diferencia un hábito de una adicción es la imposibilidad de la persona para resistir el impulso de realizar un acto que es definido como gratificante (al menos a corto plazo), a pesar del daño que le pueda ocasionar (a nivel personal y también a nivel contextual-social) (1). De alguna forma, la persona muestra una acusada compulsión por realizar una conducta que le genera recompensa. Los estudios neurobiológicos sugieren que cuando se recibe una recompensa, existe el riesgo de que el cerebro vulnerable quede atrapado en una compulsión (2).

Clásicamente, el término adicción se ha referido básicamente al abuso y la dependencia de sustancias. En la actualidad, este término se ha ampliado, y se refiere a comportamientos que pueden presentarse en ausencia de sustancia (2). Hoy en día se utiliza el término de adicciones comportamentales al referirse a la incapacidad del individuo para resistir los impulsos por realizar una conducta concreta, la cual se practica en exceso y acaba generando problemas y deterioro en la vida del individuo. Este patrón comportamental suele acabar afectando de forma importante las relaciones personales (con pareja, hijos, familiares, amigos), la vida laboral (o educativa), y en definitiva todas las áreas de funcionamiento del individuo (3).

Múltiples estudios evidencian que las adicciones comportamentales y las que cursan con sustancia/s presentan similitudes fenomenológicas. Por ejemplo, un estado de urgencia o anhelo antes de iniciar el comportamiento y una rápida disminución de estados emocionales negativos (como ansiedad o depresión), al realizar la conducta (4). Se ha observado que las adicciones conductuales presentan una alta comorbilidad con adicciones asociadas al uso de sustancias, aunque se desconoce el sentido causal de la relación (4). También se han identificado altas prevalencias de concurrencia entre las adicciones comportamentales y condiciones psiquiátricas como la depresión mayor, el trastorno bipolar, el trastorno obsesivo compulsivo y el trastorno por déficit de atención

con hiperactividad (4). Estudios de corte longitudinales sugieren que los síntomas asociados a estas condiciones psicopatológicas podrían actuar como factores predisponentes para el inicio de las conductas adictivas, particularmente los trastornos adaptativos, del estado de ánimo (5) y los trastornos de ansiedad (6). Pero también se han identificado otras variables predisponentes, como las dificultades en el empleo de estrategias de adaptación (7) y la acumulación de experiencias vitales estresantes (8) (9).

Las adicciones comportamentales pueden presentarse de varias formas. Son las más frecuentes el trastorno de juego (TJ), la compra compulsiva (CC), la adicción al sexo y el uso excesivo de los videojuegos (10). La mayoría de estas adicciones han aumentado, durante los últimos años, como consecuencia del avance de las nuevas tecnologías (11,12) y de Internet. En este sentido, la accesibilidad a diferentes formas de juego, plataformas de compra, contenidos pornográfico-sexuales, videojuegos y múltiples redes sociales, han supuesto un alto riesgo para que determinadas personas con vulnerabilidad acaben presentando y/o empeorando comportamientos adictivos (13). Situaciones de excepción, como la vivida recientemente por la crisis sanitaria originada por el virus COVID-19, han contribuido a que muchas personas hayan visto modificado su estilo de vida, incluyendo mayor distanciamiento social, confinamiento, agravamiento de problemas psicológicos y dificultades económicas. Factores, todos ellos, que también han contribuido de forma significativa al incremento de la prevalencia de las diferentes formas de adicciones comportamentales (14–16).

En la última versión del Manual Diagnóstico y Estadístico de los Trastornos Mentales (DSM-5) se incluyó la nueva categoría diagnóstica denominada “Trastornos adictivos y relacionados con sustancias”, que agrupó el TJ en el mismo nivel que las adicciones a sustancias. La justificación de esta agrupación fue la evidencia acumulada respecto a la similitud en variables neuropsicológicas, clínicas y endofenotípicas. Sin embargo, se consideró que no existían suficientes estudios concluyentes para reconocer, en esta nueva categoría del DSM-5, otras adicciones comportamentales como la compra compulsiva o la adicción al sexo, que han quedado a la espera de la publicación de más investigaciones, especialmente a nivel etiológico (17). En cambio, la versión más reciente de la Clasificación Internacional de Enfermedades (el CIE-11) presenta una categoría etiquetada como “trastornos debidos a comportamientos adictivos”, que agrupa el trastorno de juego por apuestas, junto al trastorno por uso de videojuegos y otros trastornos especificados debidos a comportamientos adictivos(18).

Separadamente, la CIE-11 incluye otra agrupación que bajo el titulo de "Trastorno del control de los impulsos" incluye condiciones como la piromanía, la cleptomanía, el trastonor por comportamiento sexual compulsivo, el trastorno explosivo intermitente y otros trastornos especificados del control de los impulsos.

En cuanto a la edad de inicio de las adicciones comportamentales, se sabe que pueden aparecer en cualquier momento del ciclo evolutivo. Existen, sin embargo, edades con mayor vulnerabilidad o riesgo, como la adolescencia y la adultez temprana (específicamente para el TJ y el uso excesivo de videojuegos), pero también en la etapa de la vejez (10,17). Acerca del sexo, los estudios epidemiológicos han mostrado que todas las formas de adicción comportamental se presentan tanto en hombres como en mujeres, aunque el riesgo es diferente en función de cada conducta concreta. Por ejemplo, el TJ es más frecuente en hombres, mientras que la CC es más prevalente en mujeres (10,19).

### 1.1.1 Trastorno de juego: definición, epidemiología y factores de riesgo

Una de las adicciones comportamentales que actualmente se observan con más frecuencia, en población general y en contextos clínicos, es la que se deriva de la actividad del juego de azar (o juego de apuesta). El juego de apuesta es una actividad de ocio que se practica en compañía o en solitario. Es importante destacar que la mayoría de las personas que practican el juego de apuesta lo hacen de una manera social y lúdica, sin padecer consecuencias negativas derivadas de esta actividad. Sin embargo, algunas personas presentan perfiles de juego intenso caracterizados por las dificultades de control de dicha conducta, a pesar de las (múltiples) consecuencias negativas que les puede acarrear en su vida diaria (20). Asimismo, en algunos países existen juegos de apuesta con alta aceptación y arraigo social. Por ejemplo, las loterías en España o las apuestas de caballos en Gran Bretaña o en Australia.

La Asociación Americana de Psiquiatría (2013), define el TJ como un patrón desadaptativo persistente y recurrente de la conducta de juego asociado a un deterioro del funcionamiento en las esferas personal, social y laboral de la vida (21). Aunque, el TJ no implica solo deterioro en estos ámbitos, sino también tiene un impacto significativo en el estado psicopatológico de la persona (22), que en algunos casos incluso conduce a comportamientos de tipo autolesivo o de conducta suicida (23,24,20).

**Tabla 1** Criterios diagnósticos del DSM-5 para el TJ

**A.** Juego patológico problemático persistente y recurrente, que provoca un deterioro o malestar clínicamente significativo y se manifiesta porque el individuo presenta **cuatro (o más)** de los siguientes criterios durante **un período de 12 meses**:

1. Necesidad de apostar cantidades de dinero cada vez mayores para conseguir la excitación deseada.
2. Está nervioso o irritado cuando intenta reducir o abandonar el juego.
3. Ha hecho esfuerzos repetidos para controlar, reducir o abandonar el juego, siempre sin éxito.
4. A menudo tiene la mente ocupada en las apuestas (p.ej. reviviendo continuamente con la imaginación experiencias de apuestas pasadas, condicionando o planificando su próxima apuesta, pensando en formas de conseguir dinero para apostar).
5. A menudo apuesta cuando siente desasosiego (p.ej. desamparo, culpabilidad, ansiedad, depresión).
6. Después de perder dinero en las apuestas, suele volver otro día para intentar ganar ("recuperar las pérdidas).
7. Miente para ocultar su grado de implicación en el juego.
8. Ha puesto en peligro o ha perdido una relación importante, un empleo o una carrera académica o profesional a causa del juego.
9. Cuenta con los demás para que le den dinero para aliviar su situación financiera desesperada provocada por el juego.

**B.** Su comportamiento ante el juego no se explica mejor por un episodio maníaco.

*Especificar si:*

- **Episódico:** Cumple los criterios diagnósticos en más de una ocasión, si bien los síntomas se apaciguan durante varios meses por lo menos entre períodos de juego patológico.
- **Persistente:** Experimenta síntomas continuamente, cumple los criterios diagnósticos durante varios años.

*Especificar si:*

- **En remisión inicial:** Tras haber cumplido previamente todos los criterios del trastorno, no ha cumplido ninguno de ellos durante un mínimo de 3 meses, pero sin llegar a 12 meses.
- **En remisión continuada:** Tras haber cumplido previamente todos los criterios del trastorno, no ha cumplido ninguno de ellos durante un periodo de 12 meses o más.

*Especificar la gravedad actual:*

- **Leve:** Cumple 4-5 criterios.
- **Moderado:** Cumple 6-7 criterios.
- **Grave:** Cumple 8-9 criterios.

El TJ es la única adicción comportamental que el DSM-5 reconoce, debido a que existe evidencia empírica que muestra similitudes en la fenomenología y en la biología con los trastornos por uso de sustancias (17). La Tabla 1 lista los criterios diagnósticos que esta taxonomía DSM-5 define para esta condición clínica. Además de un mínimo de 4 síntomas-criterios, se exige una duración mínima de 12 meses. La taxonomía, aunque de carácter básicamente categorial, facilita una clasificación de la gravedad del TJ en base al número de síntomas: leve (presencia de 4 a 5 criterios), moderado (presencia de 6 a 7 criterios) o grave (presencia de 8 a 9 criterios). Una característica de la versión última del DSM es que ha excluido como criterio la presencia de conductas ilegales, que

se cometerían con la finalidad de financiar el juego de apuesta (aunque se sabe que este comportamiento está presente entre un 30% y un 40% de los casos) (21).

Los estudios epidemiológicos estiman que la prevalencia del Trastorno de juego entre la población general en los países desarrollados está cercana al 1% y la prevalencia del comportamiento de juego problemático es próximo al 7% (25). Se ha observado que el TJ coexiste con una variedad de trastornos de salud mental, como el uso de sustancias, trastornos de la personalidad, trastornos de ansiedad y del estado de ánimo, y trastornos psicóticos, siendo los trastornos por uso de sustancias los más frecuentes (26). Además, en un estudio se encontró que próximo al 45% de los jugadores que buscan tratamiento en su muestra presentan comorbilidad con alguna otra adicción conductual, como adicción al trabajo, ejercicio, atracones de comida, sexo o CC (27).

La preferencia de juego es también un indicador asociado a diferentes correlatos clínicos y sociodemográficos. En general, es habitual diferenciar entre: a) juegos de azar no estratégicos, que se caracterizan por el hecho de que la persona no puede influir en el resultado final (que depende al 100% del azar, como loterías, ciertas máquinas recreativas con premio y bingo); b) juegos de apuesta estratégicos, cuyo resultado puede verse condicionado por el conocimiento o habilidad del jugador (como apuestas deportivas, juegos de cartas, o mercado de valores); y c) mixto (preferencia por ambos tipos, no estratégico y estratégico) (28,29). Las personas también pueden elegir jugar a estos juegos en forma presencial u *online* a través de Internet (30). Algunos factores sociodemográficos se asocian al tipo de juego (preferencia y modalidad). Por ejemplo, las personas más jóvenes, con un mayor nivel educativo, activos laboralmente y con estatus socioeconómico más elevado suelen preferir los juegos estratégicos (28,29,31).

La edad y el sexo son también variables que actúan como factores de riesgo. Por lo general, inician esta conducta a edades tempranas (generalmente en la adolescencia o a inicios de la edad adulta), y la prevalencia es muy superior en hombres (32–34). Además, los hombres suelen comenzar a jugar a una edad más temprana, aunque las mujeres se inician a edad más tardía pero con una evolución del trastorno mucho más rápida (efecto telescópico) (35,36). Se ha encontrado también que los hombres tienden a preferir juegos de apuesta estratégicos, mientras que las mujeres muestran mayor preferencia por juegos no estratégicos (28,37,38).

Existen factores de riesgo destacados, que afectan a la gravedad del TJ como la edad de inicio temprana (32,34), entre otros. Una posible explicación para esta

asociación sería el gran auge de diferentes plataformas que ofrecen juego de apuesta de forma virtual, lo cual hace que sea accesible de forma universal y con pocos elementos de control incluso a edades en las que jugar con dinero no es legal (32). De hecho, el juego en línea se considera un formato particularmente problemático, dada la relativa falta de restricciones sobre cómo y cuándo se puede acceder, su naturaleza solitaria y la amplia variedad de tipos de juego disponibles (39).

Otros factores de riesgo estrechamente vinculados al TJ son el consumo de alcohol u otras drogas ilegales (36) y un patrón de personalidad caracterizado por altos niveles de impulsividad (40), así como otras variables individuales que incluyen las conductas antisociales, depresión, número de actividades de juego diferentes, sucesos estresantes vividos, dificultades en las relaciones interpersonales (como comportamientos antisociales) e historia personal (bajo rendimiento académico, o estilos educativos de los padres) (41).

Actualmente han aparecido un número importante de trabajos que valoran el impacto de la pandemia por el Covid-19 en los hábitos de juego. Se ha comprobado que el confinamiento ocasionado como consecuencia de la situación sociosanitaria acontecida, el distanciamiento social, el cierre de locales de juego y las cancelaciones en los deporte han contribuido a la disminución del juego de forma presencial, pero también han incrementado el juego *online* (42–44).

### 1.1.2 Compra compulsiva: definición, epidemiología y factores de riesgo

Comprar es una actividad normal y necesaria que todas las personas realizan en las sociedades industrializadas, ya sea para adquirir productos de primera necesidad, como otro tipo de objetos. Para la mayoría de personas esta actividad no representa riesgo alguno, pero en ocasiones puede acompañarse de problemas y convertirse en una adicción. Es la denominada compra compulsiva (CC). Se trata de una condición clínica que todavía no está reconocida en las taxonomías de referencia en investigación y clínica, como el DSM-5 o la CIE-11 (bajo el argumento de no se dispone de suficiente evidencia empírica ) (17).

La CC es una adicción conductual caracterizada por una intensa preocupación por comprar y poseer bienes de consumo que no son estrictamente necesarios (las personas compran más productos de los que pueden pagar, y estos productos no los usan ni necesitan con frecuencia), lo que genera consecuencias adversas en la vida de las personas (45,46). Entre las consecuencias negativas habitualmente se incluyen los

problemas financieros (y en ocasiones legales), comorbilidades psiquiátricas (como la depresión y la ansiedad, o el consumo de sustancias), así como una extensa serie de conflictos interpersonales (47). Para las personas con CC los episodios de compra van acompañados de alivio y placer al realizar la conducta de adquirir los productos, pero seguidos de remordimiento y culpa por lo inapropiado del comportamiento (y muchas veces también por el gasto que realizan). Suelen acumularse numerosos artículos que no son utilizados, ya que estas personas están principalmente interesadas en el proceso de compra, pero no en el uso específico de los bienes adquiridos. Además, para muchos de estos pacientes con CC, ir de compras es una vía para mejorar sentimientos de baja autoestima y estados de ánimo negativos. Actualmente, muchos pacientes prefieren comprar por Internet (a veces atraídos por el ingente número de anuncios publicitarios y la facilidad de realizar las compras desde el propio domicilio), y otros prefieren acudir a centros comerciales (muchas veces, también prefieren los grandes comercios) (48). A modo de tentativa, se dispone de diferentes intentos de clasificación de esta condición clínica. Por ejemplo, la Tabla 2 lista los criterios para CC publicada recientemente y elaborada a partir de la consulta con un amplio grupo de expertos (proyecto Delphi) (49).

La prevalencia de la CC se ha estimado dentro de un amplio rango, entre el 1% y el 8% en países industrializados (este amplio intervalo está relacionado con la gran heterogeneidad de las muestras de estudio y las herramientas de medición), con una estimación puntual media de 5% según un metanálisis (50). Además se ha visto que las comorbilidades más comúnmente asociadas al trastorno de CC son la depresión, los trastornos alimentarios, el trastorno obsesivo compulsivo, los trastornos de ansiedad y el abuso de sustancias (47,51,52). Con respecto a la concurrencia con otros procesos adictivos asociados a alcohol y drogas, los estudios disponibles ha concluido que el impulso abrumador de comprar, la pérdida repetitiva de control sobre el gasto y la incomodidad que tiene la persona cuando no se compra se asemejan a los síntomas de urgencia y abstinencia en las adicciones a sustancias (48).

En cuanto al papel del género y la edad, las investigaciones indican que las mujeres tienen una mayor propensión a la CC que los hombres (53–55), así como que el inicio de los problemas asociados a la CC puede producirse de forma temprana (incluso en la adolescencia tardía y los primeros años de la edad adulta) (45,52,56).

**Tabla 2** Propuesta de criterios diagnósticos para la CC

**A.** Comportamientos y pensamientos disfuncionales y persistentes y/o recurrentes relacionados con la compra, tal como indican las siguientes características:

1. Urgencias y/o impulsos intrusivos y/o irresistibles y/o antojos y/o preocupaciones por comprar/ir de compras, como lo demuestran:
    a. Impulsos repetitivos para comprar
    b. Fuerte deseo o impulso irresistible de participar en actividades de compra
    c. Preocupaciones por ir de compras
    d. Anhelo o alivio mientras se está comprando
    e. Pensamientos intrusivos repetitivos acerca de comprar
2. Control disminuido sobre la compra como lo demuestra:
    a. Comprar muchas más cosas o gastar más de lo necesario o previsto
    b. Comprar muchas más cosas de las que se pueden permitir
    c. Pasar mucho más tiempo comprando de lo previsto
    d. Esfuerzos repetidos sin éxito para reducir o controlar las actividades de compras
    e. Esfuerzos repetidos sin éxito para dejar de pensar en comprar/ir de compras
    f. Comprar algo "de improviso"
3. Compra excesiva de artículos sin utilizarlos para los fines previstos.
4. Uso de las compras para regular estados internos, por ejemplo:
    a. Generar o conseguir un estado de ánimo positivo (p. ej., placer, excitación, "subidón" al comprar / ir de compras)
    b. Aliviar el estado de ánimo negativo (p. ej., nerviosismo, tensión, sentimientos y pensamientos negativos, incomodidad, aburrimiento)
5. Los síntomas persistentes y recurrentes de la compra disfuncional tienen como resultado consecuencias negativas y deterioro en áreas importantes del funcionamiento, por ejemplo:
    a. Deterioro en la vida social (p. ej., discordia familiar, relaciones en peligro)
    b. Angustia clínicamente significativa
    c. Sentimientos negativos (p. ej., lástima, culpa, vergüenza, arrepentimiento)
    d. Dificultades financieras, incluido el endeudamiento y la quiebra
    e. Perdida de interés o deterioro en otras áreas importantes del funcionamiento, por ejemplo: actividades y pasatiempos cotidianos, responsabilidades diarias
    f. Mentir a otros sobre las compras (p. ej., comprar en secreto, ocultar cosas compradas)
    g. Deterioro en el funcionamiento ocupacional (p. ej., arriesgar oportunidades profesionales)
6. La reducción o cese de las compras excesivas da como resultado
    a. Estados emocionales negativos (p. ej., ansiedad, inquietud, agitación, impaciencia, tristeza, irritabilidad, disforia, incertidumbre, inseguridad, ira, tensión sostenida) y/o
    b. Síntomas cognitivos (p. ej., preocupaciones, rumiación, distracción, constricción cognitiva al ir de compras)

**B.** Mantenimiento o escalada del comportamiento de compra disfuncional a pesar de las consecuencias negativas.

**C.** El patrón de compra no ocurre exclusivamente durante un período de manía/hipomanía.

**D.** El patrón de compra no se explica mejor por síntomas de otro trastorno mental (como la psicosis) o es atribuible a una condición médica (como psicosíndrome orgánico).

*Especificar:* Con o sin acaparamiento excesivo de ítems comprados

Se han identificado varios factores de riesgo que aumentan la posibilidad de que las personas desarrollen CC. Factores sociales como el consumismo, los estímulos de la publicidad, el gran número de centros comerciales (en especial en las grandes urbes), la disponibilidad de dinero en forma de tarjetas de crédito (48), los nuevos medios de compra (por ejemplo, por Internet), o la integración de valores propios del materialismo como signo de éxito y prestigio social (47,56). De hecho, una característica de las personas con CC es que parecen ser más vulnerables a creer que los bienes materiales son la vía principal hacia una identidad aceptable, el éxito y la felicidad (57). Dentro del contexto sociodemográfico, también se ha observado que niveles educativos bajos (58) y menor nivel de ingresos (51) se asocian a mayor gravedad de la CC.

La modalidad en la que las personas compran también es un factor de riesgo, siendo la adquisición a través de plataformas como Internet las que parecen asociarse con mayor intensidad al inicio y progresión de la CC (59). Asimismo, la literatura sobre rasgos de personalidad y la CC sugiere que altas puntuaciones en impulsividad y búsqueda de novedades, así como bajas puntuaciones en autodirección y cooperación constituyen factores de riesgo para este trastorno (60). Experimentar síntomas de ansiedad, depresión, obsesivos-compulsivos, emplear estrategias de afrontamiento de evitación pasiva ante los problemas y la autocrítica, también constituyen factores de riesgo para la CC (55).

## 1.2 Trastorno de juego y compra compulsiva en mujeres

Los estudios científicos evidencian que las adicciones comportamentales presentan similitudes en cuanto a patrones psicosociales y clínicos. En efecto, esto se ha observado cuando se comparan los perfiles de pacientes con problemas relacionados con TJ y CC. Por ejemplo, se han identificado similitudes en ciertos rasgos de personalidad, como elevados niveles de impulsividad y búsqueda de sensaciones. También variables sociodemográficas, como edad de inicio joven. E, incluso, las motivaciones percibidas por los pacientes al comienzo y en la progresión del trastorno, ya que muchos informan de que realizan las conductas adictivas como medio para aliviar sus estados de ánimos negativos. Las comorbilidades que suelen acompañar tanto al TJ como a la CC son similares, destacando la ansiedad y la depresión, además de los trastornos alimentarios y trastornos por uso de sustancias. Otras características comunes que se relacionan con el inicio y la evolución del TJ y el CC son las

dificultades en el uso de estrategias de afrontamiento, patrones de disregulación emocional y sesgos cognitivos en procesos de toma de decisión (especialmente frente a situaciones de riesgo) (61).

El TJ y la CC se presentan tanto en hombres como en mujeres. Características comunes en ambos trastornos son la ocultación relacionada con el uso del dinero, la dificultad en las finanzas personales (y familiares) y la importancia que proporcionan a los valores materialistas (la adquisición de objetos y la ganancia de premios puede valorarse como una vía para satisfacer su propio ego, y las posesiones materiales de artículos y premios para mejorar sus estados de ánimo negativos) (62,63). También es una variable común el inicio temprano de los problemas por juego de apuesta o compras excesivas. Se sospecha que, en comparación con los hombres, las mujeres suelen ocultar con mayor frecuencia estas adicciones, en gran medida por el temor a que la sociedad las juzgue y las estigmatice. En otras ocasiones, las mujeres que solicitan tratamiento por TJ y CC informan que una de las barreras de acudir a consulta era su propia resignación, que las conducía a negar los problemas asociados y minimizar el malestar. Esto hace sospechar, a la comunidad científica (y también clínica), que probablemente tanto el TJ como la CC no se diagnostican hasta que sus consecuencias son percibidas como muy perjudiciales para estas pacientes (a nivel económico, familiar y/o social).

En relación a las similitudes entre TJ y CC en mujeres, existen investigaciones que sugieren que algunos comportamientos adictivos pueden fluctuar durante el ciclo menstrual femenino. Por ejemplo, se ha observado que ciertos comportamientos de juego como la frecuencia/intensidad, el dinero en apuestas y la probabilidad de consumir alcohol mientras se juega, se exacerban durante la fase de la ovulación (64). De entrada, podría pensarse que este patrón podría extrapolarse también a la CC, aunque estos resultados deben tomarse con cautela debido a la escasa evidencia empírica y la falta de consistencia en los resultados de los estudios.

Como característica común, destacar que numerosas investigaciones sobre respuesta al tratamiento obtienen resultados similares de éxito/fracaso para el TJ y la CC, en concreto para las intervenciones como la terapia cognitivo-conductual.

Pero también existen diferencias en los perfiles de TJ y CC cuando se presentan en mujeres. De entrada, cuando se compara con los hombres, la prevalencia de TJ en sexo femenino es muy inferior, y en cambio muy superior la prevalencia de CC (33,53). Se han identificado también diferencias en variables sociodemográficas, como el estado civil y el nivel educativo: la proporción de mujeres solteras o separadas es mayor en CC

(en comparación con el TJ) (65), y además también hay mayor proporción de mujeres con niveles educativos y/o socioeconómicos más elevados que acaban presentando CC (61).

## 1.3 Trastorno de juego en pacientes con patología dual

El término patología dual se utiliza para definir una condición clínica que se da cuando los trastornos mentales se presentan con trastornos adictivos, de manera concurrente a lo largo de la vida de los pacientes (66). Aunque de forma clásica se ha utilizado para denominar la co-ocurrencia de uso o abuso de sustancias con otras patologías psiquiátricas, actualmente se acepta que se trate de cualquier forma de adicción.

Entre las personas diagnosticadas con TJ, una proporción alta cumple con criterios clínicos de otro/s trastorno/s mental/es concurrente/s (67), siendo los más frecuentes: trastorno por déficit de atención con hiperactividad, depresión, trastorno bipolar, trastornos alimentarios, ansiedad social, esquizofrenia, trastorno por uso de sustancias y trastorno de personalidad antisocial. También se consideran los síntomas desde el punto de vista dimensional, destacando que los pacientes con TJ presentan altos niveles de impulsividad y un acusado malestar emocional. Esto puede conducir a situaciones caracterizadas por conductas de autolisis o incluso por conducta suicida (66).

Estudios realizados en poblaciones clínicas han publicado datos de prevalencia más altas del TJ en pacientes psiquiátricos hospitalizados y en personas que reciben tratamiento por trastorno de uso de sustancias (6.9% y 4.3%, respectivamente), lo que se ha interpretado como una evidencia que avala que la condición dual requiere especial atención (68). Asimismo, según un informe de la encuesta Nacional de Comorbilidad (69), en los individuos con TJ, se ha estimado que el 96% tiene uno o más problemas psiquiátricos y el 64% tiene tres o más problemas psiquiátricos.

En relación a lo anterior, se sospecha que en ocasiones el TJ se diagnostica de forma tardía debido a que se presta mayor atención a las otras patologías concurrentes por las que el paciente consulta. Se cree también que algunos profesionales sanitarios podrían no prestar suficiente atención a los problemas relacionados con el juego de apuesta en las primeras consultas que se realizan en centros no especializados, por lo que estas dificultades pueden pasar desapercibidas hasta que tienen consecuencias

graves (70). Esto podría estar pasando cuando las enfermedades comórbidas al TJ se consideran altamente incapacitantes, como la esquizofrenia.

### 1.3.1 Esquizofrenia y trastorno de juego

La esquizofrenia y el TJ son dos condiciones clínicas que, en algunos pacientes, aparecen de forma conjunta. Los informes epidemiológicos sugieren que hasta una de cada cinco personas con esquizofrenia puede experimentar problemas relacionados con el juego de apuesta (71). Los estudios de prevalencia, en muestras de pacientes con psicosis, también han estimado tasas de comorbilidad con juego problemático y con TJ de entre el 12% y el 19% (71,72). Las personas con psicosis parecen tener entre 3 y 4 veces más probabilidades de presentar problemas por juego de apuesta en comparación con la población general (73). Es importante destacar que cuando los síntomas del TJ se presentan de forma conjunta con la psicosis, el perfil clínico de los pacientes es mucho más grave y disfuncional que en formas de psicosis que cusan sin comportamientos de tipo adictivo (67).

Los pacientes con esquizofrenia pueden ser particularmente vulnerables a experimentar problemas de juego de apuesta, porque las alteraciones cognitivas propias de la esquizofrenia pueden dificultar su capacidad de control, afectando a su capacidad para comprender los riesgos asociados con el juego de azar, e interfiriendo en su valoración acerca de las posibles consecuencias negativas de jugar (71). También se ha observado que la gravedad de los síntomas de la esquizofrenia se asocia con una edad más temprana de inicio del TJ, lo que reafirma la potencial relación entre las distorsiones cognitivas y el inicio temprano del juego problemático en individuos con trastornos psicóticos (74).

Aunque son escasos los estudios en pacientes con esquizofrenia con comorbilidad con TJ, se sabe que existe una alta asociación con uso-abuso de sustancias. Esto ha sugerido que, en la esquizofrenia, podrían actuar mecanismos subyacentes que son también comunes en pacientes que desarrollan comportamientos adictivos, como el TJ y/ problemas relacionados con sustancias. Se sospecha que la impulsividad podría ser uno de factores implicados en estos procesos explicativos, y también ser un elemento importante que explique la condición dual de esquizofrenia con TJ (75). Por ejemplo, algunos estudios empíricos han observado que una medida estrechamente relacionada con el concepto de impulsividad, el descuento por demora (“*delay discounting”* en inglés), podría actuar como vínculo mediacional entre los

síntomas de ambos trastornos (76). Se trata de un constructo psicológico que vincula la percepción del tiempo tiempo transcurrido con la recompensa y la toma de decisiones, y se caracteriza por el hecho de que las personas renuncian a una recompensa posterior más grande en favor de una recompensa inmediata más pequeña. Se asocia a rasgos de la personalidad como el autocontrol, la impulsividad y la consideración de las consecuencias futuras en la toma de decisiones. En población general se ha observado que las personas con altos niveles de impulsividad (y por tanto con bajos niveles de autocontrol) poseen valores superiores en tareas de descuento por demora, pero también en pacientes con TJ con esquizofrenia y con trastornos relacionados con el consumo de sustancias. Es interesante la observación de que esta medida de impulsividad asociada a la elección condicionada por la demora en la respuesta podría asociarse a la concurrencia de TJ y esquizofrenia, pero únicamente en pacientes de sexo masculino (75). Estos resultados se deben de tomar con cautela, ya que son escasos los estudios realizados y por tanto la evidencia empírica es limitada.

También se ha observado que algunas variables sociodemográficas relacionadas con la presencia dual de TJ con esquizofrenia son el estado civil (soltería), niveles educativos más bajos, desempleo, y menores índices de posición social (76). En cuanto a los rasgos de personalidad, investigaciones previas han observado que niveles más altos en evitación del daño y puntuaciones más bajas en cooperación, autodirección, dependencia de la recompensa y persistencia son características dentro del espectro esquizofrénico y también en el TJ. Se ha encontrado también que los pacientes con esta patología dual, tienen mayor probabilidad de escoger formas de juego no estratégicas, lo cual se ha relacionado con la tendencia en pacientes psicóticos por lo juegos caracterizados por la poca deliberación o que requieran pocas habilidades (76).

## 1.4 Terapia Cognitivo-Conductual

### 1.4.1 Fundamentos teóricos

La terapia cognitivo conductual (TCC), es una tipo de aproximación centrada en el problema y de duración limitada en el tiempo, que se ha aplicado con éxito a múltiples trastornos como la depresión, los trastornos de ansiedad, los trastornos de personalidad y una variedad de otros problemas. Se fundamenta en la integración de dos variedades separados de abordaje: la terapia cognitiva y la terapia conductual (77). Ambos tipos de intervención se basan en la suposición de que el aprendizaje previo

tiene consecuencias desadaptativas en el presente, y comparten el propósito de reducir la angustia y los comportamientos no deseados, ofreciendo nuevas experiencias de aprendizaje más adaptativas (78). La terapia conductual surgió en las décadas de 1950 y 1960 a partir del interés en aplicar los principios del conductismo para promover un cambio en el comportamiento en humanos. Encuentra su fundamentación teórica en los experimentos originales de Watson y Skinner (77,79). Por otra parte, la terapia racional emotiva es también uno de los principales pilares de las terapias cognitivo-conductuales, que junto con la terapia cognitiva creada por Aaron Beck sirvió de base para el desarrollo de las actuales formas de TCC. En términos globales, la idea de base es considerar las creencias irracionales como elementos centrales de la angustia emocional, lo que conduce a cambiar estos pensamientos por otros que sean de tipo racional y funcional. Este cambio estaría también en el proceso de extinción de los estados emocionales negativos y los comportamientos desadaptativos, y en su sustitución por estados emocionales y comportamientos funcionales y adaptativos (80).

Uno de los artífices de la TCC fue Aaron Beck, considerado uno de los fundadores principales de la terapia cognitiva. En sus estudios desarrolla la idea de que las personas construyen esquemas cognitivos para interpretar la realidad y sostiene que las creencias que se aprenden durante la infancia y la adolescencia tienen un rol central en la forma de percibir el mundo durante la vida adulta. El enfoque de Beck supone que los comportamientos desadaptativos son el resultado de conjuntos de síntomas, sin la necesidad de suponer la existencia de estructuras subyacentes latentes diferenciadas (como sustentas taxonomías como el DSM o la ICD). Esto supone la visión de la terapia cognitiva como una forma de intervención integradora, aplicable a múltiples condiciones clínicas, cuya aplicación se basaba en la aplicación de un conjunto de técnicas como la identificación de pensamientos irracionales, entrenamiento en relajación y entrenamiento en habilidades sociales (77–79).

El objetivo clave de las diferentes formas de TCC empleadas actualmente es ayudar a los pacientes a cambiar su forma de pensar y su forma de actuar. Durante el proceso terapéutico, los sujetos aprenden a identificar y a modificar los sesgos cognitivos que sustentan la conducta problemática, mejorando la regulación emocional. Los cambios en estos patrones de pensamiento y la mejora emocional contribuyen a interrumpir las conductas problemáticas. En los programas de TCC actuales se incluyen múltiples técnicas, como el control de estímulos, el autorreforzamiento, la exposición en vivo con prevención de respuestas, el entrenamiento de habilidades sociales, la

relajación, y las estrategias de prevención de recaídas (favoreciendo que los pacientes realicen otras actividades que también son gratificantes y no dañinas) (61). Cabe destacar que en la actualidad se dispone de un número relativamente alto de procedimientos de intervención basados en la TCC, denominadas de tercera generación. En este grupo se incluyen la terapia cognitiva basada en *mindfulness*, las terapias de aceptación y compromiso, la terapia dialéctico conductual, la psicoterapia analítica funcional, la terapia de activación cunductual, o el neurofeedback (entre otras). El propósito de estos enfoques es modificar la conducta de los pacientes partiendo de un enfoque global y contextual cuyo propósito trasciende en el control de los síntomas disfuncionales para centrarse en una reorientación del horizonte vital en términos de orientación a valores, la flexibilidad psicológica y la activación conductual (81).

