Gambling Disorder – Suicidality, Mortality and Comorbidity

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Gambling Disorder – Suicidality, Mortality and Comorbidity

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LUND
UNIVERSITY

DOCTORAL DISSERTATION

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Abstract

Background: Gambling disorder (GD) is a behavioural addiction in which a person faces negative consequences due to uncontrolled gambling, such as financial, personal, or relational difficulties. GD more often affects men but both men and women face severe consequences of GD. Psychiatric comorbidity is the rule rather than the exception and suicidality is abundant. Health issues such as obesity and cardiovascular disease are also common. Financial difficulties are common and might be both a consequence of and a risk factor for GD.

Aim and methods: To examine, through registry and qualitative research, comorbidity, intentional self-harm, suicide and mortality in GD. In Study I, standardized mortality ratios for men and women with GD were compared to the general population and potential risk factors for suicidality and mortality were investigated (N=2099). In Study II, the effect of comorbid alcohol and drug use disorders on intentional self-harm in individuals with GD was examined (N=2099). In Study III, the effects of psychiatric and socioeconomic risk factors on intentional self-harm (N=848) were examined, and in Study IV, a gender- and age-matched cohort was utilized to investigate the association between GD, suicide, and general mortality in relation to known risk factors in men and women (N=10,792). Finally, a qualitative interview study (V) investigated, through qualitative content analysis (N=7), experiences of suicidality in women with GD and potential mediators of suicidality.

Results: In the first study, mortality and suicide levels were greatly elevated in GD. Depression was associated with suicide death, and age and cardiovascular disease predicted general mortality. However, in the fourth study, GD did not appear to be a significant risk factor for the increase in suicide and general mortality when controlling for previously known risk factors. In the second and third studies, female gender, and psychiatric comorbidity such as substance use diagnoses, anxiety and depression were important risk factors for intentional self-harm. In the fifth study, the themes "internal shame and stigma", "chaotic life circumstances due to gambling (such as eviction)" and "external stigmatization" appeared important in the development of suicidality.

Conclusion: Individuals with GD suffer from increased suicide levels as well as high rates of intentional self-harm. Shame, stigma, and chaotic life circumstances might be mediators for suicidality in women with GD. Psychiatric comorbidity including substance use disorders appears to increase the risk of intentional self-harm and depression might increase the risk of suicide. This research could not determine whether GD is an independent risk factor for suicide and further research is needed. Mortality levels are higher and might be due to cardio-vascular comorbidity.

Key words: Gambling Disorder, Suicidality, Suicide, Self-Harm, Mortality, Comorbidity, Indebtedness, Socio-Economics, Gender

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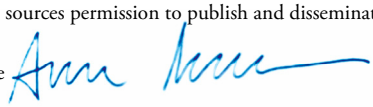
Signature  Date 04-04-2023

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For those who have lost control,

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Introduktion

Att vara beroende av att spela om pengar, att ha ett *spelberoende*, kan leda till flertalet negativa konsekvenser. Det är väl känt att personer med spelberoende ofta drabbas av bland annat skuldsättning och påverkat psykiskt mående men omfattningen av spelberoendets konsekvenser är idag ännu inte helt kartlagt. Detta avhandlingsarbete syftar till att utforska några av de allvarligaste konsekvenserna av spelberoende nämligen suicidalitet, suicid, samsjuklighet och dödlighet.

Det verkar som om människan erfarit spelandets negativa konsekvenser under lång tid eftersom såväl österländska som västerländska riken har försökt reglera spelandet under historiens gång. Spel om pengar har förekommit i flera uråldriga kulturer och man tror att småben från bland annat getter har målats och kastats i spel om värdefulla föremål. Dessa sexkantiga ben, så kallade astralger har under årtusendena utvecklats till dagens tärningar.

Gemensamt för spel om pengar är att ett element av risk ingår, till exempel genom tärningskast, och att någonting av värde kan förloras eller vinnas. Idag sker en stor del av spelandet online via bland annat internetcasinon och online betting med tillgänglighet dygnet-runt i till exempel den egna telefonen. Möjligheten att ta snabba lån ökar risken för stora förluster med potentiell överskuldsättning som följd, men även före online-spelandet kan man i historiska dokument hitta belägg för hur människor spelat bort hus och hem och hamnat i personlig konkurs.