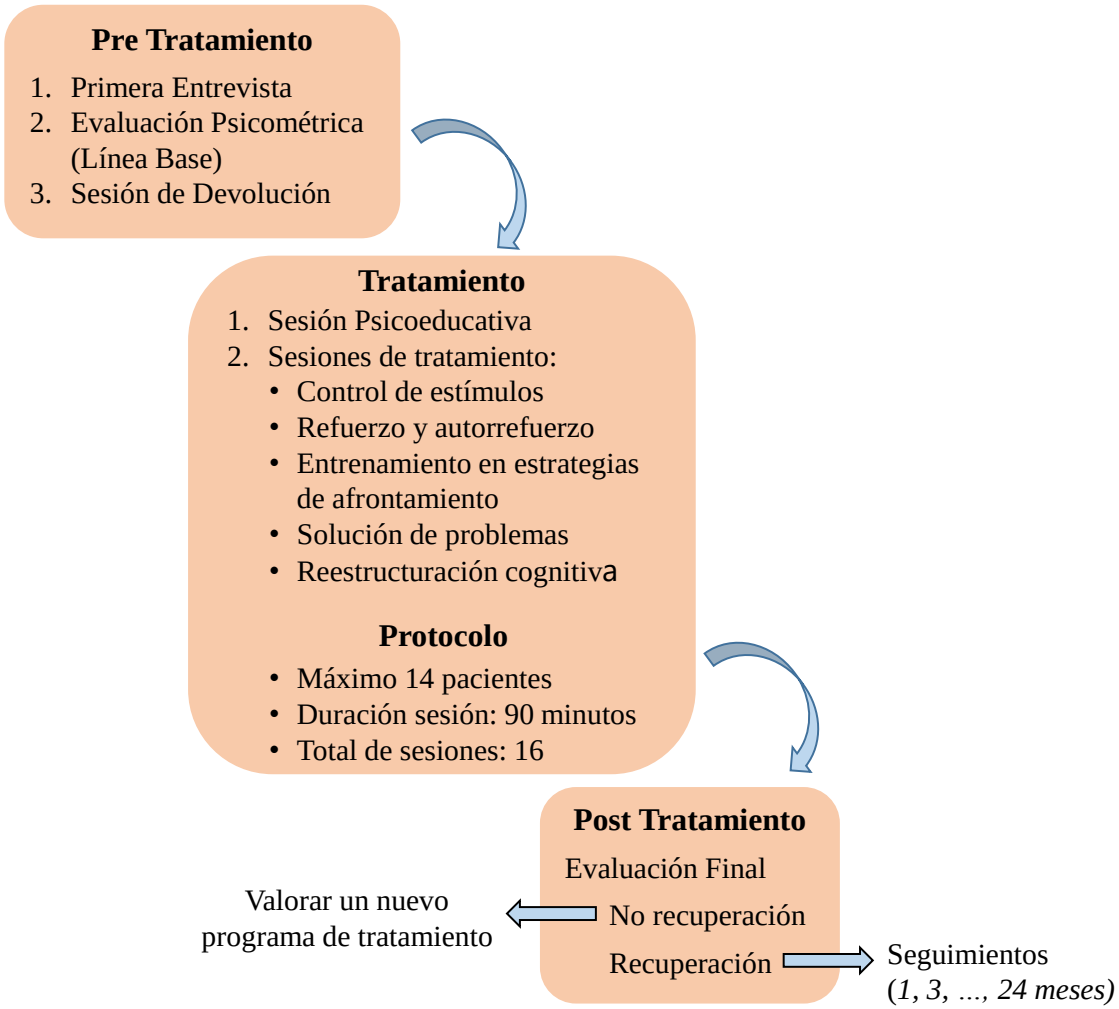
La TCC se ha utilizado con éxito en numerosos problemas mentales, hasta el punto de considerarse como un *"gold standar"* debido a sus prometedores resultados. Actualmente se emplea para el tratamiento de las adicciones, incluidos TJ (82,83), y ha demostrado ser superior a otras terapias para controlar los síntomas específicos asociados al juego de apuestas, reducir el malestar psicológico global de los pacientes y mejorar el funcionamiento general (84). La TCC también logra reducir los sesgos cognitivos y otras conductas relacionadas con el juego de azar (68,85). La mayoría de los estudios demuestran eficacia a corto plazo (en los estudios pre-post intervención) (86), aunque es más limitado el volumen de trabajos que valoran la eficiencia a medio y largo plazo.

Existen diferentes modos en que la TCC se emplea en pacientes con adicción comportamental. Por ejemplo, en forma individual o grupal. La modalidad grupal se ha mostrado efectiva en el tratamiento de pacientes con TJ, ya que logra reducir tanto los síntomas centrales del trastorno como mejora el estado emocional. Además, los resultados positivos se mantienen después de seis meses de seguimiento. En cualquier caso, también se ha observado que las primeras semanas del tratamiento son cruciales para lograr adecuada adherencia terapéutica, siendo los altos niveles de psicopatología predictores del mal resultado (también lo son edades más jóvenes, menor nivel educativo, mayor nivel de impulsividad, y personalidad más disfuncional). (85,87).

### 1.4.1 Descripción del programa de TCC aplicado en este proyecto

Los datos analizados en el presente proyecto se han obtenido de pacientes tratados con un programa de TCC en ámbito ambulatorio, que acudieron a consulta debido a TJ o CC a la Unidad de Juego Patológico y Otras Adicciones Comportamentales del Hospital Universitario de Bellvitge. El protocolo de intervención se ha aplicado en tres fases: a) la fase inicial, con una primera visita con el paciente y la evaluación en la línea base; b) la fase de tratamiento, en modalidad grupal, con 16 sesiones de duración, de 90 minutos cada una; c) fase final, con evaluación de resultados. La Figura 1 ilustra este procedimiento.

**Figura 1.** Esquema del proceso de tratamiento

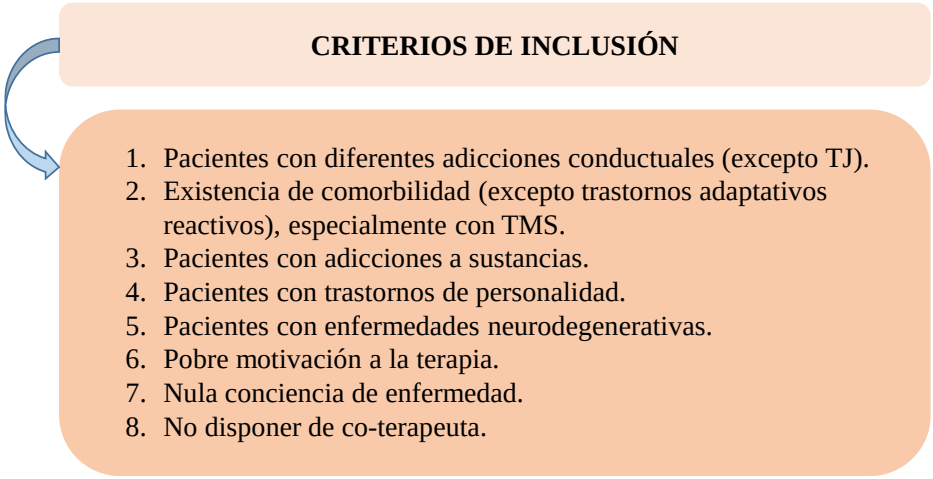


El programa de tratamiento es dirigido por experimentados psicólogos clínicos titulados. El objetivo principal del programa de tratamiento es proporcionar a los pacientes los conocimientos y habilidades necesarios para ejecutar estrategias de TCC con el fin de reducir todos los tipos de conductas de juego y lograr la abstinencia de todos los tipos de juegos de azar. Los temas abordados en el plan de tratamiento incluyeron: psicoeducación sobre el trastorno (p.ej., su curso, factores de vulnerabilidad, criterios de diagnóstico), control de estímulos, prevención de recaídas, entrenamiento en asertividad, restructuración cognitiva y auto refuerzo. Además, como parte esencial del programa de tratamiento se incentiva a los pacientes a llevar un control de dinero (como por ejemplo llevar únicamente la cantidad concreta que se necesita cada día, pedir recibos para cada gasto, anotar todos los gastos realizados en un diario), evitar situaciones de riesgo, cambiar rutas habituales y la autoprohinición de acceso a espacios de juego (como bingo, casinos o sala de juego/apuestas). En el transcurso de las sesiones el terapeuta refuerza la abstinencia lograda y las tareas cumplidas con éxito. Además, se registra la existencia de recaídas, y cuando se producen se analizan sus desencadenantes, se explora el estado anímico y los sentimientos de culpa de los pacientes. Se insiste en la necesidad de lograr la abstinencia total y permanente.

En este programa también se incluye la figura de un co-terapeuta, que generalmente es un miembro de confianza de la familia del paciente (el cónyuge, pareja o padres). Esta figura participa en 7 de las 16 sesiones de tratamiento. Sus funciones son ayudar y apoyar al paciente a gestionar situaciones de riesgo y reforzar los logros alcanzados. Se ha observado que el co-terapeuta; desempeña un papel importante y activo en el tratamiento del TJ, ya que incrementa la probabilidad de mejoras clínicas (reducción del número de síntomas asociados al TJ y mayor funcionalidad), se asocia a mayor adhesión al tratamiento, y disminuye el riesgo de abandono y recaídas durante la intervención de TCC grupal (88).

Finalizado el programa de tratamiento, se realiza un seguimiento a los 1, 3, 6, 12 y 24 meses. Cada seguimiento consiste en una sesión grupal de 90 minutos con los pacientes y sus familiares. Los objetivos de estas sesiones son comprobar y analizar posibles recaídas, gestionar posibles problemas de confianza familiar u otros problemas sugeridos por los pacientes y reforzar a los pacientes para mantener la abstinencia total de cualquier tipo de juego.

**Figura 2.** Criterios de Inclución a la terapia Individual




Este programa de tratamiento está protocolizado y descrito en el documento "*Protocolo de tratamiento cognitivo-conductual para el juego patológico y de otras adicciones no tóxicas"* (89). Ha mostrado efectividad a corto y medio plazo, tal como constatan diferentes estudios previos publicados por el grupo de trabajo de la Unidad de Juego Patológico del Hospital de Bellvitge (87,90,91).

Cabe resaltar que en ocaciones los pacientes son asignados a terapia individual. En estos casos, la estructura del tratamiento es la misma pero los sujetos son atendidos de forma más personalizada. La figura 2 ilustra los criterios de inclusión a esta terapia.

Finalmente, indicar que para este proyecto de tesis la falta de asistencia a tres sesiones consecutivas de TCC fue el criterio que se utilizó para considerar "abandono".

## 1.5 Nuevos enfoques analíticos en investigación psiquiátrica

Múltiples estudios aplican técnicas analíticas para modelos categóricos de la psiquiatría como los actuales DSM-5 o CIE-11. Sin duda, estas taxonomías han contribuido a generar un espacio consensuado para la práctica clínica y la actividad empírica, y poseen un gran valor en el ámbito científico. Se basan en modelos tradicionales de enfermedades médicas, que asumen que los síntomas son indicadores de una causa común (que se conceptualiza como una enfermedad latente subyacente) (92). Bajo este prisma, muchos estudios etiológicos diseñados para identificar factores de riesgo y el patrón de inter-relaciones entre variables han utilizado procedimientos clásicos como el modelo lineal general (que incluye el clásico análisis de la variancia, ANOVA) y los modelos de regresión.

Pero en los últimos años, la psiquiatría está incorporando una nueva conceptualización de los trastornos mentales basada en el estudio de redes, que ha sido ampliamente desarrollada por Denny Borsboom y sus colaboradores. Bajo este nuevo prisma, los trastornos psicopatológicos se conciben como sistemas dinámicos complejos formados por múltiples síntomas y factores que interactúan entre sí. Se trata un enfoque que cuestiona el enfoque categórico, y también el clásico dimensional (93).

Bajo el prisma del análisis de redes, los trastornos mentales aparecen como consecuencia de síntomas que se relacionan en una estructura subyacente, que contribuye tanto al inicio como a la evolución de los diferentes perfiles clínicos. El modelo no supone la existencia de una única estructura latente subyacente que sea la causa común de la covarianza de los síntomas. Esto sugiere que la noción misma de enfermedad mental se vuelve secundaria, ya que los síntomas no son el reflejo de este elemento basal, sino que son una expresión de un perfil endofenotípico (89,90,91).

En el análisis de redes destacan dos elementos primarios: nodos y aristas. Los nodos generalmente se visualizan como círculos y pueden representar cualquier variable imaginable y observable-cuantificable (p. ej., síntomas, pero también personas). Las aristas son líneas que conectan estos nodos y representan la relación que existe entre ellos (95). La estructura y representación de una red se definen a través de varias variables. La densidad indica el nivel de conectividad dentro de la red. La distancia indica el número de enlaces o la distancia entre dos nodos específicos. Otros conceptos importantes incluyen la noción de " *valor* " o la intensidad de la relación y la noción de signo "*señal",* indicando si la relación es positiva o negativa. Por lo general, las correlaciones más fuertes están representadas por conectores (aristas) más gruesos. Otro concepto fundamental es el de "*centralidad",* referido a la cantidad de interconexiones que posee cada nodo en la red (93).

En psicopatología, el análisis de redes suele emplearse con dos objetivos: a) estudiar las relaciones entre los síntomas que contribuyen a la aparición y la evolución de uno o más trastornos psiquiátricos; y b) identificar los síntomas centrales dentro de la estructura de inter-relaciones (94–96)

Las implicaciones de la aplicación de la teoría de redes en el ámbito de la psicopatología son múltiples, aunque pueden destacarse las dos siguientes: 1) ayudan a modelizar estructuras complejas (el modelo supone que los trastornos mentales pueden caracterizarse mejor en términos de la interacción entre diferentes componentes que mediante entidades latentes no observables); y 2) ayudan a conceptualizar y modelar

procesos complejos como la comorbilidad (en la red pueden identificarse síntomas que están más estrechamente conectados que otros y estas agrupaciones pueden interpretarse como la manifestación fenomenológica de condiciones comórbidas que suelen concurrir). Además, en términos etiológicos, la teoría de redes establece que los trastornos mentales pueden concebirse en términos de un proceso de propagación de síntomas causados por la activación de determinados nodos (94). Esto supone que un determinado perfil clínico (clásicamente un trastorno) ocurre siempre que el número requerido de síntomas se activa durante un tiempo suficiente y que la recuperación es consecuencia de la correspondiente desactivación y de la disolución de los conectores (96).

Los análisis de red se han aplicado a diferentes trastornos psiquiátricos como la depresión, ansiedad, abuso de sustancias, autismo, psicosis y personalidad (97). También en pacientes con adicciones conductuales, como el uso excesivo de videojuegos (98), el uso excesivo de telefonía móvil (99), la adicción a la pornografía (100), la esquizofrenia y el TJ (101). Sin embargo, su uso es todavía limitado, requiriéndose de estudios que aporten más conocimiento sobre los procesos subyacentes a las diferentes formas de psicopatología, en especial a las que cursan con cuadros clínicos más graves y complejos. Además, tiene aplicación directa en el ámbito de la intervención, ya que permite identificar síntomas y otros factores que poseen mayor peso (centralidad) en la red.

## 1.6 Justificación de la tesis

Las adicciones comportamentales forman parte de nuestra sociedad, con prevalencias en tendencia (alarmantemente) creciente durante los últimos años. Afectan todos los sectores de la sociedad, y además tienen mayor impacto en grupos de alta vulnerabilidad (como sexo femenino y sujetos otros trastornos mentales graves concurrentes). Es necesario disponer de nueva evidencia empírica sobre los perfiles clínicos de estos sujetos de mayor vulnerabilidad, identificar los factores de riesgo con mayor peso-contribución (ya sean sociodemográficos, psicológicos y biológicos), que permitan desarrollar planes de detección precoz y de intervención que sean más precisos y eficaces.

# 2. Hipótesis

- **1.** Los pacientes con problemas de juego de apuesta forman un grupo mixto muy heterogéneo, en el que es posible identificar subgrupos latentes empíricos que representen diferentes perfiles en términos sociodemográficos y clínicos.
- **2.** En mujeres que son tratadas con TCC debido a TJ o CC es posible identificar diferentes perfiles latentes caracterizados por la progresión de la conducta adictiva.
- **3.** El estado clínico en la línea base (mayor gravedad de la sintomatología propia de la conducta adictiva y de la comorbilidad asociada), así como la situación sociodemográfica (grupos más desfavorecidos) obtendrá capacidad discriminativa de los perfiles latentes identificados en mujeres tratadas debido TJ o CC.
- **4.** La prevalencia de la esquizofrenia en pacientes que consultan por problemas de juego de apuesta será superior a los valores estimados en la población general.
- **5.** Los pacientes con la condición dual de TJ más esquizofrenia presentarán un perfil clínico caracterizado por mayor gravedad de la sintomatología adictiva y de otros correlatos psicopatológicos que los pacientes con TJ sin esquizofrenia.
- **6.** El análisis de redes en pacientes con TJ más esquizofrenia facilitará un diagrama de relaciones complejo en el que será posible identificar diferentes clústeres de nodos (modularidades).
- **7.** Las variables de impulsividad y otros rasgos de personalidad obtendrán valores centrales (relevancia y capacidad de vinculación) en el análisis de redes en pacientes con TJ más esquizofrenia.

# 3. Objetivos

- **1.** Explorar la existencia de clústeres empíricos en una muestra clínica de mujeres que consultan por problemas relacionados con el TJ, a partir de un grupo de indicadores que incluyen factores sociodemográficos, dimensiones de personalidad, estado clínico en la línea base y resultados durante la intervención.
- **2.** Identificar clases latentes en una muestra clínica de mujeres que consultan por problemas relacionados con el TJ o con CC, a partir de la evolución de que presentan durante la TCC.
- **3.** Identificar variables en la línea base con capacidad discriminativa de los perfiles latentes identificados en mujeres tratadas debido a los problemas que les ocasiona el TJ o la CC.
- **4.** Estimar la prevalencia de esquizofrenia en pacientes que acuden a consulta debido a los problemas de la conducta de juego de apuesta.
- **5.** Comparar el perfil sociodemográfico y clínico de los pacientes con la condición dual de TJ más esquizofrenia de los pacientes con TJ sin esquizofrenia.
- **6.** Explorar la estructura de relaciones entre los síntomas centrales del TJ y otros correlatos clínicos en pacientes con la condición dual de TJ más esquizofrenia, mediante análisis de redes.
- **7.** Identificar los nodos centrales y los que poseen mayor capacidad de asociación-vinculación en la red identificada.

# 4. Material, métodos y resultados

## 4.1 Artículo 1

**Objetivo:**
En este artículo se contrasta el primer objetivo de la tesis.

> **1.** Explorar la existencia de clústeres empíricos en una muestra clínica de mujeres que consultan por problemas relacionados con el TJ, a partir de un grupo de indicadores que incluyen factores sociodemográficos, dimensiones de personalidad, estado clínico en la línea base y resultados durante la intervención.

**Título del artículo:**

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**Accesible a través de la URL:**

https://link.springer.com/article/10.1007/s10899-021-10092-5

**Resumen:**

La muestra incluyó 163 pacientes de sexo femenino, con edad dentro del rango 20 a 73 años, consecutivamente atendidas en una unidad de referencia para el tratamiento de adicciones comportamentales. El motivo de consulta fue TJ, recibiendo todas las pacientes tratamiento con TCC.
Se identificaron tres clústeres empíricos, mediante un procedimiento de clasificación bifásico (jerárquico aglomerativo). El clúster C1 incluyó 67 mujeres (41.1% del total de participantes), y se caracterizó por agrupar la mayor proporción de pacientes casadas, laboralmente activas y con los índices de posición social más elevados, niveles de gravedad medios de TJ en la línea base y valores medios más elevados en auto-dirección. Este clúster registró un 0% de abandonos y aproximadamente un 15% de recaídas. El clúster C2 incluyó 63 mujeres (38.7% del total) y se caracterizó por agrupar pacientes con los niveles más bajos de gravedad del TJ inicial, niveles medios de psicopatología en la línea base y alto riesgo de abandono durante la intervención. El clúster 3, con 33 mujeres (20.2% del total), incluyó pacientes con los niveles más graves de adicción en la línea base, mayor psicopatología global comórbida, menor nivel de auto-dirección y mayor nivel de evitación del daño. El C3 se caracterizó también por el mayor riesgo de recaída.
Los resultados aportan evidencia sobre la heterogeneidad del perfil sociodemográfico y clínico de las mujeres que acuden a solicitar tratamiento por problemas asociados al juego de apuesta. Los distintos perfiles que se registran en la línea base poseen impacto en los resultados de la intervención, concretamente en el riesgo de abandono y recaída.

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ORIGINAL PAPER

# Clustering Treatment Outcomes in Women with Gambling Disorder

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**Abstract**
The rising prevalence of gambling disorder (GD) among women has awakened considerable interest in the study of therapeutic outcomes in females. This study aimed to explore profiles of women seeking treatment for GD based on a set of indicators including sociodemographic features, personality traits, clinical state at baseline, and cognitive behavioral therapy (CBT) outcomes. Two-step clustering, an agglomerative hierarchical classification system, was applied to a sample of $n=163$ women of ages ranging from 20 to 73 years-old, consecutively attended to by a clinical unit specialized in the treatment of G. Three mutually exclusive clusters were identified. Cluster C1 ($n=67$, 41.1%) included the highest proportion of married, occupationally active patients within the highest social status index. This cluster was characterized by medium GD severity levels, the best psychopathological functioning, and the highest mean in the self-directedness trait. C1 registered 0% dropouts and only 14.9% relapse. Cluster C2 ($n=63$; 38.7%) was characterized by the lowest GD severity, medium scores for psychopathological measures and a high risk of dropout during CBT. Cluster C3 ($n=33$; 20.2%) registered the highest GD severity, the worst psychopathological state, the lowest self-directedness level and the highest harm-avoidance level, as well as the highest risk of relapse. These results provide new evidence regarding the heterogeneity of women diagnosed with GD and treated with CBT, based on the profile at pre- and post-treatment. Person-centered treatments should include specific strategies aimed at increasing self-esteem, emotional regulation capacities and self-control of GD women.

**Keywords** Clustering · Cognitive behavioral therapy · Gambling disorder · Survival analysis · Women

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## Introduction

The onset and progression of gambling disorder (GD) is characterized by clinically significant impairment in multiple areas of functioning, including psychological, working, social and even financial (Langham et al., 2016; Shannon et al., 2017). Epidemiological studies estimate the prevalence of GD among the general population in developed countries at around 1%, and the prevalence of problematic gambling behavior at around 7% (Calado and Griffiths, 2016). These rates give idea of the potential harms and social costs associated with GD, and highlight the urgent need on strength evidence-based intervention (and prevention) plans. These treatments should deliver precise strategies to patients based on the patients' individual variability.

Sex seems to have been considered a relevant risk factor for the onset and evolution of disordered gambling, and previous studies have obtained ratios of around 1/4 for frequency among females/males (Karlsson and Håkansson, 2018). However, in recent decades, the incidence of GD has risen in all sectors of the population, including women (Gainsbury et al., 2015; Håkansson and Ford, 2019). It is also known that individuals with gambling problems are often not properly diagnosed and/or untreated, even in clinical settings, which may have led to underestimation of the real prevalence of GD (Blanco et al., 2015; Quintero, 2016; Rash et al., 2016). This situation is aggravated among women, who are more reluctant to seek therapeutic help despite the severe negative consequences of GD: some women prioritize treatment for different comorbid conditions over GD (such as depression or anxiety), other women may conceal the symptoms due to the social stigma attached, and other simply accept their addiction as a lifestyle (Babić et al., 2018; Bischof et al., 2014; Braun et al., 2014; Coriale et al., 2015).

Some studies have observed that at the beginning of treatment GD severity is similar among men and women (number of gambling symptoms, level of urgency related to the gambling behavior or cognitive biases associated with gambling expectations) (Grant, Chamberlain, et al., 2012; Grant, Odlaug, et al., 2012; G. Mestre-Bach et al., 2016a, b; Smith et al., 2015). However, remarkably different results have been obtained in other studies, which suggest the existence of distinct profiles in men and women regarding gambling severity (Susana Jiménez-Murcia et al., 2020; Ronzitti, Lutri, et al., 2016; Ronzitti, Soldini, et al., 2016), as well as in other compulsive-related neurocognitive domains (Mallorquí-Bagué et al., 2021), and in the role of the urge to gamble and gambling-related cognitions in the tracking correlations of GD over time (Dunsmuir et al., 2018). Empirical evidence has also showed that patients' sex could modulate the relationships between the multiple variables that can be used to explain gambling severity and the development of the disorder. For example, comorbidity patterns have revealed that GD women report higher levels of depression and anxiety, while GD in men increases the likelihood of substance-related disorders (alcohol and drugs) (Di Nicola et al., 2015; Dion et al., 2015; Dowling et al., 2015; Pilver et al., 2013a,2013b; Ronzitti et al., 2016; Ronzitti, Soldini, et al., 2016; Sundqvist and Rosendahl, 2019; Tackett et al., 2017). It has also been claimed that the association between GD and other comorbid psychiatric conditions is stronger among women than among men (Håkansson et al., 2018; Hartmann and Blaszczynski, 2018), and that previous mental illness is also a stronger risk factor for later onset of problematic gambling among women (Haw and Holdsworth, 2016; Sundqvist and Rosendahl, 2019). The age of onset of GD and its course also evidenced a sex-related profile, characterized by the well-known telescopic effect: women tend to commence gambling activity later in life but progress to gambling-related problems more quickly compared to men (Grant et al.,

2012; Grant, Odlaug, et al., 2012; Slutske et al., 2015). Gambling preferences also seem to be strongly related with sex (Hing et al., 2016a,2016b): women tend to choose games classified as non-strategic (characterized by the subject's inability to exercise any type of control over the outcome of the bet: lotteries, bingo and slot machines, while men present a higher prevalence for strategic games (characterized by gamblers being able to use their knowledge to predict outcomes, such as poker, craps/dice games or sports betting). Finally, a number of other systematic differences have also been reported between the GD pathogenesis of men and women (Fattore et al., 2014; S. Jiménez-Murcia et al., 2014; Smith et al., 2015). For example, it has been claimed that women often use gambling activity mainly as a maladaptive coping strategy to avoid negative mood states, while many other gambling motives have been described as stronger among men [enhancement (playing for pleasure and for increasing positive emotions), avoiding boredom, socializing, excitement, competing with others or even financial reasons (making money through gambling activities)] (Grant, et al., 2012a, 2012b; Hing et al., 2016a,2016b; Mathieu et al., 2020; Moragas et al., 2015). And regarding personality traits, women with GD tend to have lower mean scores for impulsivity and sensation seeking than men (Hodgins and Holub, 2015).

Women seeking care for gambling-related problems usually follow the same treatment protocols as men, which is often cognitive-behavioral therapy, CBT (An et al., 2017). This evidence-based therapy is currently considered the gold standard for GD treatment (Abbott, 2019; Challet-Bouju, Bruneau, IGNACE Group, Victorri-Vigneau, and Grall-Bronnec, 2017; Petry et al., 2017), and its effectiveness in the short and medium terms has been widely demonstrated (Merkouris et al., 2016). And although a large number of studies have provided evidence of the effectiveness of CBT for GD (Cowlishaw et al., 2012; Merkouris et al., 2016), most research has analyzed data collected from men (Tolchard, 2017). The few studies found in the literature within clinical samples with women suggest that CBT could be more effective among male sex (in the short term and at 6 months of follow up) (Toneatto and Wang, 2009).

On the other hand, most studies exploring CBT outcomes within GD were carried out with a variable-centered methodology (the dominant approach in the field of psychopathological research), characterized by analyzing the relationships and covariances between a set of variables through classical procedures such as generalized linear models (Von Eye and Bogat, 2006). Few studies have used person-centered alternative approaches like latent classes and other classification methods, based on analysis of the specific individuals' processes, their functioning, and the behavioral expression of the different domains (Howard and Hoffman, 2017). And very few works have combined person-centered and variable-centered methods as complement analytical techniques (Laursen and Hoff, 2006; Muthén and Muthén, 2000): at the first step, person-centered methods identify subgroups of people who share specific profiles, and in the second step variable-centered methods operate on a higher level of generality with the aim of revealing the connection between features.

## Objectives

The aim of this study was to explore the existence of empirical clusters in a sample of women diagnosed with GD and treated with CBT, based on a large set of indicator/predictor variables including sociodemographics, personality traits, clinical state at baseline (prior to treatment), and therapy outcomes (mainly the risk of dropout and relapse). Based on the cumulate evidence reported in the scientific literature for men diagnosed with GD, we hypothesized that this disorder could be conceptualized as a mixed group

with differentiated latent subgroups among women. These underlying latent clusters would represent distinct GD profiles. The lack of previous research into CBT outcomes in GD women based on person-centered approaches meant we were unable to make a priori assumptions about the expected number of clusters.

## Methods

### Participants

The sample used in this study included $n = 163$ women being attended to consecutively at the Pathological Gambling and other Behavioral Addictions Unit at the Bellvitge University Hospital (Barcelona). Inclusion criteria were being female, adult age (18 and above) and meeting clinical criteria for GD (according to the DSM-5 taxonomy).

Chronological age was in the range of 20 to 73 years (mean = 47.8, SD = 11.3). Most of the participants had low education levels (primary or less, 55.2%), were single (39.3%) or married (38.0%), were employed (55.2%) and belonged to low socioeconomic levels (62.6%). The mean onset age was 36.7 yrs-old (SD = 11.5) and the mean duration of the gambling habit was 5.7 years (SD = 5.7). The most prevalent gambling preference was non-strategic (85.9%) (strategic gambling was reported by 4.9% of the participants and mixed gambling by 9.2%).

### Measures

*Diagnostic Questionnaire for Pathological Gambling* (according to DSM criteria) (Stinchfield, 2003). This self-report questionnaire was initially developed to diagnose the presence of GD using 19 items based on DSM criteria. Both GD diagnoses are available, for the DSM-IV-TR (American Psychiatric Association, 2010) and the DSM-5 versions (American Psychiatric Association, 2013). The Spanish psychometrical adaptation of this tool achieved adequate properties (Cronbach's alpha $\alpha = 0.81$ for a population-based sample and $\alpha = 0.77$ for a clinical sample) (Susana Jiménez-Murcia et al., 2009). The internal consistency achieved in this study was adequate ($\alpha = 0.77$).

*Symptom Checklist-Revised* (SCL-90-R) (Derogatis, 1997). This self-report questionnaire is used to assess psychological state by means of 90 items structured into nine primary (first order) dimensions (somatization, obsessive–compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism), and three global indices [global severity index (GSI), total positive symptoms (PST), and positive symptoms discomfort index (PSDI)]. The Spanish psychometrical adaptation of this tool obtained adequate properties (mean Cronbach's alpha $\alpha = 0.75$) (Gonzalez De Rivera et al., 1989). The internal consistency in our sample was also in the adequate to excellent range (from $\alpha = 0.77$ for paranoid ideation scale to $\alpha = 0.983$ for the global indices).

*Temperament and Character Inventory-Revised* (TCI-R) (Cloninger, Przybeck, Syrakic, and Wetzel, 1994). This self-report questionnaire was developed to assess personality traits by means of 240 items based on Cloninger's multidimensional model. The tool is structured into 7 factors [4 for temperament (novelty seeking, harm avoidance, reward dependence, and persistence), and 3 for character (self-directedness, cooperation, and self-transcendence)]. The Spanish psychometrical adaptation of the tool obtained adequate properties (mean Cronbach's alpha $\alpha = 0.87$) (Gutiérrez-Zotes

et al., 2004). The internal consistency in the study sample was in the adequate to good range (from $\alpha = 0.708$ for novelty seeking to $\alpha = 0.840$ for self-transcendence).

*Other variables.* Other additional data assessed using a semi-structured interview were also analyzed. This tool covered socio-demographic characteristics (sex, marital status, education level and employment status), as well as the socio-economic status index according to Hollingshead's scale (based on employment status, participants' level of education and occupational prestige) (Hollingshead, 2011). Patients were also asked about gambling-related variables: the onset age and the duration of the GD, bets per gambling episode, and cumulated debts due to the gambling addiction.

## CBT Program

CBT was implemented in this study as a time-limited technique across 16 weekly individual sessions lasting 90 min each. The main objective was to achieve full abstinence from all types of gambling. To achieve this purpose, different strategies were implemented to regulate the patients' negative emotions, to reduce arousal levels in the presence of any stimuli that trigger the urge to gamble, and to increase self-control of gambling. Throughout the process, women received feedback regarding the improvement of their self-efficacy and all efforts made to achieve recovery are reinforced.

All the CBT sessions were structured within an outpatient program in the Hospital Unit. The complete program was presented and developed by a qualified CBT, a clinical expert on problematic and disordered gambling. The program included a first step consisting of a psycho-education session, focused on the following topics: (a) providing knowledge about the endo-phenotypes of GD, the onset and development of the disorder, and vulnerability and protective factors related to its course (onset and progression); (b) explaining the rationale behind CBT; (c) teaching methods to identify the dysfunctional thoughts and feelings related to gambling activity; (d) explaining cognitive restructuring techniques and problem-solving techniques addressed at generating alternative functional feelings and thoughts of wellbeing (including relaxation procedures); and (e) providing knowledge regarding stimulus control procedures [such as avoidance of potential triggers, financial planning and self-exclusion (from both land-based and online gambling)].

During the initial phase of the CBT program, participants also received column sheets that they were instructed to fill in each day, detailing situations where they felt unwell (irritable or anxious), behaviors related to gambling, automatic thoughts, an objective examination of those automatic thoughts (including counterevidence), adaptive thoughts, and changes in feeling and behavior.

During the 16 treatment sessions, patients applied CBT techniques, completed the column sheets and attended individual sessions at which questions and opinions regarding the progression of the therapy were exchanged. Changes in gambling behavior and overall psychological state, as well as the learned skills, were evaluated at the end of the treatment.

Different studies have shown the short- and long-term effectiveness of the CBT used in this study in GD samples (S. Jiménez-Murcia et al., 2007, 2015, 2019; Susana Jiménez-Murcia et al., 2016; Jiménez-Murcia, Tremblay, et al., 2017; Jiménez-Murcia, Fernández-Aranda, et al., 2017).

## Procedure

The study was carried out in accordance with the Declaration of Helsinki principles, and was approved by the Ethics Committee of the University Hospital of Bellvitge (Ref: PR329/19). All patients provided signed informed consent to participate in the research. There was no financial or other compensation for being part of the study sample.

The variables recruited at baseline (prior to the treatment) were analyzed in an assessment process consisting of a single session lasting about 90 min. Data for the semi-structured interview were collected by psychologists and psychiatrists with extensive experience of the treatment of behavioral addictions. The clinicians also helped the participants to complete the self-report questionnaires in order to guarantee that no data were missing (for example, due to lack of understanding).

## Statistical Analysis

SPSS24 for Windows (IBM-Corp, 2016) was used for the statistical analysis. First, two-step clustering was used to identify the latent empirical classes. This clustering technique is an agglomerative hierarchical analysis used to explore the existence of natural groupings, useful to handle categorical and quantitative variables, and with the advantage of automatically selecting the optimal number of clusters. The log-likelihood distance was used in this study, and the best model was determined using the Schwarz Bayesian Information Criterion (BIC) and Akaike's Information Criterion (AIC). This method considers the optimal number of latent classes in the model with the largest ratio of changes for the BIC and AIC, as well as the largest ratio of distances measured when comparing the current number of clusters against the previous number. Two-step clustering uses the Silhouette index (a cohesion-separation measure to show how similar individuals are to their own cluster compared to other clusters) to assess the quality of the clustering (Rousseeuw, 1987). The Silhouette coefficient is in the range of $-1$ to $+1$, with high values indicating adequate matching in one's own cluster and poor matching in other clusters (values lower than 0.30 are considered poor fits, between 0.30 and 0.50 are fair, and higher than 0.50 are good). The indicator/predictor variables used for two-step clustering in this study were personality traits (measured at baseline using the TCI-R), global psychopathological distress (measured at baseline with the SCL-90R GSI), GD severity (number of DSM-5 criteria for gambling, debts due to the GD), age, onset age, and relapse and dropout outcomes of CBT. The final model selected for this study was based on the following criteria (Nylund et al., 2007): (a) adequate goodness-of-fit (based on a Silhouette cohesion and separation index); (b) adequate clinical interpretability; and (c) number of individuals in each group to guarantee statistical power.