Idag pratar man om *problemspelande* (en kontrollförlust över spelandet) och *spelberoende* (en beroendesjukdom där man blir beroende av spel om pengar). Spelberoende karaktäriseras av att den beroende fortsätter spela trots att hen drabbats av omfattande negativa konsekvenser till följd av spelandet. Man kan få svåra ekonomiska problem, riskera arbete och relationer, spela för större och större summor, ha svårt att sluta och bli irriterad när man hindras från spelandet. Den spelberoende spelar inte bara för att det är kul utan även när hen mår dåligt – symtom som liknar de för substansberoenden som till exempel alkoholberoende.

Ett fenomen som är särskilt utmärkande för spelberoende kallas på engelska för ”chasing losses” och innebär att den beroende hamnar i en tankefälla där hen bedömer att den enda chansen att rädda upp de ekonomiska förluster spelandet orsakat är att vinna tillbaka dem genom ytterligare spelande. Problemet är att man sällan vinner stort och även när man vunnit finns beroendet kvar och pengarna riskerar att omgående spelas bort följt av nya försök att vinna tillbaka förlusterna.

Spelberoende drabbar ungefär en halv procent av befolkningen och oftare män än kvinnor. Samsjuklighet med annan psykisk ohälsa är vanligt förekommande och spelberoende kvinnor verkar drabbas av detta i ännu högre grad. Ofta får den spelberoende också svåra ekonomiska problem och hamnar i skuldproblematik. Självskada och suicidalitet är tyvärr också vanligt förekommande.

Idag är kognitiv beteendeterapi (KBT) eventuellt i kombination med motiverande samtal den rekommenderade behandlingen för spelberoende men många får inte rätt vård eller vård över huvud taget.

Ofta kan det finnas svårigheter att vända sig till hälso-och sjukvården på grund av skuld- och skamkänslor eller okunskap. Okunskap om sjukdomen hos den drabbade och i samhället i stort kan leda till svårigheter att söka vård. Behandlingsutbudet varierar också i Sveriges olika regioner och kommuner. Personer med spelberoende kan också ofta uppleva stigmatisering och bära på skuld och skam som förhindrar att man kontaktar vården. Spelberoende kan drabba personer av olika könstillhörighet, samsjuklighet och socioekonomiska förutsättningar.

I detta avhandlingsarbete har fokus varit att utforska de negativa konsekvenserna av spelberoende med ett fokus på samsjuklighet, suicidalitet och dödlighet. Psykiatrisk samsjuklighet vid spelberoende har utvärderats i tidigare studier och bedömts vara relativt omfattande, särskilt för kvinnor. Flera studier har också visat att personer med spelberoende har en ökad förekomst av suicidtankar och tidigare suicidförsök. Dessa studier är dock ofta byggda på självskattningar varför det finns en viss osäkerhet kring resultaten. Suiciddödlighet och dödlighet över lag har tidigare inte undersökts vid spelberoende. Vidare finns frågeställningar om hur kön, samsjuklighet, socioekonomi och spelberoende samvarierar. Kvinnor med spelberoende tycks göra fler suicidförsök än män, men suiciddödligheten är fortsatt okänd.

Spelandets negativa konsekvenser i form av samsjuklighet, dödlighet och suicidalitet är viktiga att kartlägga för att kunna bemöta och behandla dessa risker hos individen, men också för att kunna reglera spelmarknad och bygga vårdsystem som utgår från evidens. På en global nivå avlider ca 700 000 människor årligen till följd av suicid. Bland unga (15-29 år) är suicid den fjärde ledande dödsorsaken och personer med psykisk ohälsa dör i snitt två årtionden tidigare än andra på grund av somatisk samsjuklighet. Trots det är det inte förrän nyligen som psykisk ohälsa inkluderades i FN:s globala mål för hållbar utveckling. Komplexa samband mellan beroendetillstånd och annan psykiatrisk samsjuklighet gör forskningen utmanande men inte desto mindre viktig.

Frågeställningarna inför avhandlingsarbetet var följande:

- Hur vanligt förekommande är suicid och medveten självskada hos personer med spelberoende och vilka är riskfaktorerna?
- Hur ser samsjukligheten ut vid spelberoende?
- Drabbas personer med spelberoende av förtida död och vilka är i så fall riskfaktorerna?
- Hur ser den suicidala processen ut för kvinnor med spelberoende?

Metod

Dessa frågeställningar har vi försökt besvara genom fyra registerstudier och en intervjustudie.

Svenska register utgör en möjlighet att följa unika individers resa genom vårdsystemet, och socioekonomiska faktorer kan kopplas till olika diagnoser tack vare våra personnummer. De fyra registerstudierna bygger på uppföljningar av individer som har fått diagnosen spelberoende i svensk specialiserad hälso-och sjukvård. Dessa personer har därefter följts i våra register och vi har kunnat se samsjuklighet och dödlighet, men också socioekonomiska faktorer såsom förekomst av brottslighet, föräldraskap och försörjningsstöd. Genom statistiska beräkningar kan därefter förekomst av samsjuklighet, dödlighet, suiciddödlighet och avsiktlig självskada kartläggas.

Den femte studien byggde i stället på intervjuer av sju kvinnor med erfarenheter av spelberoende och suicidalitet. Intervjuerna tolkades enligt en särskild teknik i vilken teman slutligen formas. Avsikten var att dessa teman skulle ta avstamp i kvinnornas berättelser och vara förklaringsmodeller för uppkomst av suicidalitet relaterat till spelberoende.

Resultat

I våra registerstudier har vi kunnat se att personer med spelberoende har en överdödlighet generellt och att samsjuklighet med hjärt-kärlsjukdomar var kopplad till den förhöjda dödligheten.

För personer med spelberoende har vi kunnat konstatera att det också finns en stor överdödlighet till följd av suicid jämfört med befolkningen. Vi ser att kvinnor med spelberoende har ett stort lidande med fler självskadehandlingar och suicidförsök men vi har inte kunnat kartlägga huruvida det finns en överdödlighet till följd av suicid.

Vi har även kunnat konstatera att det finns en relativt hög förekomst av kriminalitet hos personer diagnostiserade med spelberoende och att nästan hälften varit i behov av försörjningsstöd. Bland de personer som erhållit försörjningsstöd var suicidförsök eller självskada vanligare.

Viktiga riskfaktorer för suicid tycks vara samsjuklighet med depression. Vad gäller icke-dödliga suicidförsök verkar samsjuklighet med substansberoende, depressivitet, ångest och personlighetsstörningar spela en viktig roll.

Vi ser att kvinnorna som grupp har en än mer utpräglad psykiatrisk samsjuklighet. I vår intervjustudie ser vi även att kvinnor med spelberoende beskriver ett stort lidande vad gäller konsekvenser av spelberoendet och att flera av kvinnorna upplevt att spelberoendet varit en utlösande faktor för tidigare suicidförsök. Tre teman med möjliga förklaringsmodeller framkom mellan spelberoendet och suicidaliteten.

a) Egen skuld, skam och självstigmatisering
b) Kaos och kontrollförlust
c) Sociala konsekvenser, rädsla för skuld-och skambeläggning från andra

I det första temat beskrev flera kvinnor hur skam över det egna beteendet och en känsla av att inte vara till någon nytta ledde till suicidalitet. I det andra temat framkom berättelser om hur spelandet och skulderna lett till att man förlorat sin bostad och konsekvenser hos Kronofogden som lett till en känsla av total kontrollförlust över tillvaron och ett inre kaos som utlöst suicidalitet. I det tredje temat framkom i stället oro för hur besked om spelberoendet och den påverkade ekonomin ska tas emot av andra och en rädsla att ej bli accepterad utan snarare skuld- och skambelagd vilket har lett till ökad suicidalitet. För några kvinnor kunde flera av dessa teman återfinnas i deras berättelser medan några enbart upplevt suicidalitet till följd av en av dessa förklaringsmodeller.

Diskussion

Sammanfattningsvis har detta avhandlingsarbete belyst komplexa samband mellan spelberoende, samsjuklighet, suicidalitet och dödlighet. Mycket finns kvar att kartlägga men redan nu ser vi en förhöjd dödlighet i gruppen både vad gäller suicid och förtida död till följd av kroppsliga sjukdomar.

Förhoppningen är att denna kunskap ska kunna bidra till att öka behandlingsmöjligheter och screening för spelberoende samt påvisa vikten av suicidriskbedömning och suicidprevention vid spelberoende. Såväl psykiatrisk som somatisk samsjuklighet är vanligt och måste beaktas i behandling och bemötande av de som drabbats av spelberoende för att ge bästa möjliga vård och förhindra förtida dödlighet i gruppen.

Framöver skulle intervjustudier även behöva belysa mäns erfarenheter av suicidalitet och större studier behövs för att kunna utvärdera huruvida spelberoendet i sig är en riskfaktor för suiciddödlighet.

Dessutom behöver man arbeta brett mot det stigma som omger spelberoende. På så vis skulle förhoppningsvis fler män och kvinnor med spelberoende komma i behandling.