Second, the comparison between the latent empirical clusters obtained in this study was based on chi-square tests ($\chi^2$) for categorical variables and on analysis of variance (ANOVA) procedures for quantitative measures. The estimation of the effect sizes for the proportion and mean differences was based on the standardized Cohen's-*d* coefficient, considering poor-low effect size for $|d| > 0.20$, moderate-medium for $|d| > 0.5$, and large-high for $|d| > 0.80$ (Kelley and Preacher, 2012). In addition, the increase in Type-I errors due to the multiple statistical tests for comparing clusters was controlled with the Finner method (included in the stepwise familywise error rate procedures) (Finner, 1993).

Third, survival analysis was used to describe the hazard rate of dropout and relapse and the comparison between the empirical clusters. This technique is used for modeling censored data, which occurs in longitudinal studies when patients withdraw from the study (that is, manage to 'survive' to the end of the follow-up, or are lost to the follow-up without event occurrence at last measurement time) (Aalen et al., 2008; Singer and Willett, 2003). This study used the Kaplan–Meier (product-limit) estimator to describe the probability of women "living" to the end of the CBT (in the study, survival is considered to be the time without dropout or without the presence of relapse episodes). Comparison between the groups for the survival function was based on the Log Rank (Mantel-Cox) test.

## Results

### Clustering Procedure

The results for the two-step clustering are displayed in Table S1 (supplementary material), for models ranging from 1 to 8 clusters. The optimal number of latent clusters automatically selected by the system was the 3-cluster model: it achieved the highest ratio distance (2.49) and the highest Silhouette index (0.30, in the fair range). This 3-cluster solution was also selected as the final model since it also achieved good clinical interpretation, and discriminative capacity to differentiate between features related to the sociodemographics, the clinical profile at baseline and the CBT outcomes.

The ordered bar-chart in Fig. 1 shows the relative importance of each indicator/predictor variable in the clustering. This measure is in the range of 0 to 1, and provides an estimation of the discriminative capacity of the indicators: the greater the relevance, the less likely it is for changes between clusters for the variable to be attributable to chance. The variable with the highest relevance in the clustering in the study was the number of sessions attended during the CBT, closely followed by the presence of dropout. On the contrary, the variables with the lowest relevance were personality trait dimensions (self-transcendence, novelty-seeking and persistence). Figure 1 also contains a graphic representation of the Silhouette index in the study, and the frequency distribution for the clusters (ratio size between the largest and lowest clusters was 2.03).

### Comparison Between Clusters

The upper part of Table 1 contains a comparison between the 3 clusters for the sociodemographic variables analyzed in this study. According to the variables that achieved significant result and/or effect size in the mild-moderate to large-high range, cluster 1 was characterized by including the higher proportion of married, occupationally active patients with the highest social status index. On the contrary, clusters 2 and 3 were characterized by including the higher proportion of non-married and unemployed women with the lowest social status indexes. No differences between clusters 2 and 3 were found in terms of sociodemographics.

The lower part of Table 1 contains a comparison between the 3 clusters for the clinical measures recorded at baseline (prior the CBT). Cluster 1 was characterized as reporting medium GD severity (according to the number of DSM-5 criteria), the highest mean of debts related to the gambling activity, the best psychopathological state (lowest mean scores in the SCL-90R scales) and the highest mean in the self-directedness trait. Cluster 3,

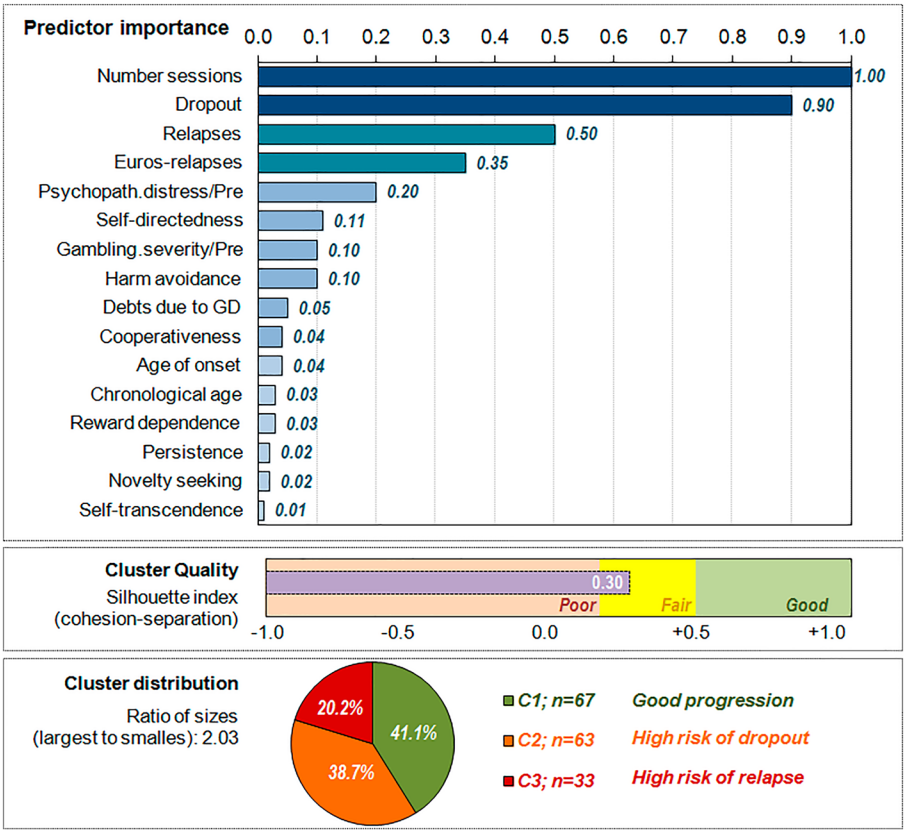


**Fig. 1** Results of the clustering procedure ($n = 163$)

however, registered the highest GD severity (according to the number of DSM-5 criteria), the worst psychopathological state, the lowest self-directedness level and the highest harm-avoidance level. Cluster 2 was characterized by the lowest GD severity (based on the number of DSM-5 criteria), medium scores in the psychopathological scales (compared to both cluster 1 and 3), a harm-avoidance level similar to cluster 1 and lower than cluster 3, and a medium score for self-directedness (compared with both cluster 1 and 2).

The first block in Table 2 contains a comparison between the 3 clusters for the risk of dropout and relapse during CBT treatment. Cluster 1 registered 0% dropouts, and only 14.9% relapses. All patients in cluster 2 drop out from the treatment, and 19% also registered relapse. Cluster 3 was defined by grouping the highest risk of relapse (97% of patients in this subgroup registered gambling-episodes during the treatment) and 21.2% dropouts.

The second block in Table 2 contains the number of relapses registered during the CBT and the euros spent on the gambling activity in the relapse episodes. While no differences emerged when comparing clusters 1 and 2 for these two measures, cluster 3 registered the highest means compared with the other subgroups.

Based on the results shown in Tables 1 and 2, the empirical clusters obtained in this study were labeled: cluster 1 "good progression", cluster 2 "high risk of dropout" and cluster 3 "high risk of relapse".

**Table 1** Comparison between the clusters for the sociodemographic and clinical variables at baseline

| | Cluster-1 | | Cluster-2 | | Cluster-3 | | Cluster-1 vs | | Cluster-1 vs | | Cluster-2 vs | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* = 67 | | *n* = 63 | | *n* = 33 | | Cluster-2 | | Cluster-3 | | Cluster-3 | |
| | *n* | % | *n* | % | *n* | % | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Education | | | | | | | | | | | | |
| Primary or less | 32 | 47.8% | 37 | 58.7% | 21 | 63.6% | .380 | 0.22 | .327 | 0.32 | .819 | 0.10 |
| Secondary | 29 | 43.3% | 23 | 36.5% | 10 | 30.3% | | 0.14 | | 0.27 | | 0.13 |
| University | 6 | 9.0% | 3 | 4.8% | 2 | 6.1% | | 0.17 | | 0.11 | | 0.06 |
| Marital status | | | | | | | | | | | | |
| Single | 24 | 35.8% | 25 | 39.7% | 15 | 45.5% | .492 | 0.08 | .083 | 0.20 | .465 | 0.12 |
| Married-couple | 31 | 46.3% | 23 | 36.5% | 8 | 24.2% | | 0.20 | | **0.51**† | | 0.27 |
| Divorced-Separated | 12 | 17.9% | 15 | 23.8% | 10 | 30.3% | | 0.15 | | 0.29 | | 0.15 |
| Employment | | | | | | | | | | | | |
| Unemploy | 22 | 32.8% | 32 | 50.8% | 19 | 57.6% | **.038*** | 0.37 | **.018*** | **0.52**† | .527 | 0.14 |
| Employed | 45 | 67.2% | 31 | 49.2% | 14 | 42.4% | | 0.37 | | **0.52**† | | 0.14 |
| Social Mean-high / High | 6 | 9.0% | 2 | 3.2% | 1 | 3.0% | **.023*** | 0.25 | .650 | 0.26 | .762 | 0.01 |
| Mean | 13 | 19.4% | 5 | 7.9% | 5 | 15.2% | | 0.34 | | 0.11 | | 0.23 |
| Mean-low | 11 | 16.4% | 12 | 19.0% | 6 | 18.2% | | 0.07 | | 0.05 | | 0.02 |
| Low | 37 | 55.2% | 44 | 69.8% | 21 | 63.6% | | 0.30 | | 0.17 | | 0.13 |
| | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Chronological age (yrs-old) | 48.7 | 11.8 | 47.9 | 11.9 | 45.8 | 9.2 | .656 | 0.08 | .227 | 0.28 | .405 | 0.19 |
| Age of onset GD (yrs-old) | 36.6 | 11.4 | 38.1 | 12.2 | 34.2 | 10.3 | .470 | 0.12 | .333 | 0.22 | .123 | 0.34 |
| Duration GD (yrs) | 6.0 | 6.2 | 5.2 | 4.8 | 6.0 | 6.3 | .448 | 0.14 | .980 | 0.00 | .552 | 0.13 |
| Number of DSM-5 criteria | 7.1 | 1.7 | 6.3 | 2.1 | 7.8 | 1.1 | **.023*** | 0.38 | **.045*** | **0.54**† | **.001*** | **0.90**† |
| Bets (mean-episode, euros) | 78 | 112 | 65 | 122 | 102 | 130 | .534 | 0.11 | .341 | 0.20 | .148 | 0.30 |
| Bets (max-episode, euros) | 488 | 752 | 421 | 680 | 746 | 1191 | .647 | 0.09 | .148 | 0.26 | .072 | 0.34 |
| Debts due to GD (euros) | 5844 | 7690 | 3098 | 6191 | 1545 | 3851 | **.017*** | 0.39 | **.002*** | **0.71**† | .268 | 0.30 |
| SCL-90R: Somatization | 1.24 | 0.78 | 1.57 | 0.78 | 2.13 | 0.77 | **.017*** | 0.42 | **.001*** | **1.15**† | **.001*** | **0.72**† |

**Table 1** (continued)

| | Cluster-1 | | Cluster-2 | | Cluster-3 | | Cluster-1 vs | | Cluster-1 vs | | Cluster-2 vs | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* = 67 | | *n* = 63 | | *n* = 33 | | Cluster-2 | | Cluster-3 | | Cluster-3 | |
| | *n* | % | *n* | % | *n* | % | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| SCL-90R: Obsessive/comp | 1.40 | 0.93 | 1.69 | 1.04 | 2.12 | 1.03 | .107 | 0.29 | **.001*** | **0.73**† | **.043*** | 0.42 |
| SCL-90R: Interper.sensitivity | 1.36 | 0.87 | 1.54 | 0.96 | 2.23 | 0.72 | .265 | 0.19 | **.001*** | **1.08**† | **.001*** | **0.82**† |
| SCL-90R: Depressive | 1.10 | 0.88 | 1.42 | 0.90 | 2.31 | 0.88 | **.043*** | 0.36 | **.001*** | **1.37**† | **.001*** | **1.00**† |
| SCL-90R: Anxiety | 1.75 | 0.94 | 2.27 | 1.00 | 2.69 | 0.89 | **.002*** | **0.53**† | **.001*** | **1.03**† | **.040*** | 0.45 |
| SCL-90R: Hostility | 1.24 | 0.93 | 1.60 | 1.02 | 2.15 | 1.00 | **.034*** | 0.38 | **.001*** | **0.95**† | **.010*** | **0.54**† |
| SCL-90R: Phobic anxiety | 0.88 | 0.82 | 1.12 | 0.92 | 1.68 | 0.92 | .113 | 0.28 | **.001*** | **0.92**† | **.004*** | **0.61**† |
| SCL-90R: Paranoid Ideation | 0.66 | 0.85 | 0.93 | 0.97 | 1.58 | 1.11 | .108 | 0.30 | **.001*** | **0.93**† | **.002*** | **0.62**† |
| SCL-90R: Psychotic | 0.95 | 0.77 | 1.30 | 0.85 | 1.87 | 0.94 | **.017*** | 0.44 | **.001*** | **1.07**† | **.002*** | **0.63**† |
| SCL-90R: GSI score | 0.94 | 0.77 | 1.19 | 0.82 | 1.80 | 0.83 | .081 | 0.31 | **.001*** | **1.07**† | **.001*** | **0.74**† |
| SCL-90R: PST score | 50.0 | 21.4 | 56.7 | 19.4 | 70.0 | 16.1 | .052 | 0.33 | **.001*** | **1.06**† | **.002*** | **0.75**† |
| SCL-90R: PSDI score | 2.07 | 0.64 | 2.34 | 0.63 | 2.66 | 0.63 | **.017*** | 0.42 | **.001*** | **0.92**† | **.021*** | **0.50**† |
| TCI-R: Novelty seeking | 109.7 | 11.5 | 109.2 | 15.2 | 110.6 | 16.6 | .827 | 0.04 | .779 | 0.06 | .648 | 0.09 |
| TCI-R: Harm avoidance | 107.2 | 16.1 | 109.3 | 17.0 | 120.5 | 20.7 | .487 | 0.13 | **.001*** | **0.71**† | **.003*** | **0.59**† |
| TCI-R: Reward dependence | 102.2 | 16.4 | 101.1 | 13.4 | 99.5 | 14.1 | .656 | 0.08 | .397 | 0.18 | .634 | 0.11 |
| TCI-R: Persistence | 104.6 | 16.7 | 104.5 | 21.8 | 102.7 | 22.3 | .969 | 0.01 | .652 | 0.10 | .679 | 0.08 |
| TCI-R: Self-directedness | 124.7 | 19.9 | 116.0 | 21.4 | 106.7 | 17.6 | **.015*** | 0.42 | **.001*** | **0.96**† | **.032*** | **0.51**† |
| TCI-R: Cooperativeness | 135.2 | 15.1 | 132.4 | 14.8 | 129.6 | 16.4 | .291 | 0.19 | .085 | 0.36 | .397 | 0.18 |
| TCI-R: Self-Transcendence | 68.0 | 14.9 | 68.9 | 19.3 | 69.7 | 19.3 | .790 | 0.05 | .663 | 0.09 | .831 | 0.04 |

Cronbach's-alpha in the sample. SD: standard deviation. *Bold: significant comparison

†Bold: effect size into the mild-moderate (\|*d*\| > 0.50) to large-high range (\|*d*\| > 0.80)

**Table 2** Comparison between the clusters for the CBT outcomes

| | Cluster-1 | | Cluster-2 | | Cluster-3 | | Cluster-1 vs | | Cluster-1 vs | | Cluster-2 vs | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *n* = 67 | | *n* = 63 | | *n* = 33 | | Cluster-2 | | Cluster-3 | | Cluster-3 | |
| | *n* | % | *n* | % | *n* | % | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Dropout | 0 | 0.0% | 63 | 100.0% | 7 | 21.2% | **.001*** | **3.14**† | **.001*** | **0.96**† | **.001*** | **2.18**† |
| Relapses | 10 | 14.9% | 12 | 19.0% | 32 | 97.0% | .531 | 0.11 | **.001*** | **2.00**† | **.001*** | **1.89**† |
| | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Number relapses | 0.25 | 0.64 | 0.27 | 0.68 | 3.88 | 4.34 | .964 | 0.02 | **.001*** | **1.17**† | **.001*** | **1.16**† |
| Euros relapses | 9.0 | 26.0 | 33.2 | 93.3 | 430.8 | 576.5 | .603 | 0.35 | **.001*** | **1.03**† | **.001*** | **0.96**† |

SD: standard deviation. *Bold: significant comparison

†Bold: effect size into the mild-moderate (\|*d*\| > 0.50) to large-high range (\|*d*\| > 0.80)

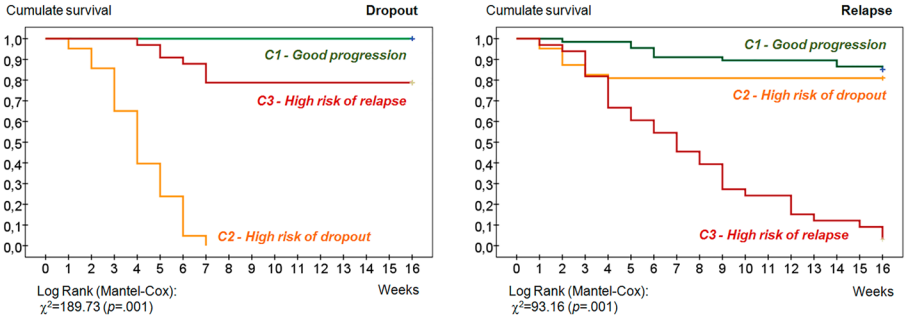


**Fig. 2** Kaplan–Meier functions for the rate to dropout and relapse ($n = 163$)

Figure 2 contains the Kaplan–Meier functions to the time of dropout and relapse. The cumulate survival to dropout shows that 100% of the patients in cluster 1 did not drop out at any stage of CBT follow-up. The dropouts registered for patients included in clusters 2 and 3 occurred during weeks 1 to 7 (before ending the second month of the treatment). Regarding relapses, the gambling episodes reported by 97% of patients in cluster 3 were registered throughout CBT follow-up. 14.9% of patients with relapses in cluster 1 also reported that these gambling episodes occurred throughout the whole treatment. The relapses registered in cluster 2 were all reported during weeks 1 to 4.

## Discussion

This study aimed to explore clusters of women seeking treatment for GD based on sociodemographic features, clinical state at baseline and CBT outcomes. The 3-cluster solution was selected as optimal: C1 clustered patients with good progression during the treatment, C2 patients with poor progression to dropout, and C3 patients with poor progression to relapse. The identification of these empirical groups evidences the heterogeneity of progression during treatment in women with GD, which can be described in separate profiles based on the demographic and clinical features.

Cluster C1 included the patients with the best progression during treatment (low rates of dropout and relapse), and was characterized by the highest proportion of women that are married, with the highest social status indexes, employed, with medium GD severity at the beginning of therapy (according to the number of DSM-5 criteria), the highest level of accumulated debts related to the gambling behavior, the best psychopathological state at baseline (lowest SCL-90R means), the highest mean self-direction and the lowest mean for harm avoidance. Regarding marital status, our results support evidence obtained in other studies that suggests that being married or having a stable partner is related to better therapeutic efficiency (S. Jiménez-Murcia, Fernández-Aranda, et al., 2017; Jiménez-Murcia, Tremblay, et al., 2017). Close relatives and friends of patients with GD usually suffer from the negative effects of the disorder, and they consequently express a positive attitude towards the treatments. These encouraging thoughts should increase the motivation for patients to seek help (Crisp et al., 2004; Dannon et al., 2006), and this better predisposition towards the therapy could also contribute to better adherence by reducing the risk of abandonment and relapse (Gomes and Pascual-Leone, 2015; Tremblay et al., 2015).

Cluster C1 is also characterized by the medium level of DSM-5 symptoms for GD, but by the highest level of accumulated debts from gambling. Financial harm has been described as one of the most commonly reported gambling problems, and gambling-related debt problems have been considered a measure of gambling severity due the strong association between this variable and poor psychosocial functioning (including adverse family impacts, comorbidity with other mental problems and distress). However, studies have also observed a moderator role of sex in the association between gambling severity and cumulate debts among GD patients: (a) among men, as the more severe the negative impacts of the gambling activity, the higher the gambling-related debts; (b) among women, as the financial consequences related with the gambling activity may be less significant for patients with severe/extreme risks of gambling compared to women with a moderate risk of gambling (Håkansson and Widinghoff, 2020). This association could explain why cluster C1 included women with the lowest number of GD symptoms but the highest level of debts. Cluster C1 also presents the best overall psychopathological state. It is known that one primary reason for gambling among women is to alleviate high levels of concurrent symptoms (mainly depression, anxiety and stress) (Marchica et al., 2020). But it is also known that a sub-group of women with better functional mental status show other motivations that explain gambling behavior, such as socialization (Ibáñez et al., 2003; Nuske et al., 2016; Potenza et al., 2006), and this specific group with better baseline functioning should obtain a better benefit from the therapy. Other motivations for gambling behavior in this cluster could also be related to the work situation: C1 grouped the highest prevalence of employed women. Previous studies have observed that active working women with managerial responsibilities could resort to gambling as a way of coping with the specific tensions that their profession causes them, or even as a way of meeting the social demands of their jobs (Toneatto and Wang, 2009). This particular profile could also be highly motivated to receive treatment for their gambling because they want to avoid the negative impacts of gambling problems on their work (such as reduced productivity and results, or damage to their reputation).

Cluster C3 is characterized by poor progression during treatment, with the highest risk of relapse. This cluster includes the highest proportion of women that are unmarried (single or divorced/separated), not actively working, with the highest number of DSM-5 symptoms for GD, the lowest level of accumulated debts due to gambling behavior, the worst psychological state, the highest level of harm avoidance and the lowest self-directedness level. Previous studies have observed that women without a stable partner, in more disadvantaged socioeconomic groups and that are unemployed reported a more severe progression of problematic gambling (Brunborg et al., 2016; R. Granero et al., 2009; Tavares et al., 2001). In this study, the lower level of gambling-related debts in cluster C3 could be related with employment status: being unemployed may explain why these women have a lower capacity to acquire debts. Other studies have also observed that patients with greater socioeconomic difficulties show greater cognitive bias associated with gambling behavior (such as illusion of control, interpretative bias, gambling-related expectancies and distortions of the inability to stop gambling) (Susana Jiménez-Murcia et al., 2020), all of which could be directly associated with greater GD severity and poorer therapeutic efficiency (Ledgerwood et al., 2020; Mallorquí-Bagué et al., 2019).

Regarding psychopathological state, different studies show that a high proportion of women who experience problems with gambling behaviors also have comorbid symptoms (such as anxiety, depression, eating or substance use) (Andronicos et al., 2015; Boughton and Falenchuk, 2007; Dannon et al., 2006; Díez et al., 2014). In fact, GD has been shown to be comorbid with a range of psychosocial and psychopathological symptoms for both

genders (Cowlishaw and Kessler, 2016), and it has been reported that more acute psychopathological comorbid states may have serious implications for the treatment benefits (Ledgerwood and Arfken, 2017; Maniaci et al., 2017; Petry et al., 2017): individuals are less likely to terminate the therapy and more likely to relapse if they are suffering from multi-morbidities and harm at baseline. In samples of women with GD, a mediational link has been reported between socioeconomic disadvantage (for example unemployment, low occupational status, low income or poverty), higher difficulties coping with stress, and poorer psychopathological functioning (Boughton and Falenchuk, 2007). This particular profile of women pertaining to low social groups who exhibit distress could use gambling as an means of escape to deal with the effects of their chronic stress [such as physical symptoms (fatigue, eating problems, sleeping disorders or general illnesses), cognitive performance (difficulty concentrating or disorganized thoughts), and other psychological correlates (irritability, low self-esteem, perceived loss of control, feeling helpless, depression or anxiety)] (Blanco et al., 2006; Hodgins and el-Guebaly, 2004; Wenzel and Dahl, 2009). Unfortunately, the progression of the GD among these women leads to even worse comorbid psychopathological symptoms (Susana Jiménez-Murcia et al., 2020; G. Mestre-Bach et al., 2016a, b), and this recursive association (the severity of the gambling-related problems and mental health) could seriously interfere with the efficacy of the therapy (Alvarez-Moya et al., 2011). Ultimately, these women with higher psychological distress may need more time, additional effort, and specific-individualized plans due to the additional care addressed at their comorbid symptoms (Yakovenko et al., 2015).

Regarding personality traits, cluster C3 was characterized by the highest score for harm avoidance and the lowest score for the self-directedness trait. Other studies have identified a profile of women seeking treatment for severe GD with a high dysfunctional psychopathological state, and a personality characterized by lower self-directedness and higher harm avoidance (R. Granero et al., 2009; Roser Granero et al., 2018; Gemma Mestre-Bach et al., 2016a, b). To our knowledge, no empirical study has found any association between this specific profile and poor treatment outcomes in samples of women seeking treatment for GD, but it has been found for males (Roser Granero et al., 2020). Harm avoidance is a personality trait that reflects a tendency towards shyness, passive avoidance behaviors, and concern in anticipation of possible danger, while self-directedness measures responsibility for one's own decisions, the availability of resources to deal with situations, self-esteem and effectiveness. This personality domain is connected with pessimistic and negativistic behavior styles (tendency to be fearful, apprehensive, discouraged and insecure), and its contribution to almost all anxiety disorders has led to the belief that harm avoidance could lead to an anxiety-prone personality (Chen, Lin, Li, Huang, and Lin, 2015; Marco, 2013). High scores for harm avoidance have been shown to contribute to poor treatment efficiency regardless of the type of gambling, the severity of the gambling problem or the duration of the addictive behavior (Maniaci et al., 2017). On the other hand, low scores for self-directedness are related to individuals described as blaming, less responsible, less mature, and driven to react to current circumstances and immediate needs. Among GD samples, low self-directedness appears to be strongly related to high levels of neuroticism-anxiety, more distressed moods, and greater difficulties with the regulation of emotions (Rogier and Velotti, 2018), and this particular profile has significantly contributed to a high risk of relapse or dropout in GD patients (Ramos-Grille et al., 2015). As a whole, these results suggest the need to develop adequate evidence-based therapies that comprise specific strategies aimed at increasing women's self-esteem and self-efficacy, as well as person-centered techniques to increase women's self-determination capacities to regulate behaviors to the demands of certain situations in order to avoid relapse.

Cluster C2 included patients with poor progression during treatment, with a high risk of dropout (all the patients in this group dropped out of the CBT, and 19% also had relapses). Regarding sociodemographic features, cluster C2 showed similar features to cluster C3, characterized by a high proportion of unmarried women (without a stable partner) of low social status. Clinically, cluster C2 presented the lowest mean for DSM-5 criteria for GD, medium levels for debts accumulated due to the GD, number of comorbid symptoms measured by the SCL-90R, and in the TCI-R harm avoidance and self-directedness scales. It is important to note that cluster C2 is associated with a high likelihood of dropout, but it is not characterized by the highest mean for the number of DSM-5 criteria or accumulated debts. Previous studies have observed that treatment dropout is related with higher scores for measures reflecting gambling severity (such as impulsivity/addiction, perceived predictive control and gambling-related cognitive distortions) (Fortune and Goodie, 2012; Ledgerwood et al., 2020). Empirical research has also observed that the risk of dropout in patients with GD is related to greater difficulty with self-regulation of behaviors, a high perception of guilt and shame for the addictive behavior, false beliefs about treatment and the presence of emotions of apathy and discouragement (Alvarez-Moya et al., 2011). Our results suggest that it is also possible that women who have not yet reached the most severe levels of affectation by the gambling problem are less aware of the need for therapy, and even consider that they can autonomously control their gambling habit.

Finally, the two treatment outcomes analyzed in this study were the presence of relapses and dropout. There has been much variation in the use of outcome measures of recovery during GD therapy (Pickering et al., 2018). Rates of relapse (and/or abstinence) have been typically reported as the main expected outcomes in a large number of studies, given that no gambling of any nature is defined as the treatment goal. Dropout is also a key therapy outcome, since it has been observed that just over half of individuals who seek treatment for gambling-related problems fail to complete outpatient therapy plans (Ronzitti, Soldini, Smith, Clerici, and Bowden-Jones, 2017). This study contributes with new empirical evidence on women from a person-centered approach, identifying separate empirical clusters that represent differentiated profiles of CBT effectiveness characterized by good progression to recovery versus poor progression to relapse or to dropout.

## Limitations and Strengths

There are some research limitations to this study that could impact the empirical evidence. First, since the data correspond to the outcomes during the CBT, the results could therefore be non-representative over a longer period (there is no way of guaranteeing that abstinence from gambling episodes will persist over time). Second, the data analyzed in the study were recruited from women who attended a specialized care center and fulfilled the inclusion criteria; therefore, our results cannot be generalized to women with gambling-related problems from the general population that do not recur to treatment centers, or men.

Strengths of this study include longitudinal data from a large sample of female GD patients. Another strength is the use of both person-centered and variable-centered approaches, the integration of which has led to a more complete understanding of the processes and patterns of individual profiles.

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## Declarations

**Conflict of interest** FFA received consultancy honoraria from Novo Nordisk and editorial honoraria as EIC from Wiley. The rest of the authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

**Ethics approval** All procedures were carried in accordance with the Declaration of Helsinki. This research was approved by the Ethics Committee of the Bellvitge University Hospital (Ref: PR329/19). All subjects were informed about the study and all provided informed consent.



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## 4.2 Artículo 2

**Objetivos:**
En este artículo se contrastan los objetivos segundo y tercero de la tesis.

> **2.** Identificar clases latentes en una muestra clínica de mujeres que consultan por problemas relacionados con el TJ o con CC, a partir de la evolución de que presentan durante la TCC.
>
> **3.** Identificar variables en la línea base con capacidad discriminativa de los perfiles latentes identificados en mujeres tratadas debido a los problemas que les ocasiona el TJ o la CC.

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**Resumen:**

La muestra incluyó 318 pacientes de sexo femenino, con edad dentro del rango 21 a 77 años, consecutivamente atendidas en una unidad de referencia para el tratamiento de adicciones comportamentales. Motivo de consulta: TJ (221 mujeres) o CC (97 mujeres). Todas recibieron tratamiento con TCC.
Se identificaron cuatro clases latentes. La clase L1 (etiquetada de "buen progreso hacia la recuperación"), agrupó pacientes con alta probabilidad de buen resultado terapéutico (bajo riesgo de abandono y recaída) y se caracterizó por los niveles más bajos de psicopatología inicial y perfil más funcional de personalidad (las puntuaciones medias más bajas en evitación del daño y auto-transcendencia, así como las puntuaciones más altas en dependencia a la recompensa, persistencia, autodirección y cooperación). Las clases L3 (etiquetada de "mala progresión hacia abandono") y L4 (etiquetada de "mala progresión hacia recaída") agruparon mujeres con la edad media más joven, inicio más precoz de la conducta adictiva y peor estado psicopatológico global en la línea base.
Los resultados aportan evidencia sobre la complejidad del perfil de las mujeres que presentan problemas relacionados con TJ y CC. Los instrumentos de evaluación deben ser sensibles para identificar las múltiples variables que interactúan en el inicio y la evolución de estos problemas, ya que deben tenerse en cuenta en los planes de intervención. Los tratamientos deben tener en cuenta herramientas para garantizar el bajo riesgo de abandono y recaída, así como también la eficacia a largo plazo.

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# Latent Classes for the Treatment Outcomes in Women with Gambling Disorder and Buying/Shopping Disorder

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**Abstract:** Background: The risk for behavioral addictions is rising among women within the general population and in clinical settings. However, few studies have assessed treatment effectiveness in females. The aim of this work was to explore latent empirical classes of women with gambling disorder (GD) and buying/shopping disorder (BSD) based on the treatment outcome, as well as to identify predictors of the different empirical groups considering the sociodemographic and clinical profiles at baseline. Method: A clinical sample of $n$ = 318 women seeking treatment for GD ($n$ = 221) or BSD ($n$ = 97) participated. Age was between 21 to 77 years. Results: The four latent-classes solution was the optimal classification in the study. Latent class 1 (LT1, *good progression to recovery*) grouped patients with the best CBT outcomes (lowest risk of dropout and relapses), and it was characterized by the healthiest psychological state at baseline, the lowest scores in harm avoidance and self-transcendence, and the highest scores in reward dependence, persistence, self-directedness and cooperativeness. Latent classes 3 (LT3, *bad progression to drop-out*) and 4 (LT4, *bad progression to relapse*) grouped women with the youngest mean age, earliest onset of the addictive behaviors, and worst psychological functioning. Conclusions: GD and BSD are complex conditions with multiple interactive causes and impacts, which need wide and flexible treatment plans. Specific interventions should be designed according to the specific profiles of women for achieving early inclusion, retention and well-maintained long-term effects.

**Keywords:** buying/shopping disorder; gambling disorder; women; cognitive behavioral therapy; latent class analysis

## 1. Introduction

Behavioral addictions refer to a form of addiction involving a compulsion to engage in a rewarding non-substance-related behavior, with concurrent maladaptative behaviors that lead to severe distress in diverse areas of the individuals' functioning: reduced quality

of life, family/social discord, comorbid physical/mental disorders, work impairment and financial problems [1–4]. During recent years, scientists and clinicians have focused attention on addictions without psychoactive substances, and the number of similarities revealed between drug addictions and non-substance addictions (in the form of addictive activity cravings, tolerance and abstinence syndrome, brain and nervous system correlates and bio-psychosocial consequences) pointed to the growing problem of these addictive behaviors within our communities [5].

GD is the only behavioral addiction included in the last version of the Diagnostic and Statistical Manual of Mental Disorders DSM-5 [6]. It has been incorporated in the broader category of "Substance-Addiction and Related Disorders" on the basis of cumulative empirical research suggesting an overlapping phenomenology, comorbidity and neurobiology with substance use disorders [7,8]. GD was also included in the latest revision of the International Classification of Diseases ICD-11 [9] as a disorder due to addictive behaviors. It is characterized by frequent concerns about gambling, gambling with larger amounts of money to receive the same level of desired experience (tolerance), repeated unsuccessful efforts to control or stop gambling, and restlessness or irritability when stopping gambling (abstinence). The most recent epidemiological studies estimate prevalence for GD close to 1% in industrialized countries across five continents [10], and considering joint problematic (non-disordered) gambling and GD, the prevalence rates increased to 6% assessing the last year of the survey, and to 10% for lifetime estimates [11].