Papers Included in the Thesis

I. **Gambling disorder, increased mortality, suicidality, and associated comorbidity: A longitudinal nationwide register study.**
Karlsson A, Håkansson A.
Journal of Behavioral Addictions 2018:1-9.
https://doi.org/10.1556/2006.7.2018.112

II. **Suicide Attempt in Patients with Gambling Disorder—Associations with Comorbidity Including Substance Use Disorders.**
Håkansson A, **Karlsson A.**
Frontiers in Psychiatry 2020;11(1240)
https://doi.org/10.3389/fpsyt.2020.593533

III. **Psychiatric Comorbidity and Economic Hardship as Risk Factors for Intentional Self-Harm in Gambling Disorder-a Nationwide Register Study.**
Karlsson A, Hedén O, Hansson H, Sandgren J, Håkansson, A.
Frontiers in Psychiatry 2021;12:688285.
https://doi.org/10.3389/fpsyt.2021.688285

IV. **Suicide and Mortality in those with Gambling Disorder and Matched Case Controls – A Swedish Nationwide Register Study.**
Karlsson A, Balem M, Hansson H & Håkansson A.
(In manuscript) 2023

V. **Personal Experiences of Suicidality in Women with Gambling Disorder – a Qualitative Interview Study.**
Karlsson, A; Håkansson, A & Hansson, H
(In review, Journal of Behavioral Addictions) 2023

Papers Not Included in the Thesis

- **Primary and Secondary Diagnoses of Gambling Disorder and Psychiatric Comorbidity in the Swedish Health Care System-A Nationwide Register Study.**
  Håkansson A, **Karlsson A,** Widinghoff C. Frontiers in Psychiatry 2018;9:426. doi:10.3389/fpsyt.2018.00426

- **Crime-Specific Recidivism in Criminal Justice Clients with Substance Use-A Cohort Study.**
  Karlsson A, Håkansson A.
  Int J Environ Res Public Health 2022;19(13) doi:10.3390/ijerph19137623

- **Gambling and COVID-19: Swedish national gambling data from a state-owned gambling sports and casino operator.**
  Balem M, **Karlsson A,** Widinghoff C, et al. Journal of behavioral addictions 2023;12(1):230-41. doi: 10.1556/2006.2022.00089

- **Mortality in substance use patients – Impact of violent criminal lifestyle in different age groups.**
  Jakobsson J, **Karlsson A,** Håkansson A, Hofvander B.
  (In review, Addiction) 2023

Abbreviations

ADHD	Attention deficit hyperactivity disorder
AH	Anders Håkansson
AK	Anna Karlsson
AUD	Alcohol use disorder
CBT	Cognitive behavioural therapy
CI	Confidence interval
DSM	The Diagnostic and Statistical Manual of Mental Disorders
DUD	Drug use disorder
EGM	Electronic gambling machine
fMRI	functional magnetic resonance imaging
GARN	The Gambling Addiction Research Network
GD	Gambling disorder
HH	Helena Hansson
HR	Hazard ratio
ICD	The International Classification of Diseases
ID	Identification number (for research)
LISA	Swedish longitudinal integrated database for health insurance and labour market studies
MI	Motivational interviewing
OR	Odds ratio
PG	Problem gambling
PET	Positron emission tomography
PIN	Personal identity number
SD	Standard deviation
SMR	Standardized mortality ratio
SUD	Substance use disorder
SWP	Social welfare payment
WHO	World Health Organization

Introduction

Gambling in History

Gambling is a global and ancient phenomenon which appears to have been associated throughout history with significant harm to individuals who have lost control of their gambling and to those close to them[1]. Indeed, several societies have regulated gambling, not only to prevent gambling related harm but also to provide income to the ruling class or state[2 3].

Although we do not know the exact origin of chance-based games, or gambling, it is believed that knuckle bones, known as *astralgi* – small "dice-like" bone from animals such as sheep and dogs – were used in prehistoric cultures as a prequel to modern dice[1]. Astralgi were used in Egyptian board games as early as 3500 BC[1]. Chance-based dice games might have been used to pass time and distract the mind during hard times such as in the famine of Lydia 1500 B.C. (situated in today's Turkey) and amongst Greek soldiers during the ten year siege of Troy[1]. Our earliest known remnants of astralgi in Sweden are made of sheep bone from around 200AD[3].