The concept of behavioral addiction is relatively new in the field of psychopathology. In this category a wide variety of clinical conditions are grouped, and gambling disorder (GD) and buying/shopping disorder (BSD) are considered most prevalent in clinical and population-based samples. While no optimal nosological classification exists towards these mental disorders when considered together, prevailing suggestions as to the preferred approach include problematic gambling and problematic buying within the impulsive–compulsive spectrum [12,13]. This spectrum -refers to a number of disorders drawn from different diagnostic categories on the basis of comparisons of phenomenology (largely, the role of obsessive–compulsive–impulsive features), natural history, family history, biological markers and treatment response. Parallel classification schemes have conceptualized GD and BSD as a dimension across a broad range of the problem symptoms continuum (valid in both clinical and community samples), being at one end the lowest risk of recreational behavior, followed by problematic behavior, and being at the other end of the dimension the highest risk of addiction [14,15]. The position along the dimensional continuum is associated with gradual increases–decreases in the level of the addiction-related harms.

BSD is considered a behavioral addiction characterized by intense preoccupations with buying and possessing consumer goods that are not strictly necessary (patients buy more products than they can afford, and these products are neither frequently used or needed), leading to adverse consequences [16,17]. Proposals to include BSD within psychiatric taxonomies (such as DSM) have not been accepted, warranting further research [18,19]. The prevalence of BSD has been estimated within a large range between 1% to 8% in industrialized countries (this wide interval is related to the large heterogeneity of the study samples and the measurement tools), with a mean point estimate of 5% according to a meta-analysis [20]. Furthermore, both clinical and population-based studies have reported an increasing trend for BSD in developing consumer societies [21], highlighting the central relevance of materialistic values among these cultures as a predisposing factor to compulsive buying attitudes [22,23]. Epidemiological research has also reported an increasing propensity toward BSD among young adults and women, suggesting a greater tolerance for women and younger age individuals to make excess purchases [24]. Recent research also demonstrated that BSD constitutes a wide-ranging clinical condition for which sociodemographic features and personality traits have proven the capacity to discriminate between empirical clusters representative of distinctive clinical profiles [25]. The level of BSD symptoms is related to female gender, young age of onset of the addictive behavior, high levels in harm avoidance, low levels in self-directedness and high likelihood of

comorbid psychopathology [26]. However, studies in this area are scarce, and some studies have failed to identify variables associated with the onset and progression of the BSD patients [27,28]. On the other hand, the scant consideration of assessment methods for impulsive buying has led to inconsistences in the research and has hampered cross-study comparability [29].

Individuals across a range of behavioral addictions show similar psychosocial and clinical patterns, both compared to control groups and as a function of the severity of the addictive behaviors. Considering the endophenotypes of GD and BSD, the role certain personality traits play in the onset and progression of the disorders, such as high levels of impulsivity (patients have a diminished control over impulses to engage in addictive behaviors) and high sensation seeking [30] have been observed to be similar. Certain sociodemographic variables have also been identified as potential risk factors, such as younger age (the age of onset is typically during young adulthood), disadvantaged social groups, and urban location (compared to rural location) [31,32]. The patients' perceived motivations for the onset and progression of the disorders also appear similar for GD and BSD; individuals associate the addictive behavior episodes with pleasure and other positive feelings during the first stages, but the addictive episodes are increasingly used to alleviate negative moods when the condition progresses to impairment stages [33]. Other central features explaining the onset and the evolution of GD and BSD are deficient coping skills, low emotion regulation capacities [34,35] and implicit cognitive biases (such as difficulties evaluating long-term negative consequences and impairment in the capacity to money manage) [36,37]. Regarding neurobiological systems and neurocognitive characteristics, studies have shown common mechanisms compared with substance-related disorders. These include abnormalities in neurotransmitter systems (dopamine, serotonin and glutamate), disturbances in the motivation–reward systems and alterations in the reward-directed behavioral circuitry (primary ventral striatum and medial prefrontal cortex) [38–44]. Within this research area, the interaction of person–affect–cognition–execution (I-PACE) model has also been proposed for describing the psychological and neurological processes of problematic addictive behaviors, including GD and BSD [45]. Steep delay discounting (considered a measure of impulsivity, strongly related to the ability to delay gratification and described as a greater preference for smaller immediate rewards instead of larger delayed rewards) has also been defined as a common cognitive phenomenon for a range of addictions, including substance-related disorders and behavioral addictions [46]. Finally, an elevated risk for other comorbid psychiatric disorders is also characteristic of GD and BSD (these disorders rarely arise as a problem in isolation), being the most frequent concurrent conditions among females with anxiety disorders, depressive disorders and other problems within the impulse-control spectrum (substance use disorders, OCD, kleptomania, trichotillomania, bulimia or binge eating) [47–51]. The study of the comorbid presence of GD with BSD has also suggested the existence of underlying common etiological pathways for these two disorders [52,53].

Regarding intervention studies, evidence-based best practice studies suggest that cognitive behavioral therapy (CBT) constitutes a *gold standard* for many mental problems [54], with promising results for a broad range of addictive behaviors, including GD [55] and BSD [56]. CBT is a problem-solving approach centered on correcting the irrational thoughts associated with the addictive behaviors and their adverse consequences. The key objective of this intervention is to help subjects change the way they think and also the way they act. During this therapy, patients learn to identify and change cognitive biases and improve emotion regulation, since the modification of these thought patterns contributes to interrupting problem behaviors. Several cognitive and behavioral techniques are included in CBT programs, such as stimulus control, self-reinforcement, live exposure with response prevention, skills training and relapse prevention strategies (through other activities that are also rewarding and non-harmful). However, despite a significant body of literature assessing the efficacy of CBT for men diagnosed with GD, few treatment studies have focused on exploring the treatment outcomes for women with GD [57] and BSD [58]. This

study is intended to provide new scientific evidence on the response to CBT in a clinical sample of women with behavioral addictions, specifically for the GD and the BSD subtypes. The results obtained in this work will allow the identification of latent groups of women with good and bad course trajectories, as well as predictive variables for the empirical latent classes.

*Objectives*

The aims of this study were to explore latent classes of women with GD or BSD considering the CBT outcomes and to identify predictors of the different empirical classes. Based on previous studies, we hypothesized that different profiles characterize the progression of the behavioral addictions during the treatment of GD and BSD and that the baseline state will achieve discriminative capacity on the empirical latent classes.

## 2. Materials and Methods

### 2.1. Participants and Procedure

The sample in this work included $n$ = 318 women consecutively attending the Pathological Gambling Unit and other Behavioral Addictions located in the Bellvitge University Hospital (Barcelona, Spain). Criteria for the study were adult age (18 years-old and older) and meeting clinical criteria for GD or BSD (according to different diagnostic measures, see below). Exclusion criteria were male sex and impairing neurological or psychiatric diseases, such as dementia, intellectual incapacity or active psychotic or bipolar episode, as determined by assessment with the tools used in the study.

The presence of GD was identified in $n$ = 221 women, while $n$ = 97 presented BSD (no participant in the study presented the dual condition of GD + BSD). In the total sample, age was between 21 to 77 years (mean = 47.3, SD = 12.3). Mean age of onset of the behavioral addiction was 36.6 years (SD = 12.1), and the mean duration of the addiction-related problems was 5.7 years (SD = 5.4). Most women had achieved primary (54.1%) or secondary (35.8%) education levels, were married or lived with a stable partner (39.6%), were employed (50.6%) and belonged to mean-low or low socioeconomic levels (78.9%).

### 2.2. Assessment

*Diagnostic Questionnaire for Pathological Gambling* (according to DSM criteria) [59]. It was initially developed as a self-report diagnostic tool to identify the presence of GD through 19 items measuring the DSM criteria. It is currently used to assess both the diagnosis of GD based on the DSM-IV [60] and DSM-5 [6] taxonomies. The Spanish version used in this study has evidenced adequate psychometrical properties (Cronbach's alpha $\alpha$ = 0.81 for a population-based sample and $\alpha$ = 0.77 for a clinical sample) [61]. In this work, this questionnaire was used to confirm the presence of GD in the subsample of women who seek treatment due to the gambling-related problems. The internal consistency achieved in this study was adequate ($\alpha$ = 0.79).

*Buying/Shopping Disorder Diagnosis* was assessed with a structured clinical face-to-face interview modeled after the SCID-I [62], developed to assess the presence of impulsive control disorders such as BSD [63,64]. The criteria used in this study have received wide acceptance in the research community [65], which must be considered due to the lack of diagnostic criteria for BSD in the most frequently used taxonomies (such as the DSM) and the recommendation of assessing the disorder through face-to-face interviews [66].

*Symptom Checklist-Revised* (SCL-90-R) [67]. This questionnaire was developed as a screening tool to assess the psychological state in multiple domains. It was planned as a self-report questionnaire, with 90 items structured into 9 primary (first order) dimensions (somatization, obsessive–compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism), and 3 global indices (global severity index (GSI), total positive symptoms (PST) and positive symptoms discomfort index (PSDI)). The Spanish adaptation of the SCL-90R used in this study has reported adequate psychometrical properties [68]. The internal consistency measured with Cronbach's-

alpha in our sample was in the range adequate to excellent: 0.92 for somatization, 0.89 for obsessive–compulsive, 0.88 for interpersonal sensitivity, 0.92 for depression, 0.91 for anxiety, 0.84 for hostility, 0.87 for phobic anxiety, 0.76 for paranoid ideation, 0.86 for psychoticism and 0.98 for the global indices.

*Temperament and Character Inventory-Revised* (TCI-R) [69]. This questionnaire was developed to obtain a measure of the personality traits according to Cloninger's multidimensional model. It was planned as a self-report with 240 items factorized in 7 general factors (4 for temperament (novelty seeking, harm avoidance, reward dependence and persistence), and 3 for character (self-directedness, cooperation and self-transcendence)). The Spanish adaptation used in this work has obtained adequate psychometrical indices (mean Cronbach's alpha in the good range, $\alpha = 0.87$) [70]. The internal consistency in the sample of the study was in the range adequate to good: 0.71 for novelty seeking, 0.83 for harm avoidance, 0.77 for reward dependence, 0.85 for persistence, 0.84 for self-directedness, 0.77 for cooperation and 0.85 and self-transcendence.

*Other Variables.* The sociodemographics and the behavioral addiction-related variables were assessed with a semi-structured interview. This tool covered sex, marital status, education level, employment status and the socio-economic position index according to Hollingshead's scale (this scale generated a classification based on the employment status, the participants' level of education and the occupational prestige) [71]. Patients were also asked about the age of onset and the duration of the addiction-related problems, the cumulated debts due to the behavioral addiction and the presence of autolysis and suicidal ideation.

Data for the semi-structured interview were collected by psychologists and psychiatrists with high experience in the treatment of behavioral addictions. The clinicians also helped participants complete the self-report questionnaires (clarifying the meaning of possible items for patients to understand) to guarantee that no data were missing (for example, due to the lack of understanding).

### 2.3. CBT Program

The CBT program used in this study has been extensively described in previous studies [72]. The complete program was developed by qualified clinicians, expert in the application of this treatment among patients with behavioral addictions. The program was implemented through 12 weekly sessions lasting between 45 and 90 min each, in individual outpatient format in a the hospital unit setting. The key primary objective was to achieve full abstinence from all types of gambling or compulsive buying/shopping episodes. Techniques covered included cognitive restructuring, assertiveness training, self-reinforcement and stimulus control (the time for this concrete technique was flexible and determined on a case-by-case basis depending on the patients' progress).

At the beginning of the CBT program, a psychoeducation session was aimed to: (a) provide knowledge about the concept of GD/BSD (as loss of control (addictive) disorders with several negative consequences on functioning); (b) provide information about the treatment (objectives, relevance to complete tasks and to remain in the intervention program, importance of total and permanent abstinence and possibility of sporadic relapses); and (c) collect diaries of baseline gambling or compulsive buying behaviors. During the next session of the treatment, the patients learned the CBT techniques (cognitive restructuring and problem-solving) and how to complete a self-monitoring diary in which to record their problematic behavior/s. Successive CBT sessions were focused on analyzing homework tasks, incidents, diaries, potential relapse/s, alternative activities carried out and attainment level with the treatment guidelines.

At the end of the CBT, patients and clinicians assessed the changes observed during the intervention and discussed expectations for the future (with regard to maintaining functional safe behaviors avoiding risk situations). Patients with GD are also encouraged on total and permanent abstinence, and patients with BSD on abstinence of compulsive buying episodes. During all the treatment, the presence of relapse (gambling or compulsive

buying episodes) were registered, as well as the time/week of these events. For patients who dropout, the time of leaving the treatment was also registered.

Regarding the reliability of the CBT program employed in this research, previous studies have shown the short- and medium-term effectiveness, including samples of women meeting clinical criteria for GD [73,74] and BSD [75].

### 2.4. Statistical Analysis

This study used Latent Class Analysis (LCA) in Mplus8.1 [76] to explore the existence of empirical sub-groups among the complete sample based on the CBT outcomes. LCA is a classification procedure employed to relate a set of an observed dataset (including both categorical and quantitative variables) to a latent unobserved variable. This method is included within the measurement models in which individuals are classified into mutually exclusive/exhaustive types (named latent classes) based on the underlying patterns on a set of indicator variables. This study used the Robust Maximum Likelihood (MLR) estimator in the *Analysis* command, defined as indicators of the main treatment outcomes (dropout, time to dropout, relapses, time to relapses and euros lost in the relapses), and including the patients' age, the diagnostic subtype (GD versus BSD), the duration of the behavioral addiction and the global psychopathological distress at baseline (SCL-90R GSI as covariates). The selection of the number of latent classes was based on the following criteria [77]: (a) the lowest Akaike (AIC) and Bayesian information criterion (BIC) indexes for the model (compared with other solutions); (b) entropy (measure of the model's discriminative capacity, that is, its ability to identify individuals following the different latent classes) above 0.80; (c) high on-diagonal average values (above 0.80) in the matrix containing the probabilities of membership (that is, high average latent class probabilities for most likely latent class membership by latent class); (d) enough sample size in a class to allow for statistical comparisons; and (e) adequate clinical interpretability.

After obtaining the latent classes, these empirical groups were compared to the sociodemographics and the baseline clinical measures (registered previous to the CBT program), with the aim of identifying factors with discriminative capacity to the treatment outcomes. Comparisons were carried out with chi-square tests ($\chi^2$) for categorical variables and with analysis of variance (ANOVA) for quantitative measures. The estimate of the effect sizes for the proportion and the mean differences were based on standardized Cohen's-*d* coefficients, considering poor-low effect size for $|d| > 0.20$, moderate-medium for $|d| > 0.5$ and large-high for $|d| > 0.80$ [78]. In addition, the increase in Type-I errors due to the multiple statistical tests for comparing latent classes was controlled with the Finner method, which constitutes a stepwise familywise error rate procedure [79].

Survival analysis was also used to describe the hazard rate to dropout and relapse and to compare the cumulative function between empirical latent classes. Survival procedures are statistical techniques used for modeling censored data, which occurs in longitudinal studies when patients withdraw from the study (that is, arrive at the end of the follow-up or is lost to the follow-up without event occurrence at the last measurement time) [80,81]. This study estimated the cumulative survival function with the Kaplan–Meier (product-limit) estimator, which provided the probability of women "living" during the CBT (in the work, survive is considered as the time without dropout or without the presence of relapse episodes). Comparison between the groups for the survival functions was done with the Log Rank (Mantel–Cox) test.

### 2.5. Ethics

The study was carried out in accordance with the Declaration of Helsinki principles, and approved by the Ethics Committee of University Hospital of Bellvitge (Ref. 307/06). All women provided signed informed consent for participating in the research. There was no financial or other compensation for being part of the sample of the study.

## 3. Results

### 3.1. Characteristics of the Sample

The first block of Table 1 displays the sociodemographics among GD and BSD patients, as well as the comparison between the groups. Compared to women with BSD, the proportion of women with lower education level and poorer social indexes was higher among women with GD. This diagnostic subtype also reported older chronological age and later age of onset of the behavioral problems (second block of Table 1). Regarding the psychopathology state and personality features at baseline, BSD was characterized by higher mean scores in the obsessive–compulsive dimension and novelty seeking trait (last block of Table 1).

**Table 1.** Descriptive for the variables of the study.

| | | GD (*n* = 221) | | BSD (*n* = 97) | | | |
|---|---|---|---|---|---|---|---|
| *Sociodemographic variables* | | *n* | % | *n* | % | *p* | \|*d*\| |
| Education | Primary | 134 | 60.6% | 38 | 39.2% | **0.001** * | 0.43 |
| | Secondary | 76 | 34.4% | 38 | 39.2% | | 0.10 |
| | University | 11 | 5.0% | 21 | 21.6% | | **0.52** † |
| Marital status | Single | 95 | 43.0% | 37 | 38.1% | 0.649 | 0.10 |
| | Married/couple | 84 | 38.0% | 42 | 43.3% | | 0.11 |
| | Divorced/Separated | 42 | 19.0% | 18 | 18.6% | | 0.01 |
| Employment | Unemployed | 110 | 49.8% | 47 | 48.5% | 0.828 | 0.03 |
| | Employed | 111 | 50.2% | 50 | 51.5% | | 0.03 |
| Social | Mean-high | 10 | 4.5% | 19 | 19.6% | **0.001** * | **0.51** † |
| | Mean | 26 | 11.8% | 12 | 12.4% | | 0.02 |
| | Mean-low | 37 | 16.7% | 26 | 26.8% | | 0.25 |
| | Low | 148 | 67.0% | 40 | 41.2% | | **0.52** † |
| *Age-onset-duration* | | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| |
| Age (yrs-old) | | 49.14 | 12.28 | 43.22 | 11.44 | **0.001** * | **0.50** † |
| Onset of the addiction (yrs) | | 37.61 | 12.22 | 34.46 | 11.61 | **0.032** * | 0.26 |
| Duration of the addiction(yrs) | | 5.62 | 5.61 | 5.75 | 5.01 | 0.841 | 0.02 |
| *Psychopathology(SCL-90R)* | | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| |
| Somatic | | 1.64 | 0.91 | 1.45 | 1.08 | 0.103 | 0.19 |
| Obsessive–compulsive | | 1.59 | 0.84 | 1.82 | 1.02 | **0.034** * | 0.25 |
| Interpersonal sensitivity | | 1.45 | 0.87 | 1.50 | 1.02 | 0.670 | 0.05 |
| Depressive | | 2.15 | 0.90 | 2.14 | 1.10 | 0.890 | 0.02 |
| Anxiety | | 1.54 | 0.92 | 1.55 | 1.07 | 0.896 | 0.02 |
| Hostility | | 1.10 | 0.84 | 1.30 | 1.00 | 0.066 | 0.22 |
| Phobic | | 0.93 | 0.92 | 0.89 | 1.00 | 0.745 | 0.04 |
| Paranoid | | 1.27 | 0.81 | 1.37 | 0.95 | 0.356 | 0.11 |
| Psychotic | | 1.19 | 0.78 | 1.22 | 0.90 | 0.793 | 0.03 |
| GSI score | | 1.54 | 0.74 | 1.56 | 0.89 | 0.838 | 0.02 |
| PST score | | 56.81 | 18.46 | 54.79 | 21.42 | 0.393 | 0.10 |
| PSDI score | | 2.28 | 0.59 | 2.36 | 0.70 | 0.308 | 0.12 |
| *Personality (TCI-R)* | | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| |
| Novelty seeking | | 109.71 | 12.08 | 115.07 | 13.78 | **0.001** * | 0.41 |
| Harm avoidance | | 110.98 | 15.62 | 111.64 | 19.78 | 0.749 | 0.04 |
| Reward dependence | | 101.14 | 13.06 | 103.53 | 16.36 | 0.168 | 0.16 |
| Persistence | | 103.86 | 17.48 | 105.05 | 19.21 | 0.589 | 0.06 |
| Self-directedness | | 117.96 | 18.09 | 121.43 | 22.77 | 0.147 | 0.17 |
| Cooperativeness | | 133.01 | 13.25 | 134.32 | 15.84 | 0.445 | 0.09 |
| Self-transcendence | | 68.29 | 15.15 | 66.89 | 16.67 | 0.460 | 0.09 |

Note. GD: gambling disorder; BSD: buying/shopping disorder; SD: standard deviation; * bold: significant comparison; † bold: effect size into the mild-moderate (\|*d*\| > 0.50) to large-high range (\|*d*\| > 0.80).

### 3.2. Latent Classes

Table 2 includes the results of the classification process for the solutions based on latent classes 1 to 6. The most optimal solution selected in this study was the 4-latent class model (abbreviated as LT1, LT2, LT3 and LT4). This solution achieved the lowest AIC and BIC indexes, as well as the highest entropy value (compared to solutions for latent classes 2, 3 and 5). Solutions for latent classes 5 and 6 were not considered due the low sample size for some groups.

**Table 2.** Results of the LCA.

| Model # Class. | Akaike (AIC) | Bayesian (BIC) | Sample-Size Adjusted BIC | Entropy | | Sample Size Count | Sample Size % | Online Probab. |
|---|---|---|---|---|---|---|---|---|
| 1 | 39,372.954 | 39,508.388 | 39,394.203 | 1.000 | T1 | 318 | 100.0% | 1.000 |
| 2 | 20,854.429 | 20,986.101 | 20,875.089 | 0.959 | T1 | 188 | 59.1% | 0.993 |
| | | | | | T2 | 130 | 40.9% | 0.983 |
| 3 | 20,713.397 | 20,916.548 | 20,745.272 | 0.924 | T1 | 44 | 13.8% | 0.951 |
| | | | | | T2 | 125 | 39.3% | 0.972 |
| | | | | | T3 | 149 | 46.9% | 0.974 |
| 4 | 20,625.497 | 20,900.127 | 20,668.587 | 0.939 | T1 | 39 | 12.3% | 0.997 |
| | | | | | T2 | 69 | 21.7% | 0.912 |
| | | | | | T3 | 109 | 34.3% | 0.997 |
| | | | | | T4 | 101 | 31.8% | 0.963 |
| 5 | 20,762.98 | 21,109.089 | 20,817.285 | 0.895 | T1 | 10 | 3.1% | 0.973 |
| | | | | | T2 | 40 | 12.6% | 0.847 |
| | | | | | T3 | 206 | 64.8% | 0.962 |
| | | | | | T4 | 52 | 16.4% | 0.916 |
| | | | | | T5 | 10 | 3.1% | 0.979 |
| 6 | 20,591.177 | 21,008.764 | 20,656.696 | 0.894 | T1 | 11 | 3.5% | 0.957 |
| | | | | | T2 | 33 | 10.4% | 0.931 |
| | | | | | T3 | 112 | 35.2% | 0.953 |
| | | | | | T4 | 100 | 31.4% | 0.903 |
| | | | | | T5 | 42 | 13.2% | 0.945 |
| | | | | | T6 | 20 | 6.3% | 0.937 |

Note. # Class: number of latent classes; AIC: Akaike's information criterion; BIC: Schwarz's Bayesian criterion.

### 3.3. Comparison between the Latent Classes for the Treatment Outcomes

Table 3 displays the risk of dropout and relapse during the CBT. LT3 accumulated the highest incidence of dropouts and LT4 the highest incidence of relapse. LT1 included the lowest risk of relapse (as well as the lowest mean of euros spent in relapse episodes). Kaplan–Meier functions for the rate of dropout and relapse in the study are plotted in Figure 1 (LT1 was the group with the highest cumulative survival estimates for both these outcomes). Results of the Log Rank test achieved significant results for the cumulative survival curves for dropouts comparing LT1 versus LT3 ($\chi^2 = 3.99$, $p = 0.046$) and LT1 versus LT4 ($\chi^2 = 5.48$, $p = 0.019$). For the relapses, Log Rank tests obtained significant results comparing LT1 versus the other latent classes ($\chi^2 = 9.99$ and $p = 0.002$ compared to LT2, $\chi^2 = 11.14$ and $p = 0.001$ compared to LT3, and $\chi^2 = 17.63$, $p < 0.001$ compared to LT4). Based on the progression during the treatment, LT1 was labeled as "good progression to recovery", LT2 as "middle progression", LT3 as "bad progression to dropout" and LT4 as "bad progression to relapse".

**Table 3.** Comparison between the latent classes for the CBT outcomes.

| | LT1; *n* = 39 | | LT2; *n* = 69 | | LT3; *n* = 109 | | LT4; *n* = 101 | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | *n* | % |
| Risk of dropout | 21 | 53.8% | 39 | 56.5% | 77 | 70.6% | 52 | 51.5% |
| Risk of relapse | 4 | 10.3% | 27 | 39.1% | 43 | 39.4% | 51 | 50.5% |
| | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* |
| [1] Number of sessions | 9.26 | 3.04 | 8.41 | 2.90 | 8.03 | 2.83 | 8.59 | 2.93 |
| [1] Number of relapses | 0.41 | 0.76 | 0.87 | 1.28 | 0.97 | 1.38 | 1.63 | 2.07 |
| [1] Euros spent/relapses | 36.8 | 37.3 | 155.6 | 156.1 | 116.9 | 117.4 | 116.5 | 117.0 |

| | Pairwise comparisons | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LT1–LT2 | | LT1–LT3 | | LT1–LT4 | | LT2–LT3 | | LT2–LT4 | | LT3–LT4 | |
| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Risk of dropout | 0.788 | 0.05 | 0.057 | 0.35 | 0.802 | 0.05 | 0.054 | 0.29 | 0.518 | 0.10 | **0.004** * | 0.40 |
| Risk of relapse | **0.001** * | **0.70** † | **0.001** * | **0.71** † | **0.001** * | **0.93** † | 0.966 | 0.01 | 0.144 | 0.23 | 0.108 | 0.22 |
| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| [1] Number of sessions | 0.156 | 0.29 | **0.028** * | 0.42 | 0.243 | 0.22 | 0.392 | 0.13 | 0.679 | 0.06 | 0.155 | 0.20 |
| [1] Number of relapses | **0.019** * | 0.44 | **0.002** * | **0.50** † | **0.001** * | **0.78** † | 0.612 | 0.08 | **0.003** * | 0.44 | **0.007** * | 0.37 |
| [1] Euros spent/relapses | **0.001** * | **1.05** † | **0.001** * | **0.92** † | **0.001** * | **0.92** † | 0.077 | 0.28 | 0.077 | 0.28 | 0.981 | 0.00 |

Note. SD: standard deviation; [1] negative binomial model; * bold: significant comparison; † bold: effect size into the ranges mild-moderate to large-high; LT1: good progression to recovery; LT2: middle progression; LT3: bad progression to dropout; LT4: bad progression to relapse.

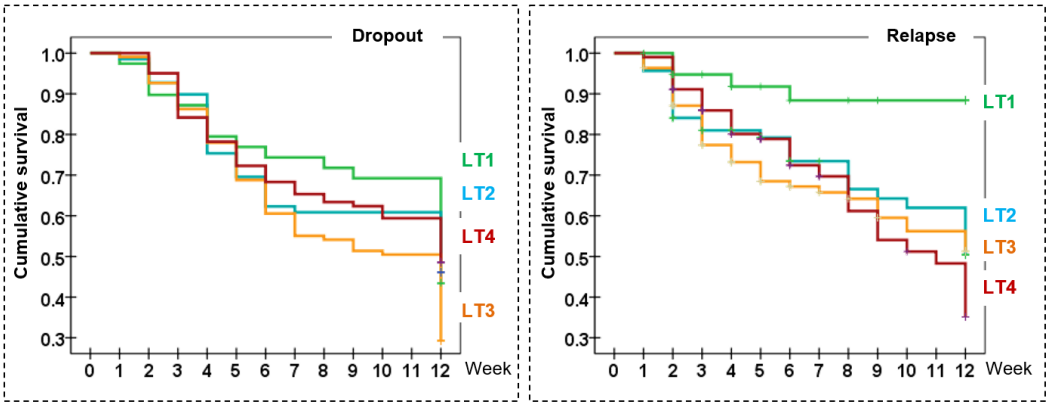


**Figure 1.** Kaplan–Meier functions for the incidence rate of dropout and relapse. Note. LT: latent class; LT1: good progression to recovery; LT2: middle progression; LT3: bad progression to dropout; LT4: bad progression to relapse.

### *3.4. Comparison between the Latent Classes for Sociodemographic and Diagnosis Profile*

The upper block of Table 4 shows the distribution of the diagnostic subtype within the latent classes (see also Figure 2). No statistical differences were found (effect size for the proportion differences were also within the low-poor range).

Table 4 also shows the distribution of the sociodemographic variables and the comparison between the latent classes. LT1 was characterized by including the highest proportion of patients with the highest education levels, employed and within the highest socioeconomic position indexes. LT2 was characterized by the highest proportion of patients with low education levels, unemployed and within the most unfavorable socioeconomic levels. No differences between LT3 and LT4 were found for the sociodemographic features.

### *3.5. Comparison between the Latent Classes for Clinical Measures at Baseline*

LT1 was characterized by the healthiest psychopathological state (the lowest scores in the SCL-90R), the lowest scores in harm avoidance and self-transcendence and the highest scores in reward dependence, persistence, self-directedness and cooperativeness (see Table 5). LT2 included patients with the oldest mean age and the latest onset of the behavioral addiction, the lowest novelty seeking score and the highest self-transcendence

level; this latent class also included the lowest proportion of patients who reported debts related to the behavioral addiction and autolysis behaviors. LT3 was defined by the youngest mean age, the earliest onset of the behavioral addiction, high scores in the psychopathological factors, high score in harm avoidance and the highest proportion of patients who reported autolysis behavior. LT4 also registered high scores in the psychopathology levels, high scores in harm avoidance and the lowest score in self-directedness.

**Table 4.** Comparison between the latent classes for the diagnosis subtype and the sociodemographics.

| | | LT1; *n* = 39 | | LT2; *n* = 69 | | LT3; *n* = 109 | | LT4; *n* = 101 | |
|---|---|---|---|---|---|---|---|---|---|
| | | *n* | % | *n* | % | *n* | % | *n* | % |
| Diagnosis | GD | 25 | 64.1% | 52 | 75.4% | 68 | 62.4% | 76 | 75.2% |
| | BSD | 14 | 35.9% | 17 | 24.6% | 41 | 37.6% | 25 | 24.8% |
| Education | Prim. | 14 | 35.9% | 50 | 72.5% | 60 | 55.0% | 48 | 47.5% |
| | Secondary | 18 | 46.2% | 14 | 20.3% | 40 | 36.7% | 42 | 41.6% |
| | University | 7 | 17.9% | 5 | 7.2% | 9 | 8.3% | 11 | 10.9% |
| Marital | Single | 12 | 30.8% | 28 | 40.6% | 52 | 47.7% | 40 | 39.6% |
| | Married | 19 | 48.7% | 27 | 39.1% | 41 | 37.6% | 39 | 38.6% |
| | Divorced | 8 | 20.5% | 14 | 20.3% | 16 | 14.7% | 22 | 21.8% |
| Employed | Unempl. | 9 | 23.1% | 46 | 66.7% | 46 | 42.2% | 56 | 55.4% |
| | Employed | 30 | 76.9% | 23 | 33.3% | 63 | 57.8% | 45 | 44.6% |
| Social | Mean-high | 7 | 17.9% | 5 | 7.2% | 10 | 9.2% | 7 | 6.9% |
| | Mean | 7 | 17.9% | 5 | 7.2% | 12 | 11.0% | 14 | 13.9% |
| | Mean-low | 8 | 20.5% | 8 | 11.6% | 29 | 26.6% | 18 | 17.8% |
| | Low | 17 | 43.6% | 51 | 73.9% | 58 | 53.2% | 62 | 61.4% |

| | | Pairwise comparisons | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | LT1–LT2 | | LT1–LT3 | | LT1–LT4 | | LT2–LT3 | | LT2–LT4 | | LT3–LT4 | |
| | | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Diagnosis | GD | 0.214 | 0.25 | 0.849 | 0.04 | 0.187 | 0.24 | 0.072 | 0.28 | 0.986 | 0.00 | 0.096 | 0.28 |
| | BSD | | | | | | | | | | | | |
| Education | Prim. | **0.001** * | **0.75** † | 0.072 | 0.39 | 0.352 | 0.24 | 0.053 | 0.36 | **0.005** * | **0.52** † | 0.528 | 0.15 |
| | Secondary | | **0.56** † | | 0.19 | | 0.09 | | 0.37 | | **0.47** † | | 0.10 |
| | University | | 0.33 | | 0.29 | | 0.20 | | 0.04 | | 0.13 | | 0.09 |
| Marital | Single | 0.553 | 0.21 | 0.184 | 0.35 | 0.521 | 0.19 | 0.524 | 0.14 | 0.973 | 0.02 | 0.323 | 0.16 |
| | Married | | 0.19 | | 0.22 | | 0.20 | | 0.03 | | 0.01 | | 0.02 |
| | Divorced | | 0.01 | | 0.15 | | 0.03 | | 0.15 | | 0.04 | | 0.18 |
| Employed | Unemplo. | **0.001** * | **0.91** † | **0.034** * | 0.41 | **0.001** * | **0.68** † | **0.001** * | **0.50** † | 0.143 | 0.23 | 0.055 | 0.27 |
| | Employed | | | | | | | | | | | | |
| Social | Mean-high | **0.018** * | 0.33 | 0.266 | 0.26 | 0.144 | 0.34 | **0.039** * | 0.07 | 0.306 | 0.01 | 0.378 | 0.08 |
| | Mean | | 0.33 | | 0.20 | | 0.11 | | 0.13 | | 0.22 | | 0.09 |
| | Mean-low | | 0.25 | | 0.14 | | 0.07 | | 0.39 | | 0.18 | | 0.21 |
| | Low | | **0.63** † | | 0.19 | | 0.36 | | 0.43 | | 0.27 | | 0.17 |

Note. GD: gambling disorder; BSD: buying/shopping disorder; BA: behavioral addiction; SD: standard deviation; * bold: significant comparison; † bold: effect size into the ranges mild-moderate to large-high; LT1: good progression to recovery; LT2: middle progression; LT3: bad progression to dropout; LT4: bad progression to relapse.

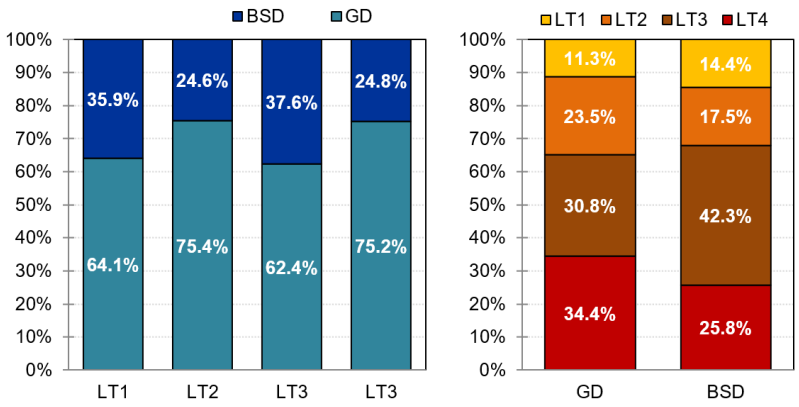


**Figure 2.** Distribution of the diagnostic subtype within each latent class. Note. BSD: buying/shopping disorder; GD: gambling disorder; LT: latent class; LT1: good progression to recovery; LT2: middle progression; LT3: bad progression to dropout; LT4: bad progression to relapse.

**Table 5.** Comparison between the latent classes for the clinical measures at baseline.

| | **LT1; *n* = 39** | | **LT2; *n* = 69** | | **LT3; *n* = 109** | | **LT4; *n* = 101** | |
|---|---|---|---|---|---|---|---|---|
| | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* |
| Age (yrs) | 44.69 | 8.45 | 61.51 | 7.05 | 35.87 | 7.50 | 51.04 | 7.79 |
| Onset of BA (yrs) | 34.37 | 8.40 | 52.94 | 6.38 | 25.00 | 5.52 | 38.96 | 6.23 |
| Duration of BA (yrs) | 5.21 | 4.58 | 4.12 | 3.70 | 7.08 | 6.60 | 5.36 | 5.01 |
| SCL-90R Somatic | 0.64 | 0.65 | 1.40 | 0.80 | 1.72 | 1.02 | 1.92 | 0.87 |
| SCL-90R Obses.co. | 0.66 | 0.56 | 1.35 | 0.73 | 1.91 | 0.84 | 2.00 | 0.83 |
| SCL-90R Sensitivity | 0.42 | 0.47 | 1.22 | 0.69 | 1.74 | 0.89 | 1.75 | 0.89 |
| SCL-90R Depressive | 0.91 | 0.79 | 1.88 | 0.79 | 2.43 | 0.80 | 2.50 | 0.85 |
| SCL-90R Anxiety | 0.46 | 0.48 | 1.27 | 0.72 | 1.76 | 1.00 | 1.92 | 0.86 |
| SCL-90R Hostility | 0.37 | 0.42 | 0.83 | 0.63 | 1.42 | 0.91 | 1.42 | 0.92 |
| SCL-90R Phobic | 0.12 | 0.17 | 0.68 | 0.69 | 1.07 | 1.01 | 1.23 | 0.98 |
| SCL-90R Paranoid | 0.49 | 0.46 | 1.03 | 0.62 | 1.47 | 0.85 | 1.62 | 0.85 |
| SCL-90R Psychotic | 0.32 | 0.40 | 0.95 | 0.62 | 1.34 | 0.80 | 1.55 | 0.78 |
| SCL-90R GSI score | 0.56 | 0.42 | 1.29 | 0.58 | 1.75 | 0.76 | 1.88 | 0.69 |
| SCL-90R PST score | 27.90 | 15.53 | 50.43 | 15.41 | 61.74 | 16.80 | 65.08 | 13.64 |
| SCL-90R PSDI score | 1.69 | 0.56 | 2.19 | 0.59 | 2.43 | 0.55 | 2.48 | 0.59 |
| TCI-R Novelty.se. | 114.4 | 13.9 | 108.3 | 12.0 | 112.4 | 12.8 | 111.1 | 12.8 |
| TCI-R Harm avoid. | 89.2 | 12.7 | 106.8 | 13.3 | 116.3 | 14.6 | 117.1 | 15.3 |
| TCI-R Reward dep. | 109.6 | 12.5 | 102.0 | 13.1 | 102.2 | 15.7 | 98.4 | 12.5 |
| TCI-R Persistence | 109.7 | 15.5 | 106.7 | 14.7 | 103.2 | 19.5 | 101.6 | 18.9 |
| TCI-R Self-directed. | 142.4 | 17.2 | 122.5 | 13.4 | 116.0 | 19.3 | 110.9 | 17.0 |
| TCI-R Cooperative. | 142.3 | 13.5 | 134.5 | 12.1 | 132.3 | 15.2 | 130.4 | 12.9 |
| TCI-R Self-Transcen. | 62.8 | 17.3 | 72.2 | 13.3 | 66.5 | 16.6 | 68.4 | 14.7 |
| | *n* | % | *n* | % | *n* | % | *n* | % |
| Debts due to BA | 19 | 48.7% | 20 | 29.0% | 57 | 52.3% | 47 | 46.5% |
| Autolysis behavior | 4 | 10.3% | 4 | 5.8% | 20 | 18.3% | 14 | 13.9% |
| Suicidal ideation | 6 | 15.4% | 15 | 21.7% | 18 | 16.5% | 22 | 21.8% |

| | Pairwise comparisons | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | LT1–LT2 | | LT1–LT3 | | LT1–LT4 | | LT2–LT3 | | LT2–LT4 | | LT3–LT4 | |
| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Age (yrs) | **0.001** * | **2.16** † | **0.001** * | **1.10** † | **0.001** * | **0.78** † | **0.001** * | **3.52** † | **0.001** * | **1.41** † | **0.001** * | **1.98** † |
| Onset of BA (yrs) | **0.001** * | **2.49** † | **0.001** * | **1.32** † | **0.001** * | **0.62** † | **0.001** * | **4.68** † | **0.001** * | **2.22** † | **0.001** * | **2.37** † |
| Duration of BA (yrs) | 0.309 | 0.26 | 0.060 | 0.33 | 0.881 | 0.03 | **0.001** * | **0.55** † | 0.138 | 0.28 | **0.020** * | 0.29 |
| SCL-90R Somatic | **0.001** * | **1.05** † | **0.001** * | **1.26** † | **0.001** * | **1.67** † | **0.021** * | 0.35 | **0.001** * | **0.62** † | 0.102 | 0.21 |
| SCL-90R Obses.co. | **0.001** * | **1.06** † | **0.001** * | **1.74** † | **0.001** * | **1.89** † | **0.001** * | **0.70** † | **0.001** * | **0.83** † | 0.392 | 0.11 |
| SCL-90R Sensitivity | **0.001** * | **1.36** † | **0.001** * | **1.87** † | **0.001** * | **1.89** † | **0.001** * | **0.66** † | **0.001** * | **0.68** † | 0.927 | 0.01 |
| SCL-90R Depressive | **0.001** * | **1.22** † | **0.001** * | **1.91** † | **0.001** * | **1.93** † | **0.001** * | **0.70** † | **0.001** * | **0.76** † | 0.543 | 0.08 |
| SCL-90R Anxiety | **0.001** * | **1.33** † | **0.001** * | **1.66** † | **0.001** * | **2.11** † | **0.001** * | **0.57** † | **0.001** * | **0.83** † | 0.167 | 0.17 |
| SCL-90R Hostility | **0.005** * | **0.85** † | **0.001** * | **1.49** † | **0.001** * | **1.47** † | **0.001** * | **0.77** † | **0.001** * | **0.76** † | 0.978 | 0.00 |
| SCL-90R Phobic | **0.002** * | **1.12** † | **0.001** * | **1.32** † | **0.001** * | **1.57** † | **0.004** * | 0.45 | **0.001** * | **0.65** † | 0.192 | 0.16 |
| SCL-90R Paranoid | **0.001** * | **0.98** † | **0.001** * | **1.43** † | **0.001** * | **1.65** † | **0.001** * | **0.60** † | **0.001** * | **0.80** † | 0.163 | 0.17 |
| SCL-90R Psychotic | **0.001** * | **1.19** † | **0.001** * | **1.62** † | **0.001** * | **1.99** † | **0.001** * | **0.56** † | **0.001** * | **0.86** † | **0.037** * | 0.26 |
| SCL-90R GSI score | **0.001** * | **1.44** † | **0.001** * | **1.92** † | **0.001** * | **2.31** † | **0.001** * | **0.67** † | **0.001** * | **0.92** † | 0.150 | 0.18 |
| SCL-90R PST score | **0.001** * | **1.46** † | **0.001** * | **2.09** † | **0.001** * | **2.54** † | **0.001** * | **0.70** † | **0.001** * | **1.01** † | 0.118 | 0.22 |
| SCL-90R PSDI score | **0.001** * | **0.88** † | **0.001** * | **1.35** † | **0.001** * | **1.38** † | **0.007** * | 0.42 | **0.001** * | **0.50** † | 0.507 | 0.09 |
| TCI-R Novelty.se. | **0.017** * | 0.47 | 0.403 | 0.15 | 0.163 | 0.25 | **0.035** * | 0.34 | 0.162 | 0.22 | 0.437 | 0.11 |
| TCI-R Harm avoid. | **0.001** * | **1.36** † | **0.001** * | **1.98** † | **0.001** * | **1.98** † | **0.001** * | **0.68** † | **0.001** * | **0.72** † | 0.660 | 0.06 |
| TCI-R Reward dep. | **0.007** * | **0.59** † | **0.004** * | **0.52** † | **0.001** * | **0.89** † | 0.944 | 0.01 | 0.094 | 0.28 | **0.049** * | 0.27 |
| TCI-R Persistence | 0.397 | 0.20 | 0.052 | 0.37 | **0.017** * | 0.47 | 0.207 | 0.20 | 0.071 | 0.30 | 0.523 | 0.08 |
| TCI-R Self-directed. | **0.001** * | **1.29** † | **0.001** * | **1.44** † | **0.001** * | **1.84** † | **0.014** * | 0.39 | **0.001** * | **0.76** † | **0.031** * | 0.28 |
| TCI-R Cooperative. | **0.005** * | **0.61** † | **0.001** * | **0.70** † | **0.001** * | **0.90** † | 0.301 | 0.16 | 0.054 | 0.33 | 0.301 | 0.14 |
| TCI-R Self-Transcen. | **0.002** * | **0.61** † | 0.201 | 0.22 | 0.054 | 0.35 | **0.016** * | 0.38 | 0.114 | 0.27 | 0.366 | 0.12 |
| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| | *p* | \|*d*\| |
| Debts due to BA | **0.040** * | 0.41 | 0.701 | 0.07 | 0.817 | 0.04 | **0.002** † | **0.51** * | **0.021** † | 0.36 | 0.404 | 0.12 |
| Autolysis behavior | 0.395 | 0.17 | 0.239 | 0.23 | 0.568 | 0.11 | **0.017** † | 0.40 | 0.093 | 0.28 | 0.378 | 0.12 |
| Suicidal ideation | 0.423 | 0.16 | 0.870 | 0.03 | 0.396 | 0.17 | 0.382 | 0.13 | 0.995 | 0.00 | 0.331 | 0.13 |

Note. BA: behavioral addiction; SD: standard deviation; * bold: significant comparison; † bold: effect size into the ranges mild-moderate to large-high; LT1: good progression to recovery; LT2: middle progression; LT3: bad progression to dropout; LT4: bad progression to relapse.

## 4. Discussion

The present study aimed to explore the existence of latent classes in women with GD and BSD based on the CBT response, and to identify the variables with discriminant

capacity in the empirical sub-groups identified in the LCA. The solution selected in this work as the optimal was the four latent classes, which achieved satisfactory fitting indexes and adequate clinical interpretation.

The diagnostic subtype (GD/BSD) was statistically equally distributed between the latent classes, regardless of the differences in the baseline. In this study, GD women reported lower education levels and poorer social indexes than BSD women, while BSD women reported younger age, earlier onset of the disorder, higher levels in the obsessive–compulsive dimension and higher scores in novelty seeking than GD women. The absence of association between the diagnosis and the latent sub-groups is a relevant result which suggests that these two forms of behavioral addiction among women may benefit from CBT and obtain similar efficacy.

LT1 was the sub-group with the most efficacious treatment responses (good recovery with a very low risk of relapse and the lowest incidence rate of dropout). This class was characterized by including the highest prevalence of patients within the highest socioeconomic levels, the lowest level of comorbid psychological symptoms and the most functional personality profile (lower harm avoidance and self-transcendence and higher reward dependence, persistence, self-directedness and cooperativeness). These results are consistent with systematic reviews conducted within GD and BSD areas, which find that less psychopathology at intake is the most consistent predictor of success after treatment across multiple time points, followed by lower addictive behavior at the beginning of the interventions, higher education levels and more adaptive personality traits [82,83]; this evidence is applicable for both genders.

LT3 and LT4 were associated with the poorest CBT outcomes (highest incidence rates of dropout and relapses). These sub-groups clustered women with the worst psychopathology, most dysfunctional personality profile (the highest scores in novelty seeking and harm avoidance and lowest scores in persistence, self-directedness and reward-dependence) and the highest likelihood of autolysis behavior. The personality profiles grouped within LT3 and LT4 are characteristic of women with distance in interpersonal interactions, social withdrawal, low interest in pleasing others, passive avoidance behaviors, concern when anticipating potential danger/s, reduced responsibility for one's own decisions, low self-esteem, lack of effectiveness to deal with daily situations and poor coping strategies. These attributes correlate with pessimistic behavior styles, the tendency towards shyness, frustration and to abandon goals at the slightest setback. Since these personality traits could contribute to poor treatment efficiency regardless of the behavioral addiction form, the severity of the addictive behaviors and the duration of the harms [58,84,85], these patients might benefit from the combination of CBT with other strategies. Such a strategy would increase motivation and make better use of treatment through motivational interventions (to improve the awareness of diseases), more flexible therapeutic guidelines, specific interventions focused on improving emotion regulation and goal setting other than definitive abstinence [86]. Patients with profiles defined by LT3 and Lt4 may even benefit from more intense treatment plans to encourage better attitudes and ensure that patients complete the follow-up and attain abstinence (for example, treatment plans with a larger number of sessions at increasing frequency). Carrying out the therapeutic strategies in group treatments (instead of individual programs, or a combination of individual and group treatments) may also feel more comfortable for patients characterized by LT3 and LT4 features. Knowing other women who share similar problems and struggles could increase interest for unmotivated patients and help them to hide their issues and avoid stigmatization/liability feelings. Even for those patients with more social difficulties, an Internet-based approach could represent an innovative and satisfactory format of CBT, enabling women with behavioral addictions to overcome many of the barriers related to conventional face-to-face formats [87].

LT3 was also defined by the youngest mean age, the earliest onset of the behavioral addiction and the longest duration of the disorder. Compared to LT3, LT4 clustered older women, later onset and shorter duration of the disorder. The mixed results regarding

age, onset and duration suggest that the contribution of these variables on the treatment response interacts with other variables of the sociodemographic and clinical profiles [58,88]. Precise treatment protocols should consider the full specific profile of each patient, with the purpose of applying those techniques with the best research evidence.

Compared to the other latent classes, LT2 showed moderate CBT outcomes (worse compared to LT1 and better compared to LT3 and LT4). Specific characteristics of this cluster are the lower likelihood of debts related to the behavioral addiction, older chronological age, later onset of the behavioral addiction and shorter duration of the disorder. First, it is not surprising that less monetary expenditure related to the addictive behaviors was associated to the cluster grouping the oldest age patients and those individuals with the shortest duration of the disease, since this specific group had probably lower incomes and placed more moderate bets. However, previous studies have identified financial harm as a strong measure of the severity of the disease [89]; therefore, it should be supposed to be closely associated with poor treatment response. It must be noted that other studies have also observed that the patients' sex interacts into the relationship between debts related to addictive behaviors and impairment levels. Moreover, it has been definitively shown that women problem gamblers with severe/extreme risks experience less significant financial consequences associated to addictive behaviors compared to women with a moderate risk [90,91]. Second, LT2 profile is representative of older individuals who exhibit a typical telescoping effect (addictive related problems develop more quickly than in younger age groups) [92] exacerbated by the typical aging-related cognitive biases [93]. Older individuals constitute a highly –vulnerable group with specific motivations for initiating and persisting in behavioral addictions (such as escaping loneliness and social isolation, relieving tension or coping with anxiety/depression symptoms due to the loss of a loved one or simply relieving boredom in retirement) [94,95]. Cognitive decline and physical–mental illness in older individuals also seem to play a central role in the onset, maintenance and escalation of addictive behaviors [96]. The absence of studies assessing the treatment response for behavioral addictions among older individuals does not allow us to know the specific role of these variables during the interventions. It seems essential that clinical settings adequately assess the concrete symptoms and negative consequences among older individuals with the aim of incorporating evidence-based integrative interventions to reduce physical and emotional problems. [97]. Healing-oriented holistic programs should include strategies to reduce chronic stress and impulsivity, and to improve social skills and emotional regulation (such as training in working memory and response inhibition). Medication should also be required in certain cases.

*Limitations*

The evidence in this study has several limitations and additional questions for future research. First, the analyses were conducted on samples of women who met clinical criteria for GD and BSD, which limits the extrapolation of the findings to men and other behavioral addictions (like gaming disorder). Additionally, while we did not consider groups of women with an explicit comorbid substance-related disorders (or other psychiatric disorders), it is not clear whether our results could be also be valid for samples including dual pathology conditions.

## 5. Conclusions

To our knowledge, this is the first intervention study focused on exploring the existence of empirical latent classes of women seeking treatment for GD and BSD based on the CBT outcomes and aimed at identifying variables with discriminative capacity on the subgroups. The identification of women-explicit features related to the treatment efficacy (that could be different from those reported for men) contribute to the knowledge of gender-specific processes involved in addictive behaviors and might be helpful for developing precise treatment plans for female patients The analysis of longitudinal data and multiple functioning areas is a further strength. Finally, the use of both person-centered and variable-

centered methods constitutes an advantage. In longitudinal designs, person-centered methods are useful to identify sub-groups of individuals who share particular attributes and provide useful techniques for addressing questions concerning differences in patterns of progressions (for example assessing the course of a treatment through LCA). Variable-centered approaches complement the analysis, providing data on the association between variables and concretely addressing the relative contribution of some predictors (in this study for exploring the variables with discriminative capacity) on a concrete outcome.

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## 4.3 Artículo 3

**Objetivos:**
En este artículo se contrastan los objetivos cuarto y quinto de la tesis.

> **4.** Estimar la prevalencia de esquizofrenia en pacientes que acuden a consulta debido a los problemas de la conducta de juego de apuesta.
>
> **5.** Comparar el perfil sociodemográfico y clínico de los pacientes con la condición dual de TJ más esquizofrenia de los pacientes con TJ sin esquizofrenia.

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**Resumen:**

La muestra incluyó 3754 pacientes atendidos de forma consecutiva en una unidad especializada en tratamiento de problemas asociados a una adicción comportamental. La prevalencia de esquizofrenia se estimó en 4.4% de los pacientes (intervalo de confianza del 95%: 3.8% a 5.1%).
Las variables asociadas a la presencia dual de TJ más esquizofrenia fueron estado civil (estar soltero/a), nivel educativo (niveles más bajos), situación laboral (inactiva), situación socioeconómica (desfavorecida), edad más joven, inicio más precoz de la conducta de juego y de los problemas de juego, peor estado psicopatológico global y perfil de personalidad más disfuncional (mayor nivel en evitación de daño y menor en cooperación, dependencia a la recompensa, persistencia y autodirección).
La presencia de esquizofrenia es aproximadamente 4 veces mayor que la que se identifica en la población general. La identificación de un fenotipo específico para pacientes con la condición dual de TJ más esquizofrenia alerta sobre la necesidad de que los protocolos de intervención para estos pacientes incluyan técnicas específicas para lograr una reducción en los comportamientos adictivos y prevenir futuras recaídas.

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# The prevalence and features of schizophrenia among individuals with gambling disorder

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Schizophrenia

ABSTRACT

*Background-objectives:* Few studies have analyzed the comorbid presence of gambling disorder (GD) with schizophrenia, its sociodemographic correlates and clinical implications. This study estimated the prevalence of the dual diagnosis (GD with schizophrenia) and the differences in the profiles of patients with and without the dual condition.

*Method:* The sample included n = 3,754 patients consecutively accepted for treatment for GD. Sociodemographics, gambling-related variables, psychopathological state and personality traits were assessed and compared between the groups.

*Results:* The prevalence of schizophrenia within patients who met clinical criteria for GD was 4.4% (95% confidence interval: 3.8%–5.1%). Variables related to the dual presence of GD with schizophrenia were single marital status, lower education level, inactive working status, socioeconomic disadvantage, younger age, earlier onset of gambling problems, worse global psychopathological state and more dysfunctional personality profile (higher level in harm avoidance and lower level in cooperativeness, reward dependence, persistence and self-directedness).

*Conclusion:* The presence of schizophrenia among patients with GD was around 4 times higher than the prevalence rate estimated in the reference general population. The differences in the profiles of GD patients with and without schizophrenia suggest that individuals with the dual diagnosis condition require unique assessment considerations and tailored treatment interventions specifically designed for the clinical and functioning higher risk.

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## 1. Introduction

Gambling disorder (GD) is defined as a psychiatric condition involving continued engagement (repeated and uncontrollable behaviors) in problematic gambling activities despite adverse problems and distress (American Psychiatric Association, 2013). Individuals with GD present a significant diminished self-control over engagement in the behavior, as well as an urge or craving state prior to engaging in the gambling activity. The prevalence of GD worldwide is estimated at between 0.1% and 5.8% during the last year of the survey across five continents, and between 0.7% and 6.5% during lifetime (Calado and Griffiths, 2016).

### 1.1. Dual presence of GD with schizophrenia

GD has been associated with high rates of multiple comorbid psychiatric conditions (Dowling et al., 2015; Sundqvist and Rosendahl, 2019; Yakovenko and Hodgins, 2018; Yau and Potenza, 2015), including psychotic states and schizophrenia. Prevalence studies in samples of patients with psychosis have estimated rates of comorbidity with problematic or disordered gambling at between 12% and 19% (Aragay et al., 2012; Desai and Potenza, 2009), and concluded that people with psychosis are between 3 and 4 times more likely to have problematic or disordered gambling compared with the general population (Haydock et al., 2015). Reciprocal relationships between GD and schizophrenia have also been obtained in some epidemiological studies, which have outlined that problematic and impaired gamblers could be at an elevated risk of experiencing psychosis compared to the general population (Cassetta et al., 2018; Corbeil et al., 2019). The study of Kim and colleagues found that 7.2% of patients seeking treatment for GD met diagnostic criteria for psychosis (Kim et al., 2018b), while other studies have published rates of schizophrenia among problematic gambling and GD at around 5% (Bergamini et al., 2018; Cassetta et al., 2018; Peritogiannis et al., 2020). Based on these epidemiological data it is likely that GD and psychotic disorders co-occur frequently, and it seems that one disorder may exacerbate the symptoms of the other (Yakovenko et al., 2016). But the extent to which individuals with GD could also exhibit psychotic symptoms is a relatively novel field, and the specific implications of this dual-disorder condition on clinical gambling profiles remain to be understood. In fact, recent research has warned that the high rates of addictive behaviors within schizophrenia (including both problem and pathological gambling and substance-use disorders) could contribute to the undetected presence of GD in clinical practices, thus far unexamined in empirical studies (Fortgang et al, 2018, 2020). In addition, the presence of active psychotic episodes in the schizophrenia spectrum is typically an exclusion criterion in most studies carried out with GD samples. As a consequence, wide gaps exist between the relatively scarce research evidence and its application in practice and public policy settings.

Several converging empirical lines have tried to obtain evidence regarding the overlap between GD and other multiple psychiatric conditions, in terms of shared etiological factors (including neurobiological performance, heritability, individual and contextual factors), clinical manifestations and treatment outcomes. These studies are currently contributing towards identifying key components for the specific concurrence between GD and schizophrenia. Impulsivity (impaired control) is one of the factors recognized as a major problem for the presence of the dual-diagnosis condition (Hodgins and Holub, 2015; Kräplin et al., 2014; Lee et al., 2013; Ouzir, 2013). In fact, the diverse impulsivity domains (cognitive, affective and motor) have been considered essential features for the onset and progression of a wide array of psychopathological problems (Krueger and Eaton, 2015; Nolen-Hoeksema and Watkins, 2011; Robbins et al., 2012), and have led to it being considered as a transdiagnostic component within the well-known *impulsive compulsive disorder spectrum*. This construct has served to harbor diverse neuropsychiatric conditions (based on the inappropriate behaviors related to maladaptive impulses), and epidemiological studies have evidenced that it is common to observe the coexistence of multiple comorbid conditions within the spectrum and/or with other disorders also characterized by impaired control mechanism, such as GD with schizophrenia (Dowling et al., 2015; Lorains et al., 2011). For example, the study conducted by Aragay and colleagues within a sample of psychiatric inpatients shows that the in terms of comorbidity, the psychotic disorder spectrum achieve a higher prevalence of gambling problems than other psychiatric disorders (Aragay et al., 2012).

Second, neuropsychological research has also found similar dysfunctions in brain pathology and neurobiological processes that could contribute towards explaining the connection between GD and schizophrenia. Alterations in the motivation-reward systems, disturbances in the reward-directed behavioral circuitry (primary ventral striatum and medial prefrontral cortex) and abnormalities in neurotransmitter systems (such as dopamine, serotonin or glutamate) have been postulated as shared characteristics in both GD and psychotic disorders (Clark et al., 2019; Howes et al., 2015; Leicht et al., 2020; Potenza and Chambers, 2001; Ruiz et al., 2020; Selvaraj et al., 2014; Zack et al., 2020).

Third, multiple clinical manifestations are also common in GD and psychosis phenotypes. For example, the age of onset is typically in adolescence or young adulthood (Gin et al., 2020; Welte et al., 2015), particularly within the male sex. Personality profiles characterized by high levels of harm avoidance and low levels of self-directedness are also common in GD and the schizophrenic spectrum (Black et al, 2012, 2013; Sundqvist and Wennberg, 2015). High difficulties in emotion regulation and impairing cognitive biases around gambling activity have also been postulated as key features explaining the comorbid presence of GD with schizophrenia (Di Trani et al., 2017; Lawlor et al., 2020; Liu et al., 2020; Livet et al., 2020; Mallorquí-Bagué et al., 2018a, 2018b; Yakovenko et al., 2016). Finally, clinical studies have observed that the dual diagnosis of GD with schizophrenia is related to worse psychopathological state, evidenced by increased gambling severity (Kim et al., 2018a) and elevated risk for other psychiatric disorders (mainly substance and non-substance addictive behaviors) (Borras and Huguelet, 2007). But the number of studies analyzing the correlates of the dual diagnosis of GD and schizophrenia is low, and therefore emerging evidences must be considered with caution. New research is required to support (or refute) the pathophysiology of the concurrence of both psychiatric conditions, and to identify key features that may complicate the course, treatment adherence and overall prognosis of the illness.

### 1.2. Objectives

In summary, the comorbid presence of GD with dual diagnosis of schizophrenia constitutes a high-risk clinical group, which causes significant morbidity and disability to patients. But this vulnerable population remains understudied, and new research is required to assess the possible interactions of the schizophrenia on the gambling phenotypes. The objectives of this study were to estimate the prevalence of schizophrenia in a large sample of GD treatment seeking patients, and to assess differences in the sociodemographic and clinical profiles of patients who reported the dual diagnostic condition (GD plus psychosis).

Based on the available empirical research studies, we hypothesized a higher prevalence of psychosis among the GD patients (compared with the prevalence reported for the general population) and worse psychopathological functioning among patients with GD comorbid with schizophrenia.

## 2. Material and methods

### 2.1. Participants

This study analyzed a sample of $n = 3{,}754$ GD patients, accepted for treatment at the Pathological Gambling Outpatient Unit at University

Hospital of Bellvitge. This is a tertiary treatment service specialized in the assessment and treatment of gambling disorder and other behavioral addictions. All the participants were recruited between January 2005 and June 2020. Inclusion criteria in the study were age 18+ years and a sufficient level of education and cognitive capacity to complete the self-report measures. Exclusion criteria were the presence of an organic mental disorder, intellectual disability or neurodegenerative disorder (such as Parkinson's disease).

The participants in this study were consecutively attended at the treatment unit. All the patients routinely signed their acceptance for facilitating their data to the research studies approved by the Ethics Committee of the institution (the acceptance rate was 100%).

All the participants in the study met DSM-5 criteria for GD. The distribution of the sex was n = 3,421 men (91.1%) versus n = 333 women (8.9%), and the mean age was 42.0 yrs (SD = 13.5). The number of single patients was n = 1,541 (41.0%), versus n = 1,709 married (45.5%) and n = 504 divorced (13.4%). Most patients reported primary level of education or lower [*n* = 2,167 (57.7%) versus n = 1,352 with secondary level (36%) and n = 235 university level (6.3%)], and were employed (*n* = 2,152, 57.3%). Social position index was distributed as follows: n = 3,126 (83.3%) into mean-low to low, n = 400 (10.7%) into mean and n = 228 (6.0%) into mean-high to high. Mean age of onset of the problematic gambling was 29.2 yrs (SD = 11.0) and the duration of the GD 6.1 yrs (SD = 6.0).

### 2.2. Measures

*Diagnostic Questionnaire for Pathological Gambling (according to DSM criteria)* (Stinchfield, 2003). This questionnaire was developed as a self-report tool with 19 items coded in a binary scale (yes-no), with the aim of assessing the diagnosis of GD according to the DSM-IV-TR (American Psychiatric Association, 2000). Currently, this DSM-IV measure has been adapted to measure DSM-5 diagnostic criteria for GD (American Psychiatric Association, 2013) by removing the illegal acts criterion and using the cutoff score of 4 symptoms-criteria. The Spanish adaptation of this diagnostic questionnaire has demonstrated good psychometric properties (Jiménez-Murcia et al., 2009). The internal consistency for this scale in the study sample was adequate (α = 0.73).

*Symptom Checklist-Revised (SCL-90-R)* (Derogatis, 1994). This self-report questionnaire was developed to assess psychopathological state with 90 items covering a broad range of psychological symptoms and problems. It is structured in nine primary dimensions/scales (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation and psychoticism) and three secondary global indices (global severity index, GSI, total positive symptoms, PST, and positive discomfort index, PSDI). This study used the Spanish adapted version, which has proved to have good psychometric features (Gonzalez De Rivera et al., 1989). The internal consistency in the sample of this study is shown in Table 2, and ranged from adequate (α = 0.78, for paranoia scale) to excellent (α = 0.98 for the global indices).

*Temperament and Character Inventory-Revised (TCI-R)* (Cloninger et al., 1994). This self-report questionnaire was developed to assess seven primary personality traits through 240 items, based on Cloninger's multidimensional model. It covers 4 dimensions of the individual's temperament (novelty seeking, harm avoidance, reward dependence and persistence) and 3 dimensions of the individual's character (self-directedness, cooperation and self-transcendence). The Spanish version of TCI-R used in the study obtained very good psychometric indexes (Gutiérrez-Zotes et al., 2004). The internal consistency in the sample of the study (shown in Table 2) was between adequate (α = 0.71 for novelty seeking) and good (α = 0.87 for persistence).

*Semi-structured clinical interview.* It was used to assess additional information, including socio-demographics (sex, marital status, education level, employment status and social position) and gambling problem-related variables (such as the age of onset of the problematic gambling, duration of the GD and the accumulated debts due to gambling behaviors). The socioeconomic status (SES) was measured according to the Hollingshead's Four Factor Index, which provides a classification based on four domains (Hollingshead, 2011): marital status, retired/employed status, educational attainment and occupational prestige. Substantive and methodological reasons have justified the widely use of the SES in medicine and public health, principally because it provides a simple recipe for combining the standard sociological variables of education and occupation. The different gambling activities were also assessed, which encompass group gambling behavior in three broad categories: non-strategic gambling (including those games which involve little decision-making or skill, and therefore gamblers cannot influence the outcome: slot-machines, bingo and lotteries), strategic gambling (including games in which gamblers attempt to use their ability to predict the outcome: poker, sports/animal betting, craps, etc.), and both non-strategic plus strategic. Finally, the presence of lifetime comorbid disorders was also assessed. This semi-structured interview was conducted by psychologists and psychiatrists with extensive experience spanning over more than 15 years in the assessment and treatment of problematic gambling and GD. This complete tool has been described elsewhere (Jiménez-Murcia et al., 2006). In addition to the assessment of the clinical and sociodemographic variables included in the semi-structured interview, the clinicians confirmed the diagnosis of GD provided by the *Diagnostic Questionnaire for Pathological Gambling,* and also helped participants to complete the self-report questionnaires to guarantee the absence of missing data.

*Diagnosis of schizophrenia.* All the participants with a diagnosis of schizophrenia had been referred to our treatment unit from local Community Mental health Centers because the psychosis was associated with GD. The condition of schizophrenia had been diagnosed after assessment by psychiatrist specialists in the treatment of this mental condition, based on the DSM-IV and the DSM-5 criteria.

### 2.3. Statistical analysis

The statistical analyses were carried out with Stata16 for windows (Stata-Corp, 2016). The comparison between the groups defined by the presence-absence of schizophrenia was based on chi-square tests ($\chi^2$) for categorical variables and the T-TEST for independent samples for quantitative measures.

The significance tests were complemented with the estimation of the effect sizes through the Cohen's-*d* measure, considered null for $|d|<$ 0.20, low-poor for $|d|>0.20$, moderate-medium for $|d|>0.50$ and large-high for $|d|>0.80$) (Cohen, 1988; Kelley and Preacher, 2012).

To control the increase in the Type-I error due to the multiple statistical comparisons, the Finner method was used, a procedure considered within the familywise error rate stepwise techniques which is more effective than the classical Bonferroni correction (Finner, 1993; Finner and Roters, 2001).

### 2.4. Ethics

All procedures were carried out in accordance with the Declaration of Helsinki of 1975, as revised in 2000. The data analyzed in this study were recruited during different research projects approved by the Ethics Committee of the Bellvitge University Hospital (Refs: PR241/11, PR286/14, PR329/19, PR338/17 and PR393/17). All subjects were informed about the study and all provided informed consent.

## 3. Results

### 3.1. Prevalence of schizophrenia in the study

The number of participants who with schizophrenia was n = 166, resulting in a prevalence rate equal to 4.42% [95% confidence interval (95%CI): 3.76%–5.08%]. At the time of the study, the number of

patients with schizophrenia was n = 132 (prevalence = 3.52; 95%CI: 2.93%–4.11%), while n = 151 reported the presence of these symptoms in the past (prevalence = 4.02; 95%CI: 3.39%–4.65%). Fig. 1 contains the line-chart displaying the evolution of the prevalence of psychosis in the study, which suggests an increasing linear trend.

### 3.2. Variables related to the presence of schizophrenia in the study

Table 1 shows the comparison of the patients with and without schizophrenia for the sociodemographic features, the age of onset of the problematic gambling and the duration of the GD. The presence of schizophrenia was related to a higher likelihood of being single, lower education level, unemployment status, and lower social position indexes. Patients with schizophrenia were also younger and reported earlier onset of the gambling problems.

Table 2 shows the comparison between the groups for the clinical measures analyzed in this work. Compared to patients without schizophrenia, the comorbid presence of schizophrenia and GD was related to worse psychopathological state (higher mean scores in the SCL-90R scales, except for hostility) and more dysfunctional personality profile (higher mean score in the harm avoidance trait, and lower means in reward dependence, persistence, self-directedness and cooperativeness) (Fig. 2). In addition, patients with schizophrenia increased the likelihood of non-strategic games as the preferred form of gambling and of tobacco use. No differences between the groups were found for the GD severity (measured with the number of DSM-5 criteria), the novelty seeking and self-transcendence personality traits, the gambling platform (offline versus online), the cumulated debts due to the gambling activity and the alcohol and drugs consumption.

## 4. Discussion

This study analyzed the presence of schizophrenia among patients seeking treatment for GD, as well as the differences in the gambling phenotypes comparing participants with and without schizophrenia. Prevalence of lifetime psychosis was 4.4%, and variables related to the dual presence of GD with psychosis were being single, lower education, unemployed status, lower social position indexes, younger age, earlier onset of the gambling problems and worse psychopathological state.