Evidence can be found of regulatory attempts towards gambling in ancient Western societies as well as in several Chinese dynasties indicating that gambling has been related to negative consequences throughout history[2]. In the Roman Empire, for example, gambling was quite regulated, although some Roman emperors gambled heavily themselves and regulations were thus at times disregarded[1]. One such example is emperor Caesar Augustus (63BC-14AD) who gambled heavily, even handing out money to guests to encourage gambling at his private dinner parties[1]. Roman emperor Claudius (10 BC-54 AD) even wrote a book on the art of dice gambling "How to Win at Dice" (which is not persevered to modern times)[1]. Other early evidence of gambling include lotteries[1].

In Sweden, Queen Hedvig Eleonora (1636-1715) is known to have lost large sums due to card gambling, perhaps influencing her daughter-in-law Queen Ulrika Eleonora (1656-1693) (with whom Hedvig Eleonora, supposedly, had a strained relationship) to impose even harder gambling regulations as well as to launch a campaign against harmful gambling[3].

Governmental regulation of gambling has long been dual in its nature, attempting to minimize harm among its citizens while also making money from gambling. In modern times, the taxation of gambling has been criticised for being regressive in its nature, mainly impacting those of lower socioeconomic status[4]. Gambling related harm appears to not only affect those who have lost control of their gambling and those close to them but also other individuals who gamble[3]. Interventions aimed at targeting everyone who gambles and not only those with a loss of control of their gambling might be most effective in reducing gambling-related harm, a phenomenon referred to as the *prevention paradox*[5]. Efforts to reduce gambling at population level have also been described as likely to diminish problems for those who have lost control of their gambling[6]. Considering this, efforts to increase primary prevention could potentially reduce harm to society at large, to many individuals who gamble and especially to those at risk of developing gambling disorder (GD).

Gambling in Sweden

In Sweden, heavy gambling prohibition started to loosen up with the opening of the state-owned lottery in 1897 providing revenue to the state[7]. This was followed by legalization of betting on horse racing and football games in in the 1920s and 30s[7]. Charity lotteries, slot machines, bingo games and land-based casinos later followed[7]. From the 1980s and 90s increasing commercialization of gambling appeared especially with the emergence of online gambling[7].

Until January 1st, 2019 gambling was to a large part controlled by the Swedish state-owned monopoly, although a large sector of illegal online gambling companies operated from locations abroad[8]. New legislation was brought on to improve control of the online gambling market and a license system was introduced[8 9]. Current legislation (2023) entails opportunities to collect taxes and aims to improve control of online gambling[8 9]. These licensed companies are now linked to "Spelpaus[a]" a national exclusion system where a gambler can exclude him or herself from gambling within the licensing system[8]. As such, national legislation aims to regulate and minimize harm due to gambling whilst still utilizing revenues from gambling, which could be considered ethically complex.

An illegal parallel gambling market still exists in Sweden today (2023), and gambling is still heavily commercialized in Sweden with roughly one in five televised commercials involving gambling, particularly online casino gambling[10]. Further, the state has little insight in to how the gambling companies operate and how the customers are affected[11].

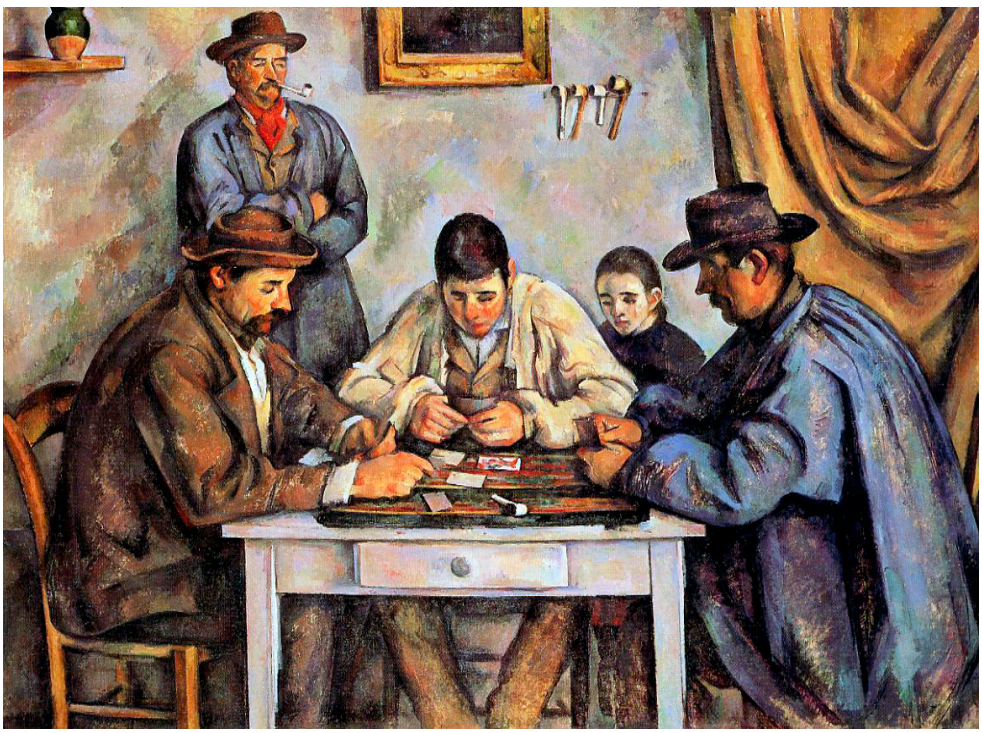
[a] "gambling pause" in English.