The study of the comorbidity of GD with other psychiatric conditions has mainly focused on substance-related problems (Graham, 2009; Grant and Chamberlain, 2020), but few studies have been conducted on the concurrence of GD with major psychiatric illness such as psychosis. To our knowledge, the first published study analyzed data recruited from n = 337 outpatients on the schizophrenic spectrum, and observed a prevalence of problematic or disordered gambling of around 20% (about 10% met criteria for GD and an additional 10% met criteria for lower severity but impairing features related with the gambling behavior) (Desai and Potenza, 2009). Next, the study of Haydock and colleagues conducted in a sample of n = 442 adults who met clinical criteria for psychosis obtained a prevalence of 4% for low-risk gambling activity, and 12% of the participants were classified between moderate to high gambling (Haydock et al., 2015). This study also found that a higher risk of gambling within the psychotic spectrum was related to lower education levels and lower socioeconomic status (as we have also observed in our research). Other empirical studies have published rates of schizophrenia among high-risk gamblers and GD patients at around 5%, an estimate four times higher than prevalence of psychosis in the reference general population (Bergamini et al., 2018; Cassetta et al., 2018; Kim et al., 2018a, 2018b; Peritogiannis et al., 2020).

The prevalence of schizophrenia in the GD patients analyzed in our study (equal to 4.4%) is consistent with the rates previously published, and our estimation is around 4 times higher than the prevalence of schizophrenia in the Spanish general population (around 1%) (Moreno-Küstner et al., 2018). This result can be interpreted in two ways: a) GD constitutes a highly vulnerable group for experiencing psychosis; and b) the presence of psychotic states represents high vulnerability to addictive behaviors, including gambling. This latter situation is particularly relevant, since a growing number of reports have related second-generation antipsychotics [such as aripiprazole (ARI), a partial D2 receptor agonist] with new onset gambling behavior or with increases in the severity of such behaviors (Corbeil et al., 2020; Gaboriau et al., 2014; Grall-Bronnec et al., 2016; Miuli et al., 2020; Smith et al., 2011). These studies suggest that the ARI-induced gambling disorder could be explained by the altered sensitization of dopamine receptors in certain genetically susceptible individuals, mostly in the early course of schizophrenia-related psychotic disorders. Studies with Parkinson's disease patients treated with dopaminergic agonistics for motor symptom management in early stages [such as pramipexole (PPX) and ropinirole (ROP)] have observed increased risk of developing behavioral complications within the impulse control disorder spectrum (including GD) (Gatto and Aldinio, 2019; Molde et al., 2018). Among Parkinson's disease with GD diminished striatal D2/D3 receptor level and increased in mesolimbic dopaminergic agonists tone has been reported, leading to an imbalance in the cortico-accumbens network implicated in reward signaling and behavioral changes (Buckholtz et al., 2010). It has also been observed that iatrogenic GD among Parkinson's disease patients may be mediated at least partly by increased activation of the intra-cellular signaling proteins GSK3β and CREB in the striatum (Cocker et al., 2019), and that the dopaminergic mesocorticolimbic system provides a role for shift behaviors in response to changing stimulus-reward contingencies (Houeto et al., 2016). But the results

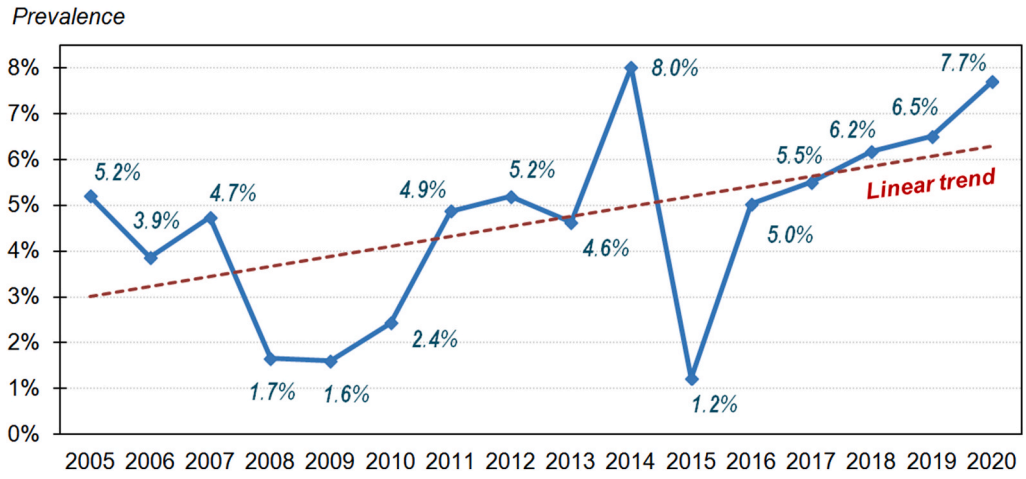


**Fig. 1.** Prevalence of patients with lifetime schizophrenia during the years 2005–2020 (n = 3,754).

**Table 1**
Descriptive for the sample and comparison between the groups.

| | | Total sample | | Schizophrenia | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | (*n* = 3,754) | | Absent (*n* = 3,588) | | Present (*n* = 166) | | | |
| | | *n* | % | *n* | % | *n* | % | *p* | \|*d*\| |
| Sex | Women | 333 | 8.9% | 319 | 8.9% | 14 | 8.4% | .840 | 0.02 |
| | Men | 3421 | 91.1% | 3269 | 91.1% | 152 | 91.6% | | |
| Marital status | Single | 1541 | 41.0% | 1428 | 39.8% | 113 | 68.1% | **<.001**[a] | **0.59**[b] |
| | Married | 1709 | 45.5% | 1677 | 46.7% | 32 | 19.3% | | **0.61**[b] |
| | Divorced | 504 | 13.4% | 483 | 13.5% | 21 | 12.7% | | 0.02 |
| Education | Primary | 2167 | 57.7% | 2060 | 57.4% | 107 | 64.5% | **.023**[a] | 0.14 |
| | Secondary | 1352 | 36.0% | 1297 | 36.1% | 55 | 33.1% | | 0.06 |
| | University | 235 | 6.3% | 231 | 6.4% | 4 | 2.4% | | 0.20 |
| Employed | Unemployed | 1602 | 42.7% | 1469 | 40.9% | 133 | 80.1% | **<.001**[a] | **0.87**[b] |
| | Employed | 2152 | 57.3% | 2119 | 59.1% | 33 | 19.9% | | |
| Social position | High | 54 | 1.4% | 54 | 1.5% | 0 | 0.0% | **<.001**[a] | 0.17 |
| | Mean-high | 174 | 4.6% | 172 | 4.8% | 2 | 1.2% | | 0.21 |
| | Mean | 400 | 10.7% | 393 | 11.0% | 7 | 4.2% | | 0.26 |
| | Mean-low | 1213 | 32.3% | 1176 | 32.8% | 37 | 22.3% | | 0.24 |
| | Low | 1913 | 51.0% | 1793 | 50.0% | 120 | 72.3% | | 0.47 |
| | *Mean* | *SD* | *Mean* | *SD* | *Mean* | *SD* | *P* | \|*d*\| | |
| Chronological age (yrs-old) | 42.02 | 13.45 | 42.12 | 13.58 | 39.83 | 10.19 | **.032**[a] | 0.19 | |
| Age of onset GD (yrs-old) | 29.20 | 10.98 | 29.29 | 11.02 | 27.25 | 9.83 | **.019**[a] | 0.20 | |
| Duration GD (years) | 6.13 | 6.03 | 6.10 | 5.99 | 6.81 | 6.87 | .138 | 0.11 | |

*Note*. SD: standard deviation.
[a] Bold: significant comparison.
[b] Bold: effect size into the range mild-moderate (|*d*|>0.50) to high-large (|*d*|>0.80).

**Table 2**
Comparison of the clinical measures.

| | | Schizophrenia | | | | | |
|---|---|---|---|---|---|---|---|
| | | Absent (*n* = 3,588) | | Present (*n* = 166) | | | |
| | α | *Mean* | *SD* | *Mean* | *SD* | *p* | \|*d*\| |
| DSM-5 criteria for GD | .727 | 7.19 | 1.52 | 7.37 | 1.43 | .141 | 0.12 |
| SCL-90R Somatization | .904 | 0.99 | 0.81 | 1.15 | 0.77 | **.013**[a] | 0.20 |
| SCL-90R Obsessive-compulsive | .877 | 1.19 | 0.81 | 1.44 | 0.84 | **<.001**[a] | 0.31 |
| SCL-90R Personal sensitivity | .869 | 1.06 | 0.81 | 1.52 | 0.95 | **<.001**[a] | **0.52**[b] |
| SCL-90R Depression | .906 | 1.56 | 0.89 | 1.76 | 0.92 | **.005**[a] | 0.22 |
| SCL-90R Anxiety | .890 | 1.06 | 0.79 | 1.31 | 0.88 | **<.001**[a] | 0.31 |
| SCL-90R Hostility | .849 | 0.96 | 0.83 | 1.03 | 0.84 | .307 | 0.08 |
| SCL-90R Phobic anxiety | .819 | 0.50 | 0.66 | 0.93 | 0.82 | **<.001**[a] | **0.58**[b] |
| SCL-90R Paranoia | .782 | 0.96 | 0.78 | 1.34 | 0.85 | **<.001**[a] | 0.46 |
| SCL-90R Psychotic | .854 | 0.94 | 0.74 | 1.26 | 0.91 | **<.001**[a] | 0.38 |
| SCL-90R GSI | .980 | 1.10 | 0.69 | 1.36 | 0.76 | **<.001**[a] | 0.36 |
| SCL-90R PST | .980 | 47.46 | 20.99 | 52.32 | 22.84 | **.004**[a] | 0.22 |
| SCL-90R PSDI | .980 | 1.92 | 0.58 | 2.14 | 0.62 | **<.001**[a] | 0.37 |
| TCI-R Novelty seeking | .707 | 110.13 | 13.01 | 108.80 | 10.20 | .193 | 0.11 |
| TCI-R Harm avoidance | .815 | 101.08 | 16.10 | 108.16 | 13.95 | **<.001**[a] | **0.51**[b] |
| TCI-R Reward dependence | .768 | 98.14 | 13.86 | 94.11 | 11.34 | **<.001**[a] | 0.32 |
| TCI-R Persistence | .867 | 108.41 | 18.72 | 103.74 | 17.96 | **.002**[a] | 0.25 |
| TCI-R Self-directedness | .847 | 126.27 | 19.62 | 120.83 | 16.80 | **<.001**[a] | 0.30 |
| TCI-R Cooperativeness | .807 | 129.77 | 15.44 | 125.04 | 13.82 | **<.001**[a] | 0.32 |
| TCI-R Self-transcendence | .830 | 63.64 | 14.14 | 65.20 | 13.63 | .163 | 0.11 |
| | | *n* | % | *n* | % | *p* | \|*d*\| |
| Gambling preference | Non-strategic | 2576 | 71.8% | 130 | 78.3% | **.012**[a] | 0.15 |
| | Strategic | 421 | 11.7% | 7 | 4.2% | | 0.28 |
| | Mixed | 591 | 16.5% | 29 | 17.5% | | 0.03 |
| Gambling platform | Offline | 3368 | 93.9% | 161 | 97.0% | .098 | 0.15 |
| | Online | 220 | 6.1% | 5 | 3.0% | | |
| Debts due to gambling behavior | 1797 | 50.1% | 71 | 42.8% | .065 | 0.15 | |
| Tobacco use/abuse | 2202 | 61.4% | 132 | 79.5% | **<.001**[a] | 0.41 | |
| Alcohol use/abuse | 574 | 16.0% | 27 | 16.3% | .927 | 0.01 | |
| Illegal drugs use/abuse | 383 | 10.7% | 24 | 14.5% | .125 | 0.11 | |

*Note*. SD: standard deviation. α: Cronbach's alpha.
[a] Bold: significant comparison.
[b] Bold: effect size into the range mild-moderate (|*d*|>0.50) to high-large (|*d*|>0.80).

suggesting a relationship between dopamine replacement therapies and the emergence of GD are still controversial and cannot prove the causality or the strength of the association (Heiden et al., 2017; Voon et al., 2017). In addition, the management of the gambling related symptoms in these patients is challenging, due the few effective treatment alternatives and/or counteractive strategies (Jeon and Bortolato, 2020).

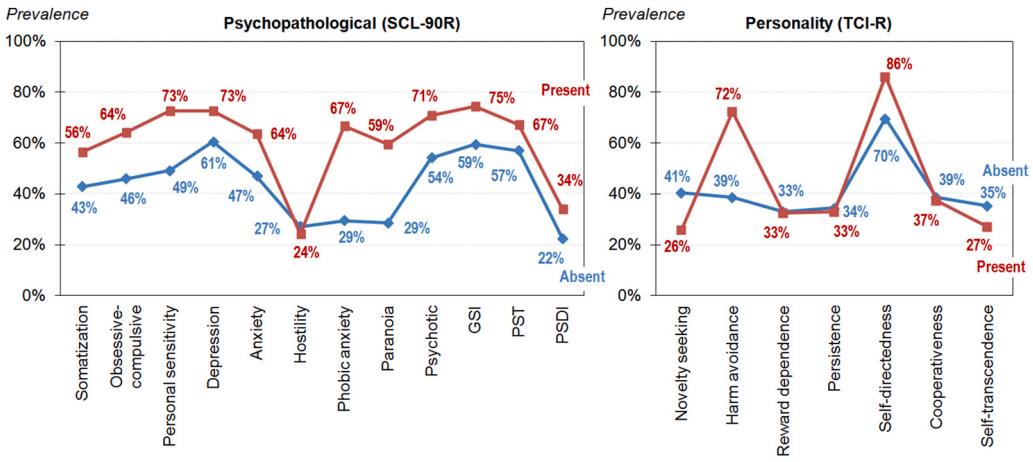


**Fig. 2.** Prevalence of patients outside the normative ranges (n = 3,754).

More details in future case reports and well-powered prospective controlled studies are required to draw reliable evidence about the specific underlying mechanisms (including individual and environmental vulnerability factors) explaining the concurrence of GD with schizophrenia.

In this study, the group of patients who exhibited gambling disorder with schizophrenia reported greater psychological distress, with higher mean scores in all the SCL-90R scales (except for hostility). This result is congruent with previous research that outlined that GD with psychosis constitutes a highly vulnerable condition which increases the risk of other poly-comorbid psychopathological conditions and suicidality (Yakovenko et al., 2016), as well as greater chasing and lower functioning (Yakovenko et al., 2018). And since previous studies have also related the concurrence of multiple psychiatric problems with worse treatment outcomes (Merkouris et al., 2016), it is crucial that clinical settings explore the presence of diverse symptoms among patients with GD with the aim of incorporating specific strategies to manage and reduce their impacts. Ultimately, the adequate identification of the diverse psychological processes underlying dysfunctional conditions such as addictive disorders (both substance use disorders and behavioral addictions) has relevant benefits during the treatment, since intervention on this specific mechanism (compared to therapies targeting a single disorder) contribute towards alleviating both primary psychopathologies and secondary concurrent psychiatric conditions (Krueger and Eaton, 2015). GD is a highly disabling mental condition which carries a great deal of stigma, and its developmental course is greatly worsened by the concurrent presence of schizophrenia (a mental health condition which impairs individuals' capacity to separate illusion from reality). Evidence-based integrative intervention plans should be specifically developed to treat the dual presence of GD with psychotic symptoms, addressed to the full range of physical and emotional problems, as well as the environmental influences that affect the patients' health. These healing-oriented holistic programs should include medication for correcting chemical imbalances, as well as other strategies to increase self-control and reduce impulsivity (such as training in working memory and response inhibition), to improve emotional regulation, to prevent or reduce chronic stress and to increase social skills. Pilot studies in this area have reported the beneficial effects of treatments particularly developed for patients with dual diagnoses of schizophrenia and GD focused on training reactive and proactive control, the ability to stop in response to a stop-stimulus, and the capacity to anticipate and prepare for a stop (these interventions have resulted in significant decreases in the number of gambling episodes and the amount of money spent on gambling) (Echeburúa et al, 2011, 2017). These studies have, however, failed to measure psychotic symptoms as an outcome of the treatments. Since few studies have analyzed the moderating role of psychiatric disorders as moderators of the efficacy of GD interventions (Dowling et al., 2016), future research is required to assess outcomes of treatments specifically matched to client GD with other comorbid conditions. For example, since emerging evidence suggest that association between schizophrenia and GD could endorse motivations for engaging in gambling activity and motivations for persisting in gambling that may be unique and not present in GD without schizophrenia (Yakovenko et al., 2016), therapeutic plans should focus in these specific mechanisms to achieve gambling abstinence and avoid relapses.

Regarding substance use, the only difference between the groups defined in our study based on the presence/absence of schizophrenia was for smoking habit (no differences emerged for the prevalence of alcohol and drugs consumption). It must be outlined that the previous cumulated evidences within this area are unambiguous: while some studies have observed that individuals with GD and psychosis are not more likely to be diagnosed with alcohol or substance use disorder (Kim et al., 2018a), other research has associated the presence of this dual-diagnostic condition with high rates of poly-substance use (Rash et al., 2016). It should be outlined that empirical studies exploring the specific mechanisms explaining the higher rates of substance use within patients with GD and schizophrenia have identified delay discounting function as a mediational link. Delay discounting refers to the loss of subjective value of a specific reward as a function of delay (it describes the concrete process by which individuals forego a larger later reward for a smaller earlier reward) (MacKillop et al., 2011). This measure represents one important type of choice impulsivity that may be informative regarding brain reward circuitry as preference for future wards (it involves the preferential selection of smaller sooner rewards over larger later rewards). Since adaptive reward processing is crucial for successful motivation, goal-directed behavior and goal-attainment across most domains of life, poor performance on delay discounting may directly impact the ability to appreciate the necessity of long-term events and planning for future. Based on the links between delay discounting to clinically relevant constructs (like treatment outcomes), this process has been suggested to be a trans-diagnostic feature underlying severe mental problems (Hamilton et al., 2015), including GD (Kyonka and Schutte, 2018) and schizophrenia (Horan et al., 2017). A current study aimed to investigate the relationship between GD and delay discounting in a sample of schizophrenia patients found that this choice impulsivity could represent a potential mechanism into the association between the dual comorbid condition (GD with schizophrenia) and substance (or poly-substance) use, but only among males (Fortgang et al., 2018). Concretely, the authors of this study observed that within the men subsample: a) the presence of GD was related with increased rates of delay discounting (compared with non-gambling); b) individuals with history of treatment for substances or poly-substances use

registered higher delay discounting (compared with non-consumers); and c) this may suggest that men who exhibit schizophrenia with substance related problems could be characterized by higher levels in some impulsivity domains, that positive reinforcement mechanisms could play a smaller role in the addictive processes within schizophrenia populations (compared to other diagnoses), and that lower levels of these features could create sensitivity to addiction. But these results should be considered with caution: mixed findings have been obtained in studies assessing the role of delay discounting, and these inconsistent evidences could be explained by the occurrence of comorbidity in chronic samples (Wang et al., 2020). Therefore, further studies should assess how choice impulsivity varies across psychiatric disorders and comorbid conditions, including the pathways between delay discounting and clinical manifestations among GD with schizophrenia.

Regarding personality traits, results obtained in this study are also consistent with previous research using the TCI-R questionnaire, which have reported higher levels in harm avoidance and lower scores in cooperativeness, self-directedness, reward dependence and persistence within the schizophrenic spectrum. High harm avoidance is characterized by excessive worrying, pessimism and shyness, as well as the tendency to be fearful, doubtful and easily fatigued; in this sense, high harm avoidance measures the tendency to respond with overall attenuation to aversive stimuli and to avoidant behavior due to the vulnerability to criticism and rejection, and it has been considered as a predictor of poor quality of life in the schizophrenic spectrum. Low cooperativeness describes the character of individuals as little empathic and callous, with a tendency to intolerance, social disinterest, unhelpfulness and revengefulness. It has been observed that high levels in harm avoidance and low levels in cooperativeness constitute a psychopathological related endophenotype of schizophrenia patients, which can contribute towards explaining some social dysfunctions observed in these patients (Fresán et al., 2015). High harm avoidance and low cooperativeness, low persistence and low self-directedness have also been reported within patients with schizophrenia compared with control subjects (Vrbova et al., 2017), and this specific profile has been linked to a higher risk of neurological soft signs (a well-known biological marker of schizophrenia, defined as minor neurological abnormalities without a definite localization in the brain, including expressions of simple sensory integration, disinhibition signs, motor coordination, complex motor sequencing) (Galindo et al., 2016; Mechri et al., 2010; Zhao et al., 2014).

Related to the personality profile identified in the GD with schizophrenia group, some studies have also explored the relationships between imaging/brain markers, personality features and its contribution to understanding the underpinnings of mental illness (Farde et al., 2018). With regard to psychosis-related traits, striatal amphetamine-induced dopamina release has been related with schizotypal personality traits and schizophrenic negative symptoms [such as social distress (discomfort in social situations and difficulty making/-keeping friendships), flat emotions or limited/inappropriate emotional responses, and incorrect interpretation of events] (Roiser et al., 2013; Woodward et al., 2011). Specific genes such as DRD4 and COMT (which regulate dopamine activity) have also been related with specific personality traits also related with the pathogenesis of psychotic disorders (concretely, sensation-novelty seeking and openness to experiences could be mediated by the pathophysiological mechanisms at the neurotransmitter level among psychotic patients) (Peritogiannis, 2015). A recent study has also found that polygenic risk for schizophrenia is associated with disordered gambling, concluding that that common genetics factors could have pleiotropic effects on both psychiatric conditions (one disorder could act as an intermediate phenotype providing a crucial link in a causal chain and setting the required conditions to facilitate the onset of the second disorder) (Piasecki et al., 2019). Anyway, the results of this study must be adequately contextualized. Two groups of patients were compared in this work: GD without schizophrenia and GD with schizophrenia. The different personality profile associated with the dual comorbid condition, although being consistent with previous results reported in samples within the schizophrenic spectrum, does not evidence a more severe dysfunctional personality profile than usual pronounced endophenotype traits of personality among schizophrenia patients. Future studies should detail the potential similarities and differences of the complete clinical profiles (symptoms, psychopathological distress and personality traits) comparing GD schizophrenia versus non GD schizophrenia patients.

Our study did not find a relationship between the concurrent presence of schizophrenia with GD and a greater level of gambling behavior. This result is not consistent with previous research, which observed higher gambling severity within problematic gamblers with psychosis (Fortgang et al., 2020). However, it is important to outline that this potential relationship could be explained by the mediating role of impulsivity, as stated by previous research (Kim et al., 2018b). Since our study did not include a measure of the impulsivity levels, it was not possible to assess this potential mediational role. Therefore, the absence of a direct relationship between the presence of schizophrenia and greater gambling severity levels in our study does not exclude an indirect effect through some impulsivity domain.

Finally, our study also obtained a higher likelihood for non-strategic gambling forms (slot-machines, bingo and lotteries) among the group of GD with comorbid psychosis state. Previous studies have outlined that the selection of a concrete form of gambling is clinically significant and provides a means of subtyping individuals with GD (Odlaug et al., 2011; Stevens and Young, 2010). It has been observed that two socioeconomic factors contribute towards increasing the odds of reporting non-strategic high-chance games: lower educational levels and disadvantaged socioeconomic status (Moragas et al., 2015), features characteristics of the group with the dual GD and psychosis condition. On the other hand, non-strategic gambling has also been related to disadvantageous cost-benefit decision-making (Jiménez-Murcia et al., 2020). Previous researchers reveal that patients with schizophrenia experience deficits in decision-making tasks, expressed by a systematic failure in the contingency learning required to distinguish between advantageous and disadvantageous selections when valuing frequencies and magnitudes of loss and gains (these patients show reinforcement learning deficits incorporating experiences of outcomes on previous tasks to assess the expected value of each new selection) (Boka et al., 2020; Brown et al., 2015; Kim et al., 2016). These characteristics of decision-making under risk typical of psychotic states could lead to a preferred non-strategic gambling, characterized by little deliberation or few skills (in these games, the potential result is totally dependent on chance).

### 4.1. Limitations and strengths

This study should be interpreted in the context of some limitations. First, the cross-sectional nature of the data, which did not allow cause-effect relationships to be determined. Second, this work was conducted within a sample of patients who met clinical criteria for GD, and therefore our findings cannot be generalized to complete original populations of problematic or non-treatment-seeking individuals. Third, among schizophrenia patients the antipsychotic medication and the presence/impact of the negative symptoms was not available (future research should examine the potential interactive contribution of these measures to the clinical profile and the GD treatment efficiency). Finally, this work was based on the comparison of two groups (GD versus GD with schizophrenia), and the lack of a non-gambling schizophrenia group do not allow to know if the phenotype obtained in the dual condition is actually more accurately characterizing schizophrenia rather than a comorbid picture. However, it must be outlined that our aim was to assess the differential characteristics related with the presence of schizophrenia among GD patients, since knowing this particular profile is required for developing more inclusive GD treatment approaches (patients with schizophrenia attended in centers specialized in GD treatment usually receive the standardized programs initially developed for patients without the dual comorbid condition). It is also important to

note that GD and schizophrenia share some common characteristics, such as specific community and sociodemographic features (poor academic performance and low socioeconomic status), personality traits (high scores in impulsivity and harm avoidance and low scores in persistence and self-directedness), and clinical features [such as cognitive difficulties (impaired decision making and planning), and the presence of multiple comorbid psychopathologies (such as substance related disorders, anxiety and depression)]. Therefore, it is relevant to assess the increased risk in the GD with schizophrenia profile compared to only GD for developing adequate assessment tools and personalized intervention plans.

The strengths of the study were its novelty (few research projects to date have explored phenotypes for GD with schizophrenia), the clinical origin of the data, the large sample size and the sampling procedure (consecutive patients over a long period).

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## Declaration of competing interest

All authors declare no conflicts of interest.

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## 4.4 Artículo 4

**Objetivos:**
En este artículo se contrastan los objetivos sexto y séptimo de la tesis.

> **6.** Explorar la estructura de relaciones entre los síntomas centrales del TJ y otros correlatos clínicos en pacientes con la condición dual de TJ más esquizofrenia, mediante análisis de redes.
>
> **7.** Identificar los nodos centrales y los que poseen mayor capacidad de asociación-vinculación en la red identificada.

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**Resumen:**

El análisis de redes se aplicó a una muestra de 179 pacientes (con edad dentro del rango 19 a 70) con TJ más esquizofrenia que consultaron debido a problemas de juego de apuesta. En el modelado se tuvieron en cuenta los síntomas centrales del TJ (tal como se define en la taxonomía DSM-5), los síntomas de ideación paranoide y psicótica (que se miden con el SCL-90R), la gravedad del TJ (deudas acumuladas por la conducta de juego y la presencia de conducta ilegal), consumo de sustancias (tabaco, alcohol y drogas ilegales) y perfil de personalidad (medido con el TCI-R).
Los nodos con la máxima autoridad fueron variables de personalidad y de malestar psicopatológico. Se identificaron también 4 clústeres de nodos, y los nodos con la mayor capacidad de vinculación fueron la búsqueda de novedad (una medida estrechamente relacionada con la impulsividad) y la dependencia a la recompensa.
La identificación de variables con la máxima centralidad/vinculación es particularmente útil para desarrollar herramientas de detección precoz temprana y también programas de intervención que tengan en cuenta las especificidades de estos pacientes.

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ORIGINAL ARTICLE

# Network Analysis of the Structure of the Core Symptoms and Clinical Correlates in Comorbid Schizophrenia and Gambling Disorder

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**Abstract**
Few studies have analyzed the clinical profile of treatment-seeking patients with the comorbid presence of schizophrenia (SCZ) and gambling disorder (GD), which warrants new research to assess the network structure of this complex mental condition. The aim of this study was to explore the organization of the symptoms and other clinical correlates of SCZ with GD. Network analysis was applied to a sample of $N = 179$ SCZ patients (age range: 19–70 years, mean=39.5, SD=9.9) who met clinical criteria for gambling disorder-related problems. Variables included in the network were the core GD symptoms according to the DSM-5, psychotic and paranoid ideation levels, global psychological distress, GD severity measures (debts and illegal behavior related with gambling), substances (tobacco, alcohol, and illegal drugs), and personality profile. The nodes with the highest authority in the network (variables of highest relevance) were personality traits and psychological distress. Four empirical modules/clusters were identified, and linkage analysis identified the nodes with the highest closeness (*bridge* nodes) to be novelty seeking and reward dependence (these traits facilitate the transition between the modules). Identification of the variables with the highest centrality/linkage can be particularly useful for developing precise management plans to prevent and treat SCZ with GD.

**Keywords** Network · Schizophrenia · Gambling disorder · Personality · Self-transcendence · Novelty seeking

Gambling disorder (GD) is a mental condition defined by persistent, repeated, uncontrollable, and maladaptive patterns of gambling activity, despite the multiple adverse problems and impaired functioning. GD is the only behavioral addiction classified in the latest edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), specifically as a "Substance-Related and Addictive Disorder"

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(American Psychiatric Association, 2013). The term behavioral addiction is employed for a set of behaviors that individuals become dependent on and crave, in the absence of physical substances. While discussions on whether or not to classify these non-substance addictions as mental disorders continue (Petry et al., 2018), the rationale for grouping GD into the same category than physical addictions into the DSM-5 lies in the growing body of empirical studies showing similarities in many features related to the endophenotype, concretely in the features affecting the neural circuitry of the brains' reward system (such as lack of control, tolerance, craving, and withdrawal) (Stefanovics & Potenza, 2022). Common treatment responses to interventions planed for addictive conditions have also been observed comparing GD with substance addictions (Hasanović et al., 2021; Li et al., 2020; Loo et al., 2019), as well as comorbidity patterns (Grant & Chamberlain, 2020).

The worldwide prevalence of GD is estimated at around 1% in the latest year of the survey, and between 0.7 and 6.5% of calculated lifetime (Calado & Griffiths, 2016). The large range for the point-estimated prevalences has been related to multiple features, such as the composition of the samples (clinical or population-based), the different assessment tools (screening or diagnostic tools), and the geographical areas (cultural differences and legislation about accessibility to gambling). For example, the lowest rates for problematic gambling have been observed in Oceania (between 0.4 and 0.7%), followed by Europe (between 0.1 and 3.4%), Asia (between 0.5 and 5.8%), and North America (between 2 and 5%) (Calado & Griffiths, 2016). A national multi-center research carried out by a government agency in Spain has estimated the prevalence of GD around 1% in the general population, the percentage of individuals who exhibit moderate- to high-risk behaviors related to gambling around 5%, and around 76% the subjects who reported participation in any gambling activity during the last 12 year (Dirección-General-Ordenación-Juego, 2017). This study also outlined significant gender differences, being the ratio of men versus women treatment seeking for gambling problems around 9:1.

Schizophrenia (SCZ) is a mental disorder that presents significant disability, characterized by a heterogeneous constellation of cognitive and behavioral symptoms associated with high affectation in all areas of life (including personal, family, social, educational, and occupational). According to the DSM-5 taxonomy, typical SCZ symptoms are delusions, hallucinations, disorganized speech, disorganized or catatonic behavior, and other negative mood states (such as diminished emotional expression) (American Psychiatric Association, 2013). Neurological studies differentiate between positive versus negative symptoms (Correll & Schooler, 2020; Marder & Galderisi, 2017; McCutcheon et al., 2019): (a) the positive symptom profile is defined by the disorganization of thinking and behaviors, and is reflected as an excess or distortion of normal functions (such as delusions, hallucinations, paranoia, or disorderly communication); and (b) negative symptoms are related to the motivation/interest and verbal/emotional areas, and are reflected as a diminution of normal behaviors (such as anhedonia, apathy, blunted affect, alogia, or avolition). Updated epidemiological reviews have shown that approximately one in 150 individuals are diagnosed within the psychosis disorder spectrum (SCZ and other forms of non-affective psychosis) at some point of their lifetime (Moreno-Küstner et al., 2018). And according to the latest report published by the World Health Organization, SCZ affects approximately 24 million people worldwide (around 1 in 300, 0.32%), the rate among adults being 1 in 222 (0.45%) (World Health Organization, 2022).

## Dual Presence of GD with SCZ

Epidemiological and clinical studies have observed multiple psychiatric conditions that are comorbid with GD (Dowling et al., 2015; Sundqvist & Rosendahl, 2019; Yakovenko & Hodgins, 2018; Yau & Potenza, 2015), including psychopathologies within the psychotic spectrum (SCZ as well as schizoaffective, schizophreniform, paranoid, and other disorders). It has been observed that the likelihood of problematic gambling behavior is at least 3 times higher among patients with psychosis compared with control population-based samples (Haydock et al., 2015), and gambling-related harm has been reported in the range of 12 to 30% of patients with psychotic disease (Aragay et al., 2012; Desai & Potenza, 2009).

It is also common for people with SCZ to exhibit other comorbid symptoms, including substance-related disorders and/or other behavioral addictions (Johnstone et al., 2022). It has been found that about half of those with SCZ use drugs, usually as coping mechanisms to deal with negative mood states (depression, anxiety, boredom, and loneliness), and during the course and prognosis of SCZ, a global prevalence of around 42% has been found for any substance use disorder (illicit drugs or alcohol) (Hunt et al., 2018). Unfortunately, the presence of comorbid conditions in patients with severe mental illness like SCZ is commonly underdiagnosed and treated (Onyeka et al., 2019), which might lead to interference with antipsychotic medication, less adherence to interventions or even to aggravation/exacerbation of the psychotic symptoms. Treatments of SCZ (typically antidopaminergic antipsychotics, complemented [or not] with psychotherapy) have basically been focused on managing the positive symptoms, proving efficacious for relieving these signs and reducing the risk of hospitalization and relapse (Bighelli et al., 2021; de Bartolomeis et al., 2022; Kishimoto et al., 2021). However, fewer effects have been obtained for negative and cognitive symptoms (such as processing speed, problem-solving, reasoning, and attention) and other psychological problems that are comorbid with SCZ (Haddad & Correll, 2018; Spark et al., 2022). It has also been found that aripiprazole, an antipsychotic (a partial dopamine agonist) used for the treatment of various mental disorders (including SCZ), has been related with the onset of gambling-related problems (Corbeil et al., 2019, 2020). Due to the nature of the dopamine dysfunction found in addictions (substance-related disorders and gambling disorder) (Lachance et al., 2019), pharmacovigilance studies are currently focusing on this association (Grall-Bronnec et al., 2016).

Research in samples characterized by comorbid psychiatric profiles has sought to identify explanatory mechanisms of the dual presence of GD with SCZ. It has been observed that impulsivity (including motor, cognitive, and affective dimensions) can act as a transdiagnostic construct (Hodgins & Holub, 2015; Kräplin et al., 2014; Lee et al., 2013; Ouzir, 2013). Alterations to brain and neurobiological processes have also been proposed as an explanation for the reciprocal relationships between GD and SCZ (mainly disturbances in the motivation-reward and neurotransmitter systems including dopamine, serotonin, or glutamate) (Clark et al., 2019; Howes et al., 2015; Leicht et al., 2020; Potenza & Chambers, 2001; Ruiz et al., 2020; Selvaraj et al., 2014; Zack et al., 2020). Other psychological variables contributing to the dual presence of GD with SCZ are male sex and young age (Gin et al., 2021; Welte et al., 2015), typical cognitive distortions related with the gambling activity (di Trani et al., 2017; Lawlor et al., 2020; Liu et al., 2020; Livet et al., 2020; Mallorquí-Bagué et al., 2018a, b; Yakovenko et al., 2016), severe difficulties in emotion regulation (Szerman et al., 2020), and personality profiles defined by high harm avoidance and low levels of self-directedness (Black et al., 2012, 2013; Sundqvist & Wennberg, 2015).