The Swedish government proposed a set of new legislative changes in their bill "en förstärkt spelreglering, 2022[b]", further increasing the regulation of the gambling market[11], which was accepted partially by parliament late in 2022. As of 2023 licensed gambling companies are obliged to share certain information with Swedish authorities, regulations are further enhanced and increased opportunities to exclude non-licensed operators have been introduced[12]. However suggestions to further regulate the gambling commercials were disapproved[12]. Thus, the Swedish gambling market is very much changing.

[b] "a stronger gambling regulation, 2022" in English

Gambling in Art

Gambling has inspired artists throughout history. Games and gambling motifs are portrayed in ancient societies across the world[1]. Some of the more well-known paintings are Heintz Narr's woodcut from 1494 depicting four individuals involved in a game of dice, "Players and courtesans under a tent" (1600-1651) by Cornelis de Vos, "A Madwoman and Compulsive Gambler" portraying an elderly woman from 1820 by Théodore Géricault (page 25), Paul Cezanne's "the card players" (1890-1892) as seen below, Edward Munch's "By the Roulette" from 1892 (page 33), as well as the series of paintings called "Dogs playing poker" (1903) by American artist Cassius Marcellus Coolidge which have been referenced in, among other places, contemporary musician Snoop Dog's 1993 music video for the song "What's my name".



Gambling in Art: Paul Cezanne, Les Joueurs des Carte (1890-1892).

What is Gambling Disorder?

Today, we know that some individuals develop an addiction to gambling; what we refer to as GD. GD comes with symptoms similar to those of substance use disorder (SUD) but with a specific trait of "chasing losses" where increased gambling is utilized in an attempt to regain lost money[13]. Some individuals experience some of the negative effects of gambling but do not fully meet the criteria of addiction and are typically referred to as suffering from problem gambling (PG). Approximately 0.5 % of the population are estimated to suffer from GD[14 15], and roughly 2.3 % might be affected by PG[16], although it has been suggested that these prevalence figures might be much higher when accounting for selection bias[17]. Below is the definition of GD according to the American Psychiatric Association manual *Diagnostic and Statistical Manual of Mental Disorders (DSM), 5th version*, a classification widely used in clinical practice.

DSM-5 Basic Diagnostic Criteria for Gambling Disorder

A. Persistent and recurrent problematic gambling behaviour leading to clinically significant impairment or distress, as indicated by the individual exhibiting four (or more) of the following in a 12-month period:

a) Needs to gamble with increasing amounts of money to achieve the desired excitement.

b) Is restless or irritable when attempting to cut down or stop gambling.

c) Has made repeated unsuccessful efforts to control, cut back, or stop gambling.

d) Is often preoccupied with gambling (e.g., having persistent thoughts of reliving past gambling experiences, handicapping or planning the next venture, thinking of ways to get money with which to gamble).

e) Often gambles when feeling distressed (e.g., helpless, guilty, anxious, depressed).

f) After losing money gambling, often returns another day to get even ("chasing" one's losses).

g) Lies to conceal the extent of involvement with gambling.

h) Has jeopardized or lost a significant relationship, job, or educational or career opportunity because of gambling.

i) Relies on others to provide money to relieve desperate financial situations caused by gambling.

B. The gambling behaviour is not better explained by a manic episode.

The international classification of diseases (ICD) 11th version is another important classification system provided by the World Health Organization (WHO)[18]. The ICD system is used in Swedish and international registers although the DSM-5 system is also in clinical use.

ICD-11 Diagnostic Criteria for Gambling Disorder Essential (Required) Features:

- A persistent pattern of gambling behaviour, which may be predominantly online (i.e., over the internet or similar electronic networks) or offline, manifested by all of the following:
- Impaired control over gambling behaviour (e.g., onset, frequency, intensity, duration, termination, context);
- Increasing priority given to gambling behaviour to the extent that gambling takes precedence over other life interests and daily activities; and
- Continuation or escalation of gambling behaviour despite negative consequences (e.g., marital conflict due to gambling behaviour, repeated and substantial financial losses, negative impact on health).
- The pattern of gambling behaviour may be continuous or episodic and recurrent but is manifested over an extended period (e.g., 12 months).
- The gambling behaviour is not better accounted for by another mental disorder (e.g., Manic Episode) and is not due to the effects of a substance or medication.
- The pattern of gambling behaviour results in significant distress or impairment in personal, family, social, educational, occupational, or other important areas of functioning.

The DSM-5 and ICD-11 criteria for GD are quite similar to each other and to the diagnostic criteria describing other addictive disorders. Further, the GD diagnosis can be found in the chapters dealing with addictive disorders in both classification systems. However, GD, previously referred to as 'pathological gambling', was in the earlier DSM-IV in the chapter "Impulse-Control Disorder Not Elsewhere Classified"[19]. Further, a previous criterion in the DSM-IV of committing illegal acts was removed and the cut off was lowered in the 5th version with the requirement of four criteria compared to the previous five which also included an illegal acts criterion[20]. These changes were brought up due to a growing body of literature describing the close similarities between GD and other addictive disorders such as similarities in tolerance,

comorbidity, overlapping genetics, neurobiological mechanisms, and response to treatment[20]. Altogether these changes have appeared to increase the sensitivity of the diagnosis and manifest the status of GD as an addictive disorder[21 22]. The removal of the illegal acts criterion appeared to have very little effect on the population diagnosed with GD[22].

Why do Some Develop a Gambling Disorder?

The reasons why some develop GD appear multifactorial and might differ from individual to individual. The complexity of its development might best be described in a biopsychosocial model in which genetic, biological, environmental, psychological, and social factors all impact the risk of developing PG or GD[23 24]. The following sections will briefly explain the different components believed to play a role in the development of GD.

The pathways model

Alex Blasszynski and Lia Nower published an article in Addiction in 2002 introducing the since well-known "Pathways model"[25]. The authors describe three distinct pathways to developing GD. These are summarized in brief below.

1) "Behaviourally conditioned problem gamblers" are described as a group of individuals without previous vulnerability who develop an addiction due to behavioural conditioning. For example, a previously healthy individual engages in gambling as a leisure activity and develops distorted cognitions surrounding his or her likelihood of winning, loses control of the gambling and develops GD. These previously healthy individuals might then develop later psychiatric comorbidity due to their gambling disorder such as an alcohol use disorder (AUD) or depression.

2) "Emotionally vulnerable problem gamblers" are instead described as individuals with previous vulnerabilities such as psychiatric comorbidities, negative life-events, and previous poor coping or problem-solving mechanisms, who also become behaviourally conditioned, develop distorted conditions but might also gamble to regulate affective stress or negative moods. For example, a person engages in gambling to get relief from a negative mood and later develops distorted cognitions and an addiction to gambling.

3) "Antisocial impulsivist problem gamblers" includes individuals who have a different kind of vulnerability. In this pathway, impulsivity, anti-social personality disorder and attention deficit hyperactivity disorder (ADHD) are common. Individuals are often easily bored, seek adventure, and often engage in a multitude of activities such as

gambling and substance use. Gambling often occurs in binge episodes and commences at an early age.

This model demonstrates how different individuals might develop GD and how heterogenous the group can be. Indeed, individuals with GD range from previously highly functioning individuals to individuals with quit severe experiences of external and internal struggles and difficulties. Although individuals with GD are quite heterogenous in background a few concepts appear to be of importance for the group in developing and maintaining the addiction such as "cognitive distortions", "conditioning" and "biological factors".

Cognitive distortions

The "cognitive distortions" mentioned in the pathways model are thought patterns which are erroneous or distorted beliefs increasing an individual's confidence in winning which are thought to play an important role in the development and maintenance of GD[26]. Some of the more strongly supported cognitive distortions include "the gambler's fallacy" (also called "the Monte Carlo fallacy") and "illusion of control"[26].