However, empirical studies focused on the dual pathology of GD with SCZ are scarce and limited. One reason for this is that one of the usual exclusion criteria in GD research is the existence of SCZ, and vice versa (many clinical studies focused on SCZ exclude other severe psychopathological forms such as addictions). Moreover, in clinical practice, and despite the proven reciprocal relationship between GD and SCZ (Cassetta et al., 2018; Corbeil et al., 2019), it is common not to assess the gambling behavior profiles of patients undergoing treatment for SCZ (clinicians usually consider SCZ to be the "primary" diagnosis and prescribe treatments that are specifically focused on monitoring positive and cognitive symptoms) (Fortgang et al., 2018, 2020). And since the presence of GD may not be reflected in the medical histories of individuals seeking treatment for SCZ, an accurate measure of the prevalence of the dual condition of SCZ plus GD remains unknown, as well as the structure of the clinical profile of this complex condition.

In summary, patients who exhibit GD plus SCZ are a highly vulnerable group because of the significant morbidity and disability caused by the complex structure of symptoms. But this high-risk population remains understudied, and new research is required to explore the underlying mechanisms of its clinical profiles. The objectives of this network study were to examine the structure of the core symptoms and other clinical correlates of GD and SCZ, as well as to identify the central nodes, those with the highest closeness and the existence of empirical modules-clusters of symptoms.

To our knowledge, this is the first study to have explored the network basis among patients with the dual presence of GD with SCZ; hence, we were unable to define empirical hypotheses regarding the most relevant nodes or those with the greatest linkage. However, according to an integrative model of mental illness based on the interaction between multi-level mechanisms, which posits that psychopathological states can be conceptualized as interactive systems of mutually reinforcing groups of symptoms that contribute to the onset and progression of diseases (Robinaugh et al., 2020), we expected (a) the existence of distinct modularity classes formed by nodes (symptoms/features) more densely connected together than to the rest of the network and (b) the identification of nodes referred with emotional withdrawal, impulsivity, and difficulty in socialization, as central and bridge nodes.

## Material and Methods

### Participants

The sample included $N$=179 consecutive treatment-seeking patients of the Pathological Gambling Outpatient Unit, Bellvitge University Hospital (Barcelona, Spain). This is a tertiary treatment service specialized in the assessment and treatment of gambling disorder and other behavioral addictions.

Participants were recruited between January 2005 and March 2022 (this long period was required to generate a large enough sample for statistical analyses). Inclusion criteria were age 18+ years, and meeting clinical criteria for GD and SCZ. Exclusion criteria were the presence of an organic mental disorder, intellectual disability, other mental disorder whose symptoms evolve paranoid and psychotic ideation, or neurodegenerative disorder (such as Parkinson's disease) (the presence of these conditions meant the measurement tools could not be used due the low reliability of the responses).

Most of the 179 participants were men ($n$=163, 91.1%), single ($n$=123, 68.7%), unemployed ($n$=140, 78.2%), reported primary education levels ($n$=116, 64.8%), pertained to a low social position index ($n$=129, 72.1%), and were born in Spain ($n$=168, 93.9%) (Table 1). Age was in the range of 19 to 70 years old (mean age was 39.5 years, SD=9.93). Mean onset of the GD was 26.5 years (SD=9.85), and mean duration of the GD-related problems was 6.8 years (SD=6.86).

Regarding gambling profile, the prevalence of patients achieving each DSM-5 criterion was between 71.5% for symptom-5 "often gambles when feeling distressed" and 92.7% for symptom-3 "repeated unsuccessful efforts to control-stop gambling." Regarding the preferred gambling activity, 76.0% of patients reported engaging in only non-strategic forms of gambling (this category encompasses gambling that involves little decision-making or skill, and hence no influence on the outcome, such as slot-machines, bingo, and lotteries) (Jiménez-Murcia et al., 2020). The percentage of patients who reported engaged in only strategic forms of gambling (in which gamblers attempt to use their ability to predict the outcome, such as poker, sports/animal betting, and craps) was 5%, and mixed types were reported by 19% of the participants. Regarding the modality of gambling, 92.2% did so in person, 3.9% did so online, and 3.9% reported mixed modalities. The presence of gambling-related debts was reported by 44.7% of patients, and gambling-related illegal behaviors (such as robbery or theft) were observed among 29.6% of patients.

The point prevalence of substance use was 78.2% for tobacco, 17.3% for alcohol, and 14.5% for illegal drugs. For the SCL-90R measures, the number of patients in the clinical group in the paranoid ideation scale was $n$=102 (57.0%), in the psychotic ideation $n$=122 (68.2%), and in the GSI $n$=132 (73.7%).

Table S1 (supplementary material) displays the frequency distribution for the variables of the study among women and men sub-samples. No statistical differences were found comparing women versus men.

## Materials

**Symptom Checklist-Revised (SCL-90-R) (Derogatis, 1994)** This is a widely used tool that was initially developed to assess the presence and level of a large set of symptoms and other psychological problems. It contains 90 items arranged in nine primary scales (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychotic ideation) and three secondary global indices (global severity index, [GSI], total positive symptoms [PST], and positive discomfort index [PSDI]). The version used in this study (Spanish version) has been proven to have good psychometric indexes (Gonzalez De Rivera et al., 1989). This study used two primary scales for the assessment of the symptoms related to the SCZ condition (paranoid ideation and psychotic ideation), since no other specific measure of the SCZ symptom level and the SCZ functional level were available, and it was not considered adequate to perform a network excluding SCZ indicators. In addition, the global psychology distress (GSI) was used as a measure of the global distress in the sample. The internal consistency in this study for these three scales was from good to excellent: Cronbach-alpha $\alpha$=0.780 for paranoid ideation, $\alpha$=0.895 for psychotic ideation, and $\alpha$=0.982 for GSI.

**Temperament and Character Inventory-Revised (TCI-R) (Cloninger et al., 1994)** This tool was developed to assess personality profile based on Cloninger's multidimensional model. The questionnaire includes 240 items and covers 4 dimensions of the individual's

**Table 1** Descriptive of the variables of the study

| Sociodemographic | | *n* | % | GD measures | Mean | SD | |
|---|---|---|---|---|---|---|---|
| Sex | Women | 16 | 8.9% | Onset GD (yrs-old) | 26.50 | 9.85 | |
| | Men | 163 | 91.1% | Duration GD (years) | 6.85 | 6.86 | |
| Marital | Single | 123 | 68.7% | DSM-5 criteria: | n | % | |
| | Married | 34 | 19.0% | A1: Gambling with increasing amounts of money | 134 | 74.9% | |
| | Divorced | 22 | 12.3% | A2: Restless-irritable when stop gambling | 158 | 88.3% | |
| Education | Primary | 116 | 64.8% | A3: Repeated efforts to control-stop gambling | 166 | 92.7% | |
| | Secondary | 58 | 32.4% | A4: Preoccupied with gambling | 135 | 75.4% | |
| | University | 5 | 2.8% | A5: Often gambles when feeling distressed | 128 | 71.5% | |
| Employed | Unemployed | 140 | 78.2% | A6: Chasing one's losses | 142 | 79.3% | |
| | Employed | 39 | 21.8% | A7: Lies to conceal the extent of gambling | 161 | 89.9% | |
| Social position | Mean-high | 3 | 1.7% | A8: Has lost relationships, job, education | 160 | 89.4% | |
| | Mean | 7 | 3.9% | A9: Relies related with financial issues | 150 | 83.8% | |
| | Mean-low | 40 | 22.3% | Preference | Only non-strategic forms of gambling | 136 | 76.0% |
| | Low | 129 | 72.1% | | Only strategic forms of gambling | 9 | 5.0% |
| Born in… | Spain | 168 | 93.9% | | Mixed forms of gambling | 34 | 19.0% |
| | Other | 11 | 6.1% | Modality | Only land-based | 165 | 92.2% |
| Chronological age | | Mean | SD | | Only online | 7 | 3.9% |
| Age (yrs-old) | | 39.53 | 9.93 | | Mixed | 7 | 3.9% |
| Psychopathology (SCL-90R) | | Mean | SD | Debts due to GD (yes) | | 80 | 44.7% |
| Paranoid ideation | | 1.30 | 0.85 | Illegal behavior (yes) | | 53 | 29.6% |
| Psychotic ideation | | 1.22 | 0.89 | | | Mean | SD |
| Global distress (GSI) | | 1.34 | 0.74 | SOGS total score | | 10.73 | 2.74 |
| Personality (TCI-R) | | Mean | SD | Substances | | n | % |
| Novelty seeking | | 108.77 | 10.19 | Tobacco | | 140 | 78.2% |
| Harm avoidance | | 108.90 | 13.49 | Alcohol | | 31 | 17.3% |

**Table 1** (continued)

| Sociodemographic | *n* | % | GD measures | Mean | SD | |
|---|---|---|---|---|---|---|
| Reward dependence | 94.13 | 11.43 | Illegal drugs | | 26 | 14.5% |
| Persistence | 103.09 | 17.72 | | | | |
| Self-directedness | 120.99 | 17.39 | | | | |
| Cooperativeness | 126.18 | 14.07 | | | | |
| Self-transcendence | 64.98 | 13.80 | | | | |

temperament (novelty seeking, harm avoidance, reward dependence, and persistence) and 3 dimensions of the individual's character (self-directedness, cooperation, and self-transcendence). Novelty seeking is a measure of the exploratory excitability, extraversion impulsivity levels (example of an item: "I do things just for fun"). Harm avoidance measures anticipatory worry, fear of uncertainly, shyness, and fatigability (items like "I worry more than most people that something might go wrong in the future"). Reward dependence measures dependence and openness to warm communication ("I like to please people as much as I can"). Persistence measures eagerness of effort, work hardened, and perfectionism ("I've been called a workaholic because of my enthusiasm for working a lot"). Self-directedness measures responsibility, purposeful, self-acceptance, and resourcefulness ("I almost always feel free to choose what I want to do"). Cooperativeness measures social acceptance, empathy, and helpfulness ("I tend to accept others as they are"). And self-transcendence measures self-forgetful and spiritual thinking patterns ("I feel a powerful sense of bonding with all the things around me"). The version used in this study (Spanish adaptation) has been shown to have good psychometric indexes (Gutiérrez-Zotes et al., 2004). The internal consistency in the study sample was between adequate ($\alpha$=0.705 for novelty seeking) and very good ($\alpha$=0.867 for persistence).

**South Oaks Gambling Screen (SOGS) (Lesieur & Blume, 1987)** This tool was designed as a measure to identify the presence of probable, problem, and non-problem gambling, and it has usually been used as a measure of gambling symptom severity. It consists of 20 items aimed at discriminating between probable pathological, problem, and non-problem gambling. The version used in this study (Spanish adaptation) has been shown to have good psychometric indexes (Echeburúa et al., 1994). The internal consistency in this study was adequate, $\alpha$=0.738.

**Diagnostic Questionnaire for Pathological Gambling (According to DSM Criteria) (Stinchfield, 2003)** This is a self-report tool formed by 19 items coded in a binary scale (yes-no). It was used to assess the presence of GD according to the DSM-IV-TR (American Psychiatric Association, 2000). This DSM-IV measure has been adapted to measure DSM-5 diagnostic criteria for GD (American Psychiatric Association, 2013) by removing the illegal acts criterion and using the cutoff score of 4 symptoms-criteria. The version used in this study (Spanish adaptation) has been shown to have good psychometric indexes (Jiménez-Murcia et al., 2009). The internal consistency for this scale in the study sample was adequate, $\alpha$=0.785.

**Diagnosis of SCZ** All the participants in the study were referred to the treatment unit from local Primary Care Centers and Community Mental Health Centers whose clinicians had identified the presence of GD. The presence of SCZ was diagnosed after assessment by psychiatrist specialists in the treatment of this mental condition, based on DSM-IV and DSM-5 criteria.

**Semi-structured Clinical Interview** This tool was used to assess additional information, including socio-demographics (sex, marital status, education level, employment status, and social position) and gambling problem-related variables (such as the age of onset and duration of the GD, and the presence of accumulated debts due to gambling behaviors). In this study, the social position index was calculated according to Hollingshead's Four Factor Index, which provides a classification based on four domains (Hollingshead,

2011): marital status, retired/employed status, educational attainment, and occupational prestige. This semi-structured interview was also used to identify gambling preferences (only non-strategic, only strategic, or mixed), gambling modality (only in person, only online, or mixed), and the use of substances (patients reported the consumption of tobacco, alcohol, and other illegal drugs). This complete tool has been described elsewhere (Jiménez-Murcia et al., 2006).

## Ethics

The study was carried out in accordance with the Declaration of Helsinki of 1975, as revised in 2000. The participants in this study were recruited for different research projects approved by the Ethics Committee of Bellvitge University Hospital (Refs: PR241/11, PR286/14, PR329/19, PR338/17 and PR393/17). All subjects were informed about the research and they all provided informed consent (the acceptance rate was 100% of all the consecutive patients of the treatment unit who met the inclusion criteria).

## Procedure

Data analyzed in this study correspond to a cross-sectional design. In addition to the assessment of the clinical and sociodemographic variables included in the semi-structured interview, the clinicians confirmed the diagnosis of GD provided by the *Diagnostic Questionnaire for Pathological Gambling*, and helped the participants to complete the self-report questionnaires to guarantee that they adequately understood all the items and completed the tools. All the clinicians involved in the recruitment of the sample pertained to the treatment unit, were specialized in the GD area, and had great experience in the assessment and treatment of patients seeking for problematic and disordered gambling.

Throughout the CBT for GD, SCZ patients maintained their antipsychotic medication plans, following the guidelines and management of the clinicians from the Primary Care Centers or Mental Health Centers.

## Network Approach

Network theory offers an outstanding methodological platform to explore complex system of reciprocal interactions (based on the graph theory), as well as to visualize intricate multifaceted phenomena (Borsboom, 2017; Borsboom et al., 2018; Borsboom & Cramer, 2013; Epskamp et al., 2018; Hevey, 20218; McNally, 2016). In the psychiatric area, the network methodology proposes the study of mental disorders as complex phenomena resulting from the underlying interactions between causally connected symptoms/symptoms (which include biological, psychological, and social aspects) (Boschloo et al., 2015; Goekoop & Goekoop, 2014). This approach has proved being useful for discovering the symptoms/features of greatest relevance to the onset and progression of mental problems ("central nodes") (Fried et al., 2017; Fried & Cramer, 2017). And since this approach does not consider the existence of any single latent entity as the cause of concrete disorders (as is the case with categorical taxonomies), boundaries between diagnostic categories become vague, and comorbid profiles (overlapping symptoms) are explained by means of "transition/bridge" nodes (symptoms that facilitate the paths between structures) (Braun et al., 2018; Cramer et al., 2010).

In the clinical research area, the underlying structure of variables through is displayed through two elements: (a) nodes (symptoms and other sociodemographic-clinical variables), which are represented through circles; and (b) edges (relationships between variables), which are represented as connecting lines (Borgatti et al., 2009). The effect size of the associations between the nodes is visualized in the thickness of the edges (for example, a large effect size is reflected through a thick edge, while two unrelated variables are reflected by two unconnected nodes). The effect size of the associations can be calculated using several statistical procedures, such as the partial correlations matrix, adjusted regression coefficients, adjusted odds ratio coefficients, or factorial loads (these parameters need to be adjusted to avoid biases due to the impact of possible confounding variables) (Bringmann et al., 2013; Clifton & Webster, 2017; Hevey, 20218).

## Statistical Analysis

The network analysis was conducted with Gephi 9.2 for Windows (Bastian et al., 2009) (available at http://gephi.org), a software package that was specifically developed for exploring and visualizing networks within datasets. The system enables a powerful spatialization process and the computation of essential parameters of centrality, density, and modularity clustering.

In this study, a network for the total sample ($n$=179) was obtained. Due the strong asymmetry for the sex distribution, a complementary network among the men sub-sample was also identified ($n$=179). Nodes analyzed in the study were the nine DSM-5 criteria for GD, severity of the GD (total SOGS as a measure of symptom level, the presence of debts, and illegal behavior), psychotic and paranoid ideation levels (according to the SCL-90R), the global psychology distress (SCL-90 GSI), the presence of substance addictions (tobacco, alcohol, and illegal drugs), and personality profile (measured with the TCI-R). The effect size and the signal of the edges were calculated through partial correlations between nodes. The initial data structure for the network resulted in 25 nodes and 300 potential edges, most of which had very low weights (partial correlations around 0). To simplify this initial complex structure, edges that did not reach significance ($p$<0.05) were excluded, resulting in a final structure with 91 edges (around 30.3% of all potential connectors).

The prominence and linkage capacity of the nodes within a network can be measured through distinct indexes, such as centrality and closeness (Epskamp et al., 2018). In this study, node-level relevance within the network was measured with centrality parameters, concretely eigenvector centrality, and authority (these coefficients are obtained from the weighted sum of centrality measures of all nodes connected to a node). High centrality indexes indicate that the information contained in a concrete node is highly valuable for the whole graph.

The node-level linkage was measured in the study using the closeness parameters (which measure how close the node is to all the other nodes in the graph). High closeness indexes indicate a short average distance between one node and all the other nodes, and therefore, nodes with high closeness values have a high capacity to promote relevant changes in other parts of the network (and they are also highly vulnerable to the impact of modifications to any part of the structure).

The presence of empirical clusters of nodes (also called communities or modules in Gephi) was automatically identified (Blondel et al., 2008), as well as the clustering coefficient for each node (these values measure the importance of a node within its community).

Node clusters are identified for those variables that are most highly interconnected to each other and poorly connected with nodes outside the cluster.

Other graph distance measures used in the study were (a) the (average) path length, calculated as the mean of the shortest paths between all pairs of nodes (this value represents a measure of the efficiency of information transport in the network), and (b) the diameter, calculated as the greatest distance between the two furthest nodes (representing the maximum eccentricity of any vertex in the graph) (Brandes, 2001). The density of the graph was also estimated as the number of connections divided by the number of possible connections, which provides a measure of how close the network is to being complete (a complete graph includes all possible edges and achieves a density measure equal to 1).

## Results

The graph of the network obtained in the study is shown in Fig. 1 (the statistics for this analysis are included in Table S2, supplementary material). The diameter achieved a value equal to 4 and the average path length was 2.297.

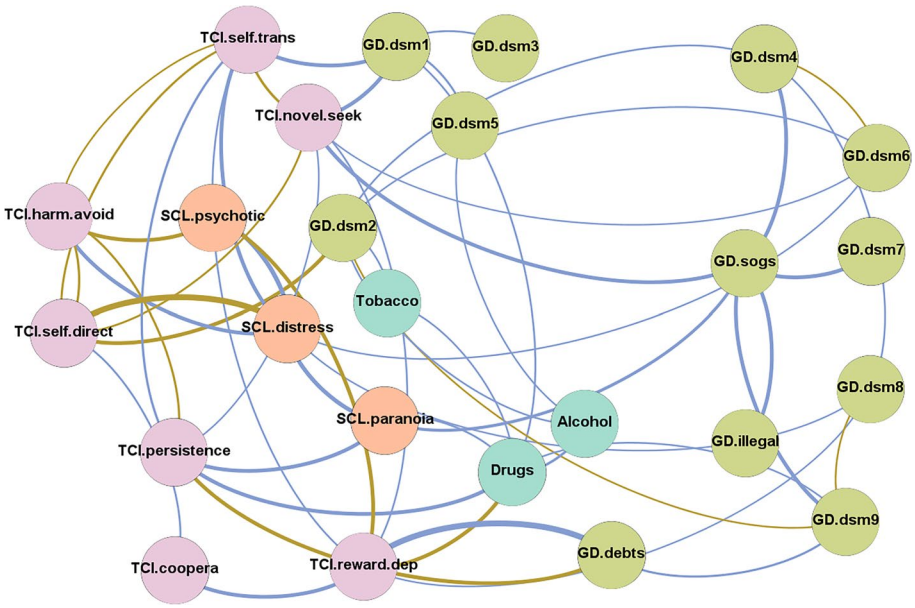


**Fig. 1** Visualization of the network. *Note*. Positive edges are represented by blue lines, and negative edges are plotted in brown-ochre. As thicker the edge, as stronger the connection weight. Nodes are plotted in colors depending on the dimension: personality (purple), psychopathology (orange), gambling-related measures (light blue), substances (pistachio). Nodes: DSM-5 symptoms for gambling disorder (GD.dsm1 to GD.dsm9), debts related with gambling (GD.debts), illegal behavior related with gambling (GD.illegal), GD symptom level (GD.sogs), global psychopathology distress (SCL.distress), paranoid ideation (SCL.paranoia), psychotic ideation(SCL.psychotic), substances (tobacco, alcohol, and drugs), novelty seeking (TCI_NS), harm avoidance (TCI_HA), reward dependence (TCI_RD), persistence (TCI_PE), self-directedness (TCI_SD), cooperativeness (TCI_CO), self-transcendence (TCI_ST), Tobacco (tobacco use), Alcohol (alcohol use), Drugs (drug use)

The first bar chart in Fig. 2 shows the nodes ordered by eigenvector centrality, which provides a measure of the relevance of each variable in the network. Personality profile, global psychology distress, and the use of illegal drugs achieved the greatest influence. Concretely, self-transcendence and novelty seeking were the nodes with the greatest influence.

The second bar chart in Fig. 2 shows the nodes ordered by closeness centrality, which constitutes a measure of linkage capacity, calculated as the reciprocal of the sum of the length of the shortest paths between the node and all other nodes in the graphon. In this analysis, personality traits and use of drugs also achieved the highest linkage. Concretely, novelty seeking was the closest node to all others in the network.

Figure 3 shows the main linkage for the two variables of greatest centrality in the study (eigenvector and closeness). The activation of the novelty seeking node had a major impact on the other personality traits (except for cooperativeness), the DSM-5 criteria for GD 1 "gambling with increasing amounts of money," and 6 "chasing one's losses", and the GD symptom severity level (SOGS total score). Activation of the "self-transcendence" node also had a major impact on the remaining personality traits (except for cooperativeness), as well as DSM-5 criterion 1 for GD ("gambling with increasing amounts of money") and global psychology distress (SCL-90R GSI).

Four latent modularities (clusters of nodes) were identified (Fig. 4 shows the nodes grouped into each cluster). Cluster 1 (C1) included self-transcendence, novelty seeking, and the DSM-5 criteria for GD 1 "gambling with increasing amounts of money," 3

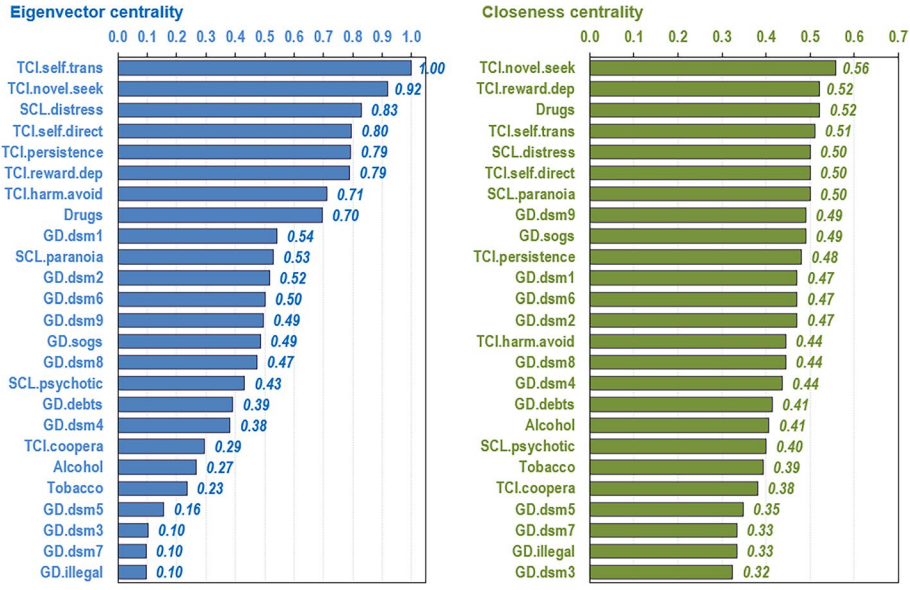


**Fig. 2** Relevance of centrality and linkage of the nodes. *Note*. Nodes: DSM-5 symptoms for gambling disorder (GD.dsm1 to GD.dsm9), debts related with gambling (GD.debts), illegal behavior related with gambling (GD.illegal), GD symptom level (GD.sogs), global psychopathology distress (SCL.distress), paranoid ideation (SCL.paranoia), psychotic ideation(SCL.psychotic), substances (tobacco, alcohol, and drugs), novelty seeking (TCI_NS), harm avoidance (TCI_HA), reward dependence (TCI_RD), persistence (TCI_PE), self-directedness (TCI_SD), cooperativeness (TCI_CO), self-transcendence (TCI_ST), Tobacco (tobacco use), Alcohol (alcohol use), Drugs (drug use)

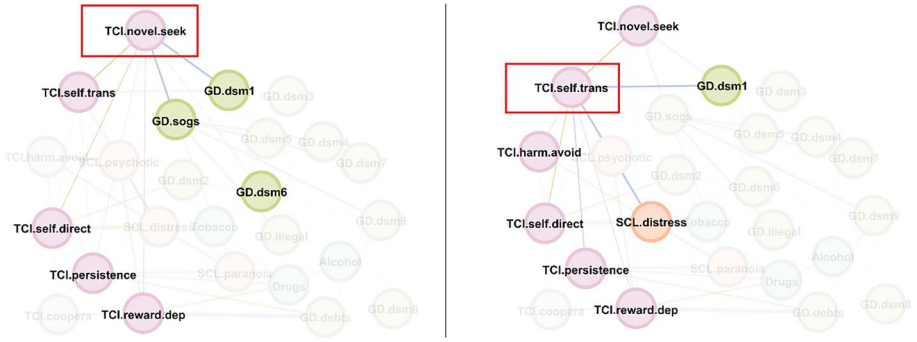


**Fig. 3** Main linkages for the variables with the highest closeness centrality and eigenvector centrality. *Note*. Nodes: DSM-5 symptoms for gambling disorder (GD.dsm1 to GD.dsm9), debts related with gambling (GD.debts), illegal behavior related with gambling (GD.illegal), GD symptom level (GD.sogs), global psychopathology distress (SCL.distress), paranoid ideation (SCL.paranoia), psychotic ideation(SCL.psychotic), substances (tobacco, alcohol, and drugs), novelty seeking (TCI_NS), harm avoidance (TCI_HA), reward dependence (TCI_RD), persistence (TCI_PE), self-directedness (TCI_SD), cooperativeness (TCI_CO), self-transcendence (TCI_ST), Tobacco (tobacco use), Alcohol (alcohol use), Drugs (drug use)

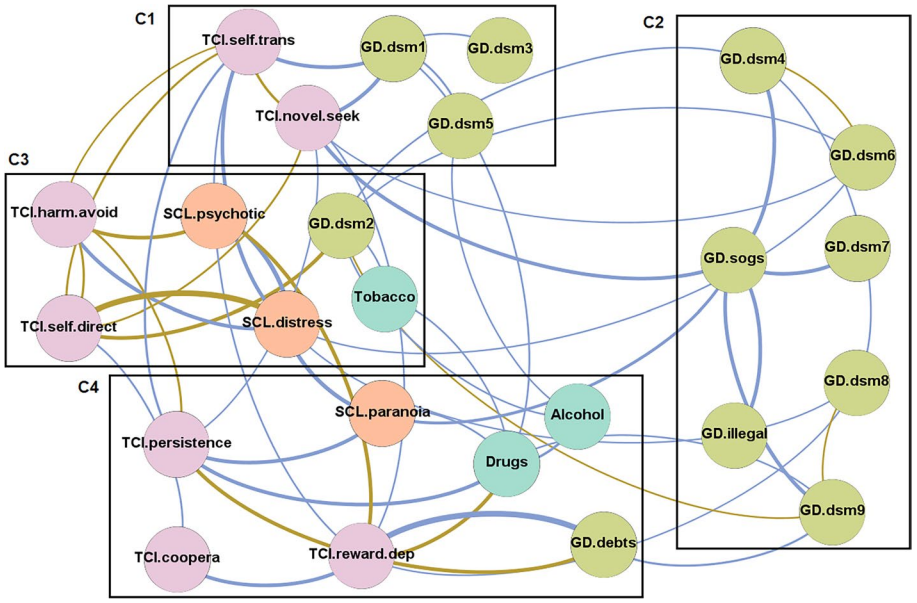


**Fig. 4** Network grouping the nodes within module-class-clusters. *Note*. Positive edges are represented by blue lines, and negative edges are plotted in brown-ochre. As thicker the edge, as stronger the connection weight. Nodes are plotted in colors depending on the dimension: personality (purple), psychopathology (orange), gambling-related measures (light blue), substances (pistachio). Nodes: DSM-5 symptoms for gambling disorder (GD.dsm1 to GD.dsm9), debts related with gambling (GD.debts), illegal behavior related with gambling (GD.illegal), GD symptom level (GD.sogs), global psychopathology distress (SCL.distress), paranoid ideation (SCL.paranoia), psychotic ideation(SCL.psychotic) , substances (tobacco, alcohol, and drugs), novelty seeking (TCI_NS), harm avoidance (TCI_HA), reward dependence (TCI_RD), persistence (TCI_PE), self-directedness (TCI_SD), cooperativeness (TCI_CO), self-transcendence (TCI_ST), Tobacco (tobacco use), Alcohol (alcohol use), Drugs (drug use)

"repeated efforts to control-stop gambling," and 5 "gambling when feeling distressed". Cluster 2 (C2) grouped another five DSM-5 criteria for GD (criterion 4 "gambling-related preoccupations," 6 "chasing one's losses," 7 "lies related to the gambling impacts," 8 "losses of relationships, job, or educational opportunities," and 9 "lies related with financial problems"), the GD symptom level (total SOGS), and gambling-related illegal behaviors. Cluster 3 (C3) grouped the nodes harm avoidance, self-directedness, the DSM-5 criterion for GD 2 "restless-irritable when stopping gambling," psychotic ideation level, global distress, and tobacco use. Cluster 4 (C4) included the nodes persistence, cooperativeness, reward dependence, paranoid ideation level, gambling-related debts, and the use of drugs and alcohol.

### Network Model Among the Men Sub-sample

Figure S1 (supplementary material) shows the graph of the network obtained among the men sub-sample (*n=163*), and the bar chart with the nodes ordered by the eigenvector centrality and the closeness centrality. The diameter achieved a value equal to 4 and the average path length was 2.397. The node with the highest relevance was self-transcendence, followed by novelty seeking. The node with the highest linkage capacity was novelty seeking, followed by the drug use. Regarding the latent modularities, 5 latent clusters of nodes emerged: C1 included self-transcendence, novelty seeking, persistence, and the DSM-5 criteria for GD 1 "gambling with increasing amounts of money," 3 "repeated efforts to control-stop gambling," and 5 "gambling when feeling distressed"; C2 grouped four DSM-5 criteria for GD (criterion 4 "gambling-related preoccupations," 7 "lies related to the gambling impacts," 8 "losses of relationships, job, or educational opportunities," and 9 "lies related with financial problems"), the GD symptom level (total SOGS), and gambling-related illegal behaviors and debts; C3 included harm avoidance, self-directedness, and the SCL-90R scales measuring paranoia ideation, psychotic ideation, and global distress; C4 grouped criterion for GD 2 "restless-irritable when stopping gambling" with the substances; and C5 was defined for cooperativeness and reward dependence.

## Discussion

This study has explored the network structure of the core symptoms for GD, gambling-related impairment measures (debts and illegal acts), psychotic and paranoid ideation levels, emotional distress, substance use, and personality profile, among treatment-seeking patients with comorbid GD plus SCZ. Among the total sample, the variables with the highest impact on the underlying structure were two personality traits: novelty seeking and self-transcendence. Four modularity classes were identified, each including nodes with information on different functionality domains. Among the men sub-sample, the highest relevance was obtained for the nodes self-transcendence and novelty seeking, and the highest linkage capacity was achieved for novelty seeking followed by the use of drugs.

Two personality characteristics appeared as the nodes with the highest centrality indexes, self-transcendence and novelty seeking. Several studies have identified the major contribution of different personality domains to the onset and progression of multiple mental disorders, including schizophrenia and gambling-related problems. Research investigating the influence of personality domains on these two mental disorders has related patients' risk decisions/choices to the big five factor personality theory (Buelow & Cayton, 2020).

Concretely, high neuroticism and low conscientiousness seem to be related to risk-adverse selections in patients with problematic gambling (Brunborg et al., 2016; Takeuchi et al., 2016; Teal et al., 2021). Poor schizophrenia outcomes in terms of symptomatology and quality of life have also been linked with high neuroticism and low extraversion levels (Franquillo et al., 2021), and these two personality features have also helped to explain the heterogeneity within the psychotic disorder spectrum and to conceptualize their comorbidities (Cicero et al., 2019). Therefore, identification of the personality traits implied in patients' clinical profiles, and the directions and strengths of the associations, is crucial in order to design precise treatment plans and optimize the effectiveness of psychiatric interventions.

In this study, self-transcendence was a central node of the network. As defined in the TCI-R questionnaire, this measure of the individuals' character covers several factors such as self-forgetfulness, unconscientiousness, and dissolution of the self in experience (Schimmenti et al., 2017). When compared with healthy control samples, patients with high scores for self-transcendence exhibit a profile characterized by negative emotions, introversion (closeness to experience), and absorption (losing track of time and space, focusing all attention on a specific task, and disregarding any other external or internal stimuli) (Anglim et al., 2020; Cloninger et al., 1993; Rezaei et al., 2020). High scores for self-transcendence have been linked to psychotic tendencies and paranoid-schizotypal traits among population-based and clinical samples, especially the cognitive-perceptual component associated with magical thinking (Galindo et al., 2016) and unusual perceptions (such as delusions and bizarre-unconventional beliefs) (Miskovic et al., 2018). This profile is typical of emotionally unstable individuals with a tendency to perceive any event as potentially stressful, and therefore highly vulnerable to anxiety and to the use of unhealthy behaviors to cope with these negative states (Zhou et al., 2017). And among SCZ patients, self-transcendence has been related with multiple unhealthy correlates, such as the social function (troubled and non-satisfying interpersonal relationships) (Kashiwagi et al., 2022), suicidal behavior (Canal-Rivero et al., 2021), and the presence of dual diagnoses characterized by substance-related disorder (Río-Martínez et al., 2020). These results could elucidate the results obtained in our network, suggesting that self-transcendence among SCZ could increase patients' propensity to engage in risky situations, while predisposing them in an isolated-closed world (these are, precisely, two relevant signs of the onset and progression of gambling-related problems). In addition, based on the connections between self-transcendence and negative affectivity, detachment and poor social support observed in previous studies, high scores in this personality domain could act as a "bridge node" in SCZ patients towards uncontrolled gambling as a way to inhibit harmful feelings (Kayiş et al., 2016; Laier et al., 2018; Müller et al., 2014; Wittek et al., 2016). It is likelihood that context that accompanies gambling behaviors could be perceived by SCZ patients as a safe environment in which they are not exposed to ridicule (or rejected), since face-to-face social skills are not required. And since the preferred form of gambling among SCZ patients is largely non-strategic face-to-face games, especially slot machines (which do not require special skills or technological knowledge), while they are gambling patients are not exposed to the failure they usually perceive in their real-life experiences.