The Monte Carlo Fallacy	**Illusion of Control**
The name of this cognitive distortion is believed to stem from a situation at the Monte Carlo Casino, Las Vegas, 1913, where at the roulette the ball had fallen on black for several turns. People gathered around betting on the ball to fall on red again – because of a cognitive distortion where one perceives that the odds are better for red since the ball has already landed on black for so many spins. However, the ball continued to land on black for 26 turns and millions of dollars were supposedly lost.[27]	This cognitive distortion implies that one perceives that one has control of a random event. The gambler might perceive that he or she has a skill to predict whether the ball will fall on red or black at the roulette table. In fact individuals with GD might even show a greater illusion of control in situations other than gambling as well.[28]

Gambling in Art: Edward Munch, By the Roulette (1892).

Conditioning

The pathway model also contains a concept referred to as "conditioning", in which maladaptive learning reinforces GD. There are several different aspects of conditioning including *classical conditioning* where the arousal from winning might be conditioned on the gambling situation at large[29]. Thus gamblers who retain control of their gambling experience arousal related to winning whereas gamblers who have lost control often experiences arousal with regards to the gambling situation at large[30]. Another example is *aversive classical conditioning*. This is a process of learning that a certain stimulus is often related to a negative outcome. For example, learning that gambling often leads to financial losses. Individuals with GD appear to have a diminished capacity to form associations between aversive events and stimuli that predict aversive events, even outside the gambling situation[29].

Biological Factors in Gambling Disorder

Genetics appears to play a considerable role in the risk of developing GD with a heritability estimated to around 50 % in men as well as women, based on results from an Australian twin study on 4,268 pairs of twins born between 1964 and 1971[31 32]. Further, it could also be concluded from the Australian twins study that GD and AUD appear to share genetic underpinnings[32]. Results from studies on American twins

estimated the heritability to around 60 % among men (based on studies on "The Vietnam Era Twin Registry" consisting of 4,774 male American pairs of twins born between 1939 and 1957 with both brothers having served in the United States military during the Vietnam War)[33].

Many different *neurotransmitters and hormones* have been shown to be involved in GD including serotonin, cortisol, glutamate, adrenaline, dopamine and opioids[34]. Their addictive potentials are presented in brief in Table 1.

Table 1 Hypothesized addictive aspects of neurotransmitters and hormones in gambling disorder as explained by Potenza, 2017[34].

Substance	Classification	Addictive potential
Serotonin	Neurotransmitter	Impulse control
Cortisol	Hormone	Stress
Glutamate	Neurotransmitter	Compulsiveness, cognitive flexibility
Adrenaline	Hormone	Arousal, excitement
Dopamine	Neurotransmitter	Reward, learning
Opioids	Neurotransmitter	Pleasure, urge

The importance of dopamine and opioids are clinically interesting and are thus further discussed below.

Dopamine is a neurotransmitter involved in many functions of the brain including reward and learning[34 35]. Behaviours that drive dopamine release appear to have the potential to become addictive[36]. In gambling it is theorized that dopamine will be released upon a win. In games of luck the win is always random and the dopamine release might then evoke a maladaptive learning – *conditioning*[34]. Dopamine might then be released upon contact with stimuli associated with gambling rather than winning. Indeed a raclopride positron emission tomography (PET) study showed that dopamine was released irrespective of gambling outcome suggesting that the mere expectation of reward was sufficient to induce dopamine release (although also in individuals without GD interestingly enough)[37]. Such "reward expectancy" appeared to disappear among individuals with GD where a dopamine antagonist (haloperidol) was administered (in a placebo controlled study) before playing on slot machines[38]. In line with this, dopamine agonists used to treat Parkinson's disease as well as the antipsychotic dopamine modulator aripiprazole, appear to increase the risk of being diagnosed with GD[39]. This indeed calls for an awareness of GD amongst neurologists and psychiatrics treating individuals with Parkinson's disease as well as psychotic disorders. Further,

different variations in genes coding for dopamine receptors appear to influence the risk of developing GD[40 41].

It has been suggested that several regions of the brain such as the striatum[42], prefrontal cortex[42], amygdala[43 44], hippocampus[44] and the pathways between them are affected by gambling and GD. Table 2 displays some of the regions of interest. Indeed, functional magnetic resonance imaging (fMRI) and regular MRI studies have shown differences in connections between regions of the brain at resting states powerful enough to be able to differentiate healthy controls from individuals with GD[45]. In general, the morphology of the brain appears similar to that of other SUDs as well as internet gaming disorder[46]. Affected areas could be potential treatment targets for brain stimulation. Non-invasive brain stimulation studies involving magnetic stimulation or stimulation through creating a current within the brain are hypothesized