Novelty seeking also achieved a very high centrality index in the network modeled in this work. Measured by the TCI-R, this personality trait is defined as the tendency towards excitement and exploratory activity in response to novel stimulation, avoidance of frustration, and impulsive decision-making (Cloninger et al., 1993). Previous studies observed that this trait is strongly related to impulsiveness, a complex multifaceted trait proposed as a vulnerability marker (Marín-Navarrete et al., 2018) and a transdiagnostic sign within

multiple mental disorders (Dalley & Robbins, 2017), including SCZ (Peritogiannis, 2015; Şenormanci et al., 2022) and GD (Szerman et al., 2020). Impulsiveness has also been proven in previous research to be a key feature for explaining the correlations between SCZ and multiple psychiatric symptoms, such as substance use (Dondé et al., 2020) and GD (Granero et al., 2021; Hodgins & Holub, 2015; Kräplin et al., 2014; Lee et al., 2013; Ouzir, 2013). In this study, novelty seeking obtained the highest closeness centrality, and this suggests that it could be a strong transition-bridge node within the comorbid profile of SCZ and GD patients. In network analysis, nodes with high transition-bridge capacity are interpreted as triggers of symptoms/signs from different disorders, thus promoting psychiatric comorbidity (Fried et al., 2017; Fried & Cramer, 2017). Since this study analyzed a sample of patients with a dual comorbid condition, high transition-bridge capacity could be interpreted as expanding the activation of other nodes related with the worst functional state. Concretely, the activation of novelty seeking in this work strongly impacted the total SOGS score (a measure of GD symptom severity), but also DSM-5 criterion 1 for GD ("gambling with increasing amounts of money," a tolerance measure) and DSM-5 criterion 6 for GD ("chasing one's losses," one of the central characteristics of problematic gambling). Other studies have found that in SCZ or schizoaffective disorder, chasing was associated with greater gambling involvement and with greater problems with substance use (Yakovenko et al., 2018; Yakovenko & Hodgins, 2018). Impulsivity has also been identified as the most relevant personality trait associated to the presence of GD and the severity of this disorder (Ioannidis et al., 2019).

It must be also outlined that cognitive inhibitory control deficits associated with impulsivity have been linked with psychopathological disorders such as addictive behaviors and SCZ (Dixon et al., 2022). Medication use is other related important factor, since impulsive responses have been associated in some patients within the impulsive spectrum disorders with dopamine agonist therapy during chronic treatments (Napier & Persons, 2019). Pharmacological research published in the last 20 years has related the increase in impulsivity-related problems in SCZ patients to dose response to some dopamine agonist drugs (Kim et al., 2021; Kishi et al., 2021; Pahwa et al., 2021), including clinical cases with dual mental conditions (Clerici et al., 2018). These studies show that aripiprazole (an atypical anti-psychotic drug), as well as other dopamine replacement therapies, contributes to the development of impulsive responses, and these medications therefore constitute risk factors for the onset and progression of GD among SCZ populations. This specific association has been explained by the hyperdopaminergic state in the mesolimbic pathway (reward system) through the predominant action on dopamine D2 and D3 receptors of these medications (Tuplin & Holahan, 2017). But while these studies are consistent with the relevance of impulsiveness among patients with the dual condition of SCZ with GD, the results must be considered with caution: although aripiprazole could contribute to the onset of gambling-related problems in the early stages of SCZ, the causality, strength (effect size), and specific process (direct, indirect, or mixed effect) have not been proven in terms of causality (Qian et al., 2021). The impact of long-term medication use on the neurometabolite levels is still not fully understood among SCZ patients, and future longitudinal research is needed to analyze the complex relationships between specific changes due to medication uses from specific disease-related changes. On the other hand, the pharmacological plan (medication and dose) was not available for SCZ in this study, which does not permit attribution of the central role of impulsivity to a potential dose response to antipsychotic treatments.

Regarding the analysis of modules-clusters in this study, it should be noted that the procedure used in the network approach is different from conventional classification analysis. For example, analytical techniques such as k-means or two-step-cluster are focused on the

grouping of elements (usually individuals) by the degree of similarity-difference between the set of components. However, the network approach identifies empirical groups of nodes (which can be defined for individuals, but also for variables) based on their edges (the key element is the linkage) and their attributes (identity relationships between classes). The evidence of different modules/clusters in a network suggests that groups of nodes could be part of specific processes, with the condition that some of these nodes may be closely interacting with nodes pertaining to other processes (that is, high linkage is possible intra-cluster and also between clusters). And although some of the modules/clusters may include sets of symptoms/criteria as defined in classical categorical taxonomies such as the DSM or the ICD, the activation of a node belonging to a module can transcend the cluster itself, thus increasing the likelihood of activating related nodes belonging to other groups (Borsboom, 2017; Boschloo et al., 2015). This would be, precisely, the role of "bridge nodes," which in clinical research are usually called "transdiagnostic symptoms." In this study, four clusters have been identified, and three of them include variables that measure patients' heterogeneous domains. Specifically, cluster C1 grouped the two personality variables with the highest centrality indexes in the study (self-transcendence and novelty seeking), along with three DSM-5 symptoms for GD. Clusters C3 and C4 grouped personality factors, DSM-5 criteria for GD, variables related to substance use, and psychopathology levels according to the SCL-90R.

## Limitations and Strengths

This study should be interpreted in the context of some limitations. First, the network has been modeled with several nodes that measured multiple aspects of the psychological and functional areas. However, other nodes that previous research relates to the GD and SCZ phenotypes were not available for this study (such as specific neurological and physical variables), so it was not possible to assess their contribution to the pattern of the relationships. In relation with this first limitation, in our network, the nodes related to the core/specific symptoms of GD were overrepresented compared to the nodes related to the core/specific symptoms of SCZ (the complete list of DSM-5 criteria for SCZ was not available), and this hinders the ability to identify with greater reliability-validity the true central and bridge nodes among the sample of patients with the comorbid condition GD and SCZ (after all, any analytical procedure analysis is be highly influenced by the variables analyzed). Future studies should explore the centrality (relevance and linkage) of alternative networks with additional nodes specifically focused on the SCZ profile.

Second, the sample in this study can be considered low in view of the analytical plan, but large in view of the specific composition (treatment-seeking patients with dual GD and SCZ, a comorbid condition uncommon even in tertiary treatment centers specialized in behavioral addictions). The sex distribution was asymmetrical (the number of women was particularly low), but this distribution is consistent with the ratio of men/women observed in clinical settings (any case, the limited proportion of female participants must be considered for generalization purposes). Regarding the impact of the sample size on the statistical procedures, it must also be outlined that there is no consensus rule on the optimal number of participants to ensure the reliability and validity of the network analysis, but like other statistical analysis, it is important that the sample size allows to accurately estimate the statistical parameters for safeguarding against erroneous conclusions which contribute to the robustness and replicability of the research. A current simulation study has observed that sample requirements for network are into a very broad range depending on different

design factors, such as the network architecture, network connectedness, number of nodes, and type of data (Constantin et al., 2022). Our study has been performed with large number of nodes and edges, and this could impact in the capacity of the model to achieve accurate parameters. Therefore, our results must be interpreted with caution, in the context of being a pioneering study whose results must be corroborated/refuted by future studies with larger samples.

Third, the cross-sectional nature of the data does not enable interpretation of the results in causal terms (in this study, the network was modeled by defining undirected edges). Finally, the lack of previous research on the subject matter (network studies applied to the etiology of GD and SCZ) impacts the interpretation of the findings, since there is no solid theoretical framework with which to contextualize the new empirical evidence generated by this study.

The last limitation is the long recruitment period for the sample. This is a typical procedure in studies analyzing (un)healthy conditions with few prevalence even in specialized clinical settings. In our study, the selection of all the participants was done according to the same inclusion-exclusion criteria, the same assessment tools were used, and the diagnostic of GD was homogeneous (based on the DSM-5 criteria). However, sociocultural changes have occurred during the recruitment period (including the COVID-19 pandemic), as well as pharmacological/treatment plans for SCZ. Related with this fact, the specific antipsychotic medication was not registered and controlled (nor the presence/impact of the negative symptoms). Future research should examine the potential interactive contribution of these measures, which should be considered in the interpretation of the results of our study.

This study has various strengths. First, there is the use of the network methodology to visualize the structure of interrelations between nodes and modules-clusters, and to identify the central nodes/variables in the clinical profile of patients with the comorbid/dual profile of GD and SCZ (this is a clinical condition that has a considerable effect on the patients' functionality level). One advantage of network analysis is its focus on the concrete nodes/variables that form the complete clinical profile (instead of focusing on single underlying latent constructs, the disorders), with the aim of measuring the relevance and closeness of each node, providing the pattern of relationships and exploring potential sub-groups.

## Conclusions

To the best of our knowledge, this is the first study to focus on the analysis of centrality (relevance and linkage) within the profile of patients with SCZ who are receiving treatment for gambling-related problems. The role of personality traits as the most central features, the identification of distinct modularity classes (grouping nodes that contain information from different functional dimensions), and the patterns of interrelations between the nodes support the hypothesis of a complex process sustaining the clinical profile. These results illustrate the difficulty of conceptualizing GD and SCZ as two well-defined, separate nosological entities, acting as single latent factors. On the contrary, the clinical phenotype of patients with GD and SCZ seems to be the result of a dense pattern of associations between psychological symptoms, personality traits, and other functional measures. And this complex structure suggests the involvement of common neurobiological impairments and the affectation of common brain systems, which should be participating in the expression of the distinct mental disorders. Therefore, profiles such as dual conditions should be approached from a transdiagnostic perspective, including personality traits such as impulsivity.

Finally, the objective of this study was not to assess the structure of the core symptoms/criteria for GD and SCZ as described in categorical taxonomies such as ICD-11 or DSM-5, but to explore the network of these core symptoms plus other sets of variables measuring the gambling-related impacts, the concurrence of substance uses, and personality traits. The conclusions of the study must also be contextualized to the specific population of individuals with the comorbid condition of SCZ with GD. Among these patients, the assessment of the contribution of the multiple nodes (relevance, linkage capacity, and clustering in modularity classes) provides evidence regarding the endophenotypes of GD and SCZ and suggests the suitability of a paradigm shift in the way that patients with this dual condition are conceptualized, diagnosed, and treated. Upcoming studies should also validate the underlying structure of symptoms in samples of pure SCZ and pure GD patients. Future research is crucial, particularly studies focused on clinical neuroscience and precision psychiatry.

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## Declarations

**Ethics Approval and Consent to Participate** The study was carried out in accordance with the Declaration of Helsinki of 1975, as revised in 2000. The participants in this study were recruited for different research projects approved by the Ethics Committee of Bellvitge University Hospital (Refs: PR241/11, PR286/14, PR329/19, PR338/17, and PR393/17). All subjects were informed about the research and they all provided informed consent (the acceptance rate was 100% of all the consecutive patients of the treatment unit who met the inclusion criteria).

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# 5. Discusión

## 5.1 Discusión global

Los artículos que forman parte de esta tesis doctoral aportan nuevas evidencias acerca del perfil clínico en pacientes con adicciones comportamentales, en este caso en una muestra de mujeres con TJ y CC y de sujetos con patología dual, caracterizada por TJ y esquizofrenia. Los estudios que analizan los datos de mujeres usan un enfoque analítico centrado en la persona, para identificar grupos empíricos (clases latentes) que representan perfiles diferenciados en la respuesta a la intervención con TCC. En el caso de los pacientes con patología dual se estimó la prevalencia de esquizofrenia en pacientes con TJ y se usó metodología de redes para visualizar las interrelaciones de las variables más importantes del perfil clínico e identificar los nodos con mayor relevancia y capacidad de vinculación en el grafo.

Los trabajos que exploran la existencia de clústeres empíricos latentes de mujeres con TJ y CC evidencian que los perfiles con mejor respuesta a la intervención con TCC se caracterizan por incluir una mayor proporción de mujeres casadas, en posiciones sociales más elevadas, laboralmente activas, con menor psicopatología general comórbida y perfil de personalidad más adaptativo, como es el caso del Clúster C1 en el primer estudio de la presente tesis. Otras intervenciones ya han constatado que estar casada y disponer de apoyo de la familia u otras personas significativas para la paciente contribuyen a una mejor adherencia a las terapias y a reducir el riesgo de recaídas y de abandono, particularmente en el TJ (88,102–104). Menor vulnerabilidad socioeconómica y comorbilidad asociada a mejor respuesta terapéutica también es un resultado congruente con estudios previos, que han observado que las mujeres con mejor posición sociolaboral y menor psicopatología asociada, usan el juego con una motivación básicamente dirigida a la socialización (105,106) y también como una forma de desconectar de los estresores que les puede generar su profesión (107). Estas mujeres estarían especialmente motivadas para recibir tratamiento y evitar las consecuencias negativas del TJ en el ámbito laboral, emocional, familiar y social.

El clúster C3 caracterizado por alto riesgo de recaídas durante la intervención incluyó mayor proporción de mujeres solteras o divorciadas/separadas, laboralmente inactivas, con mayor gravedad del TJ al inicio de la TCC, mayor comorbilidad

psicopatológica y un perfil de personalidad caracterizado por mayor evitación al daño y menor autodirección. Este clúster también incluyó el porcentaje más bajo de mujeres con deudas acumuladas. Estos resultados son congruentes con estudios previos que han observado que las mujeres sin pareja estable, en grupos socioeconómicos más desfavorecidos y que están desempleadas muestran peor progresión del TJ (33,108,109). Otros estudios también informan de la alta proporción de mujeres que experimentan problemas asociados a la conducta de juego, que presentan síntomas comórbidos como ansiedad, depresión, trastornos en la alimentación o consumo de sustancias (104,110,111) y que, precisamente, una de las principales razones de mantenimiento de la conducta de juego, en este grupo de mujeres, es aliviar estos síntomas concurrentes con la conducta adictiva (112). La gravedad que conforma la concurrencia del TJ con otros síntomas psiquiátricos pueden interferir seriamente en la eficacia de la terapia (30,113). Respecto al perfil de personalidad, se ha observado que puntuaciones altas en evitación del daño y bajas en autodirección se asocian a peor eficacia de los tratamientos y a mayores dificultades con la regulación de emociones (114,115), siendo este perfil concreto predictor de recaídas y abandono en pacientes con TJ (116).

El Clúster C2, que también incluyó pacientes con mala progresión durante el tratamiento caracterizado por alto riesgo de abandono (todos los pacientes de este grupo abandonaron el tratamiento y un porcentaje tuvo recaídas antes de abandonar), también presentó un perfil sociodemográfico de mayor vulnerabilidad y puntuaciones medias en la gravedad del estado psicopatológico. Estudios previos han concluido que el abandono del tratamiento está relacionado con una mayor dificultad para la autorregulación de conductas, falsas creencias sobre el tratamiento y la presencia de apatía y desánimo (117). Estos hallazgos sugieren que el perfil de mujeres con menor afectación a consecuencia de los problemas de juego son, probablemente, menos conscientes de la necesidad de hacer un tratamiento específico para este trastorno, llegando a pensar que pueden resolverlo de forma autónoma. En definitiva, los resultados obtenidos en los tres perfiles de mujeres con TJ, sugieren la necesidad de desarrollar terapias específicas, destinadas a mejorar la autoestima y autoeficacia, para ayudarlas así a regular comportamientos inapropiados que las conduzcan a recaídas y abandonos.

El segundo estudio, que planteó como objetivos explorar la existencia de clases latentes en mujeres con TJ y CC en base a la evolución que presentan durante la TCC, así como también identificar las variables en la línea base con capacidad discriminativa, se obtuvo que la solución óptima era la de cuatro clases latentes. El clúster con las

respuestas al tratamiento más eficaces (buen pronóstico de recuperación, riesgo bajo de recaída y la tasa de incidencia de abandono más baja en comparación a los demás subgrupos), se caracterizó por mayor nivel socioeconómico, mejor estado psicopatológico y perfil de personalidad más funcional. Estos resultados son consistentes con revisiones sistemáticas realizadas en TJ y CC, en las que se encontraron que menor psicopatología, menor comportamiento adictivo al inicio de las intervenciones, niveles de educación más altos y rasgos de personalidad más adaptativos, eran predictores de éxito después del tratamiento (118,119).

Las clases latentes caracterizadas por peores resultados de la TCC (tasas de incidencia más altas de abandono y recaídas), incluyeron mujeres con peor estado psicopatológico, perfil de personalidad más disfuncional (puntuaciones altas en evitación del daño y bajas en autodirección) y mayor tendencia a comportamientos autolíticos. Investigaciones previas han evidenciado que estos rasgos de personalidad disfuncionales (retraimiento social, baja autoestima, déficits en estrategias de afrontamiento) pueden contribuir a un pobre resultado del tratamiento, independientemente de la adicción comportamental (114,120,121). Una característica interesante en estos dos subgrupos es que el LT3 incluyó pacientes más jóvenes. El inicio más temprano de la adicción comportamental y mayor evolución del trastorno también se ha asociado a una respuesta terapéutica limitada, aunque se sabe que ambas variables pueden interactuar con otras, sociodemográficas y clínicas (120,122).

Finalmente, la clase latente con resultados moderados de respuesta al tratamiento incluyó mujeres con la mayor edad cronológica, el inicio más tardío de la adicción comportamental y menor duración del trastorno. Estos resultados son congruentes con estudios que indican que las personas mayores constituyen un grupo altamente vulnerable con motivaciones específicas para iniciar y persistir en este tipo de trastornos (como escapar de la soledad y del aislamiento social, evitar el sufrimiento por la pérdida de un ser querido o aliviar el aburrimiento en la jubilación) (123,124). Este grupo suele también caracterizarse por mayor deterioro cognitivo y mayor presencia de enfermedades físicas y mentales, aspectos que también pueden desempeñar un papel central en el inicio, mantenimiento y la escalada de conductas adictivas (125).

El tercer estudio de esta tesis doctoral tuvo como objetivos estimar la prevalencia de esquizofrenia en pacientes que solicitan tratamiento por problemas de juego de apuesta, y comparar el perfil sociodemográfico y clínico de estos pacientes con pacientes con TJ sin esquizofrenia. La prevalencia de la esquizofrenia se estimó en el

4.4% en el grupo total de pacientes que consultaban por TJ, lo cual es consistente con tasas publicadas en estudios previos (prevalencias de esquizofrenia unas cuatro veces superior a la de la población general [próxima al 1%]) (126). Estos resultados pueden evidenciar que las personas con un TJ constituyen un grupo vulnerable para el desarrollo de sintomatología del espectro psicótico, o que la presencia de estados psicóticos representa una condición de alta vulnerabilidad para el inicio y la progresión de conductas adictivas (incluido el TJ). Esta última situación es particularmente relevante, ya que hay un creciente número de informes que han relacionado la medicación con antipsicóticos de segunda generación (como Aripripazol, un antagonista parcial del receptor D2), con la aparición de conductas de juego o con aumentos en la gravedad de estas conductas adictivas (127–131).

En este tercer estudio se encontró que las variables más relacionadas con la presencia dual de TJ con esquizofrenia fueron la soltería, niveles educativos más bajos, desempleo, posición social más baja, edad cronológica más joven, inicio más temprano de los problemas de juego, peor estado psicopatológico comórbido y perfil de personalidad más disfuncional. En cuanto al peor estado psicopatológico, este resultado es congruente con investigaciones anteriores que señalaron que el TJ con psicosis constituye una condición altamente vulnerable que aumenta el riesgo de otras condiciones psicopatológicas (70), y con la concurrencia de otros múltiples problemas psiquiátricos que podrían interferir en los resultados del tratamiento (119).

En cuanto al perfil de personalidad, los resultados obtenidos en el tercer artículo son consistentes con investigaciones previas que reportaron niveles más altos en evitación del daño y puntuaciones más bajas en cooperación, autodirección, dependencia a la recompensa y persistencia, dentro del espectro esquizofrénico. Se ha observado que niveles altos de evitación del daño y niveles bajos de cooperación constituyen un endofenotipo relacionado con la psicopatología de los pacientes con esquizofrenia, lo que puede contribuir a explicar algunas limitaciones sociales observadas en estos pacientes (132). Es importante destacar que en este estudio se compararon pacientes con TJ sin esquizofrenia con pacientes con TJ con esquizofrenia, de manera que identificar un perfil de personalidad diferente asociado a la condición dual, aunque es consistente con los resultados previos informados en muestras dentro del espectro esquizofrénico, no evidencia ningún perfil de personalidad disfuncional más severo que los rasgos endofenotípicos habituales de la personalidad entre los pacientes con esquizofrenia. En este estudio tampoco se encontró relación entre la

presencia concurrente de esquizofrenia con TJ y un mayor nivel de conducta de juego. Este resultado no es consistente con investigaciones previas, que observaron una mayor gravedad del juego en jugadores problemáticos con psicosis (74). Sin embargo es importante señalar que esta potencial relación podría explicarse por el papel mediador de la impulsividad identificado en otras investigaciones (133), y puesto que el presente estudio no incluyó una medida para los niveles de impulsividad no fue posible evaluar este papel mediador. Finalmente, el tercer estudio obtuvo una mayor probabilidad de formas de juego no estratégicas (máquinas tragaperras, bingo y loterías) en el grupo de pacientes con TJ comórbido con esquizofrenia. Investigaciones previas observaron que los pacientes con esquizofrenia experimentan déficits en las tareas de toma de decisiones y aprendizaje (134–136). Por este motivo estos pacientes podrían preferir jugos no estratégicos caracterizados por la escasa habilidad y conocimientos que requieren.

El cuarto artículo de la tesis planteó como objetivos principales visualizar mediante análisis de redes la estructura de relaciones entre los síntomas centrales del TJ y otros correlatos clínicos en pacientes con la condición dual de TJ más esquizofrenia, e identificar los nodos centrales y con mayor capacidad de asociación/vinculación. Se observó que los nodos con mayores índices de centralidad fueron la autotrascendencia y la búsqueda de novedad. Son varios estudios los que identificaron la contribución principal de diferentes dominios de la personalidad al inicio y progresión de múltiples trastornos mentales incluidas la esquizofrenia y los problemas relacionados con el juego. En este artículo, la autotrascendencia es una medida que caracteriza a los sujetos con falta de conciencia y disolución del yo en la experiencia. Estudios previos sugieren que este perfil es propio de individuos emocionalmente inestables con tendencia a percibir cualquier evento como potencialmente estresante, y por lo tanto muy vulnerables a la ansiedad y al uso de conductas poco saludables para hacer frente a estos estados negativos (137). Y entre los pacientes con esquizofrenia, la autotrascendencia se ha relacionado con correlatos como la dificultad en las relaciones interpersonales, la conducta suicida y la presencia de diagnósticos duales relacionados con el consumo de sustancias (138,139). Estos resultados podrían explicar los hallazgos obtenidos en el presente estudio de red, puesto que las puntuaciones elevadas en autotrascendencia en pacientes con esquizofrenia podrían aumentar la propensión a involucrarse en situaciones de alto riesgo, al mismo tiempo que los predispone al aislamiento (factores de riesgo para la aparición y la progresión de los problemas relacionados con el juego

de apuestas). Además, puesto que la autotrascendencia se asocia a afectividad negativa, desapego y escaso apoyo social, las puntuaciones altas en este factor de personalidad podrían actuar como un "nodo puente" en pacientes con esquizofrenia hacia conductas de juego descontrolado como una forma de inhibir sentimientos dañinos (140–142).

La búsqueda de novedad obtuvo en este artículo un índice de centralidad muy alto. Este rasgo de personalidad se caracteriza por la tendencia a la excitación, la actividad exploratoria en respuesta a estímulos novedosos, evitación de la frustración y toma de decisiones impulsivas (143). Este resultado sugiere que esta dimensión de la personalidad también podría ser un "nodo puente" (con alta capacidad de vinculación) dentro del perfil comórbido de los pacientes con esquizofrenia y TJ. En el análisis de redes, los nodos con alta capacidad de puente de transición se interpretan como desencadenantes de síntomas/signos de diferentes trastornos, lo que favorece la comorbilidad psiquiátrica (144,145). En este artículo, cabe resaltar que la impulsividad también ha sido identificada como el rasgo de personalidad más relevante asociado a la presencia de TJ y la gravedad de este trastorno (146). Otras investigaciones encontraron que los déficits de control inhibitorio asociados a la impulsividad se relacionan con trastornos psicopatológicos como las conductas adictivas y la esquizofrenia (147). En este contexto, otro factor importante a destacar es el uso de medicamentos antipsicóticos, ya que se han asociado a respuestas impulsivas en algunos pacientes (148). La investigación farmacológica publicada en los últimos 20 años ha descrito un aumento de los problemas relacionados con la impulsividad, en pacientes con esquizofrenia, con la respuesta a la dosis de algunos fármacos agonistas de la dopamina (149–151), incluyendo casos clínicos con condiciones mentales duales (152). Estos estudios muestran que el Aripiprazol (un fármaco antipsicótico atípico), así como otras terapias de reemplazo de dopamina, contribuyen al desarrollo de conductas impulsivas, por lo que estos medicamentos constituyen factores de riesgo para la aparición y desarrollo del TJ entre las poblaciones esquizofrenia. Son necesarias investigaciones longitudinales que analicen las relaciones complejas que se dan en el uso de medicamentos en estas enfermedades psiquiátricas duales, que forman un endofenotipo muy complejo. Puesto que en el presente estudio no se incluyó la información sobre el tratamiento farmacológico de los pacientes con esquizofrenia, no fue posible atribuir el papel central de la impulsividad a una posible dosis-respuesta a los tratamientos antipsicóticos.

En síntesis, la esquizofrenia es una enfermedad mental grave que afecta de forma significativa la capacidad de las personas para tener un juicio conservado de la realidad, con síntomas positivos: como alucinaciones (visuales y auditivas), delirios, alteraciones graves en el pensamiento (inusual e ilógico), desorganización del comportamiento y síntomas negativos con alteraciones graves en el estado de ánimo (anhedonia, inhibición social, aislamiento, que son más devastadoras para la persona) y también alteraciones en las funciones cognitivas. Debido a que un número importante de personas presentan TJ comórbido con esta condición, es preciso identificar los elementos centrales del perfil clínico y sociodemográfico de estos pacientes, que contribuya a desarrollar planes de intervención integradores, que tengan presente la amplia esfera de problemas físicos y emocionales, así como las múltiples influencias ambientales que afectan el bienestar de estos pacientes. Estos programas holísticos deben incluir tratamiento farmacológico apropiado para corregir los desequilibrios químicos, así como otras estrategias psicológicas para aumentar el autocontrol y reducir la impulsividad (como el entrenamiento de la memoria de trabajo y la inhibición de respuestas), y también para mejorar la capacidad de regulación emocional, prevenir o reducir el estrés crónico y aumentar las habilidades sociales.

## 5.2 Limitaciones

Los estudios que forman esta tesis doctoral deben interpretarse en el contexto de algunas limitaciones. En primer lugar, algunos trabajos analizan muestras de poblaciones con características específicas (mujeres con TJ y CC y pacientes en su mayoría varones con esquizofrenia comórbida con TJ) por lo que los resultados no podrían generalizarse a poblaciones de diferente sexo a los que conforman las investigaciones. Asimismo las muestras también cumplieron con criterios de exclusión específicos; ya que no se incluyeron otras adicciones conductuales, además la muestra forma parte de una población clínica ya que fue obtenida de un centro de atención especializada, debido a esto los resultados conseguidos no podrían generalizarse a pacientes con otras adicciones comportametales y a pacientes que no recurren a centros de atención especializada, de la población en general.

Por otro lado, destacar que los estudios que valoran resultados de la intervención se basan en el cambio pre-post tratamiento, y por consiguiente los resultados podrían no ser representativos de períodos de tiempo más largos.

En segundo lugar, en los estudios con pacientes con diagnóstico de esquizofrenia no se disponía del tratamiento farmacológico con antipsicóticos, ni de la gravedad de los síntomas negativos de la enfermedad. Investigaciones futuras deberían examinar la posible interacción de estas variables en el perfil clínico de los sujetos en la línea base.

En tercer lugar, el trabajo que utiliza el análisis de redes analiza nodos que miden múltiples aspectos de las áreas psicológica y funcional. Sin embargo, otras variables que investigaciones previas relacionaban con los fenotipos de TJ y esquizofrenia no se incluyeron (el tamaño de la muestra no permitía ampliar los parámetros de la red). Podría suceder que variables no consideradas en este estudio pudieran tener medidas de centralidad alta, incluso superior a la que obtienen los nodos centrales de nuestra investigación. De hecho, la muestra de este estudio concreto podría considerarse limitada en términos estadísticos, aunque teniendo en cuenta que se trata de pacientes con la condición comórbida de TJ con esquizofrenia (poco común incluso en centros de tratamiento terciarios especializados en adicciones comportamentales), el número de pacientes es significativo en términos clínicos. En cuanto a la distribución del sexo, la asimetría en la ratio hombres/mujeres es consistente con la proporción observada en entornos terapéuticos. Además, la naturaleza transversal de los datos no permite la interpretación de los resultados en términos causales, y la falta de investigación en esta área dificulta la interpretación de los hallazgos porque no se dispone de un marco teórico sólido para contextualizar los hallazgos obtenidos, aunque debe también destacarse que se mantuvieron homogéneos los criterios de inclusión–exclusión y se emplearon los mismos instrumentos de evaluación y la definición diagnóstica del TJ.

## 5.3 Fortalezas

Existen diferentes aspectos que pueden ser interpretados como fortalezas. En el primer estudio se incluyen datos longitudinales para una gran muestra de mujeres, con diagnóstico de TJ, que habían solicitado tratamiento por este trastorno. Además, usa un método analítico que combina el enfoque centrado en la persona y el enfoque centrado

en las variables. La mayoría de los estudios que exploran los resultados de la TCC dentro del TJ se realizaron con una metodología centrada en las variables (es el enfoque dominante en el campo de la investigación psicopatológica). Este trabajo incluye resultados de un enfoque alternativo, basado en un procedimiento de clasificación que identifica clases latentes empíricas. Estos procesos basados en el individuo se han mostrado especialmente útiles para identificar la heterogeneidad de los procesos psicopatológicos, y su expresión conductual en los diferentes dominios de funcionamiento. En nuestro estudio, estos métodos centrados en la persona se han empleado para explorar la existencia de subgrupos de personas con perfiles similares, y conocer variables con capacidad discriminativa entre las clases, lo que podría incluirse dentro de las estrategias de la terapéutica de alta especificidad o individualizada.

Otro aspecto a destacar, de los estudios que conforman es tesis doctoral, es el análisis de variables que valoren múltiples aspectos, como el perfil sociodemográfico, los estados psicopatológicos, los rasgos de personalidad, y otras variables particularmente relacionadas con los comportamientos por adicción (inicio de los problemas, duración, subtipos y modalidad, y consecuencias).

La novedad de los estudios es también un aspecto a destacar. Hasta donde sabemos, el segundo artículo es el primer trabajo publicado en la literatura científica que versa los resultados de la intervención con TCC y explora clases latentes empíricas en mujeres que buscan tratamiento para el TJ y la CC, e identifica variables en la línea base con capacidad discriminativa sobre los clústeres. La identificación de las características que impactan en la eficacia del tratamiento en muestras de mujeres contribuye a un mejor conocimiento de los procesos específicos de género involucrados en las conductas adictivas, y por consiguiente resulta de gran utilidad para elaborar planes de tratamiento precisos capaces de dar respuesta a las diferencias individuales en género femenino. Por otro lado, el tercer y cuarto estudios son también pioneros en lo que se refiere al estudio del perfil de pacientes con patología dual de TJ con esquizofrenia, y utilizan metodología de redes para visualizar la estructura de interrelaciones entre nodos y módulos, y para identificar módulos/agrupaciones de clústeres de nodos/variables.

## 5.4 Implicaciones

La presente tesis doctoral aporta nueva evidencia empírica acerca de los perfiles sociodemográficos y clínicos de pacientes que constituyen grupos de alta vulnerabilidad, mujeres y condiciones duales complejas. Se sabe que las mujeres encuentran mayores barreras para solicitar tratamiento por adicción comportamental, en gran medida por el estigma social que les ocasiona hacer visible estos problemas. En pacientes con TJ comórbido con esquizofrenia, es habitual que los problemas por juego de apuesta queden relegados a un segundo plano, ya que las intervenciones se focalizan en controlar la sintomatología positiva del cuadro psicótico.

El análisis de datos de corte longitudinal también aporta información valiosa acerca de la progresión de los pacientes durante la TCC, y facilita nueva evidencia para el desarrollo de planes de detección precoz y de intervenciones precisas que den respuesta a las diferencias individuales entre los pacientes. El enfoque centrado en la persona de estos estudios facilita también un método empírico muy valioso para discernir perfiles con características similares en grupos de pacientes cuya composición es muy heterogénea en aspectos sociodemográficos, psicológicos y funcionales.

# 6. Conclusiones

1. Las mujeres que solicitan tratamiento por TJ y CC forman un grupo heterogéneo con distintos síntomas psicológicos y conductuales, que permiten identificar clústeres empíricos en base al resultado de la intervención con TCC.
2. Los clústeres empíricos con peor respuesta al tratamiento (mayor riesgo de abandono y recaída) se caracterizan por incluir mujeres más jóvenes, con inicio más precoz de los síntomas del TJ y la CC, mayor gravedad del trastorno adictivo, mayor comorbilidad psicopatológica y un perfil de personalidad más disfuncional.
3. Los instrumentos de evaluación del TJ y la CC deben ser sensibles para identificar tanto los síntomas específicos de la adicción como del conjunto de variables sociodemográficas y clínicas, que influyen en la eficiencia de las intervenciones.
4. Se deben diseñar tratamientos específicos que tengan en cuenta las diferencias individuales de las mujeres con TJ y CC, para lograr abordajes precisos que sean eficientes en pacientes de alta vulnerabilidad a estos trastornos y a la respuesta a las intervenciones.
5. La presencia de esquizofrenia es aproximadamente 4 veces mayor que la que se estima en la población general en pacientes con TJ.
6. Los pacientes con patología dual caracterizada por TJ más esquizofrenia presentan un perfil sociodemográfico y clínico más vulnerable y disfuncional que los pacientes con TJ sin esquizofrenia.
7. En pacientes con patología dual por TJ más esquizofrenia el análisis de redes revela que los nodos con mayor centralidad (relevancia global y capacidad d vinculación) son variables de personalidad y de malestar psicopatológico.
8. La identificación de variables con alta centralidad/vinculación en pacientes con TJ y esquizofrenia es particularmente útil para desarrollar herramientas de detección precoz temprana, y para elaborar programas de intervención precisos que tengan en cuenta las especificidades de estos pacientes.

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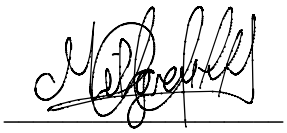
# Declaración de código ético y buenas prácticas

**LA DOCTORANDA**

Doña **Milagros Lizbeth Lara Huallipe,** con NIE Y4261531J

declara que la tesis que presenta no contiene plagio, manifiesta conocer y consiente en que la tesis podrá ser sometida a procedimiento para comprobar su originalidad.



*Firma doctoranda*

**LAS DIRECTORAS**

La Doctora **Susana Jiménez Murcia,** con DNI 40432581F

La Doctora **Roser Granero Pérez,** con DNI 34745763P

declaran que se han cumplidos los códigos éticos y de buenas prácticas, y que no tiene conocimiento de que se haya producido ningún plagio.

Susana Jiménez-Murcia

Roser Granero Pérez

*Firma directoras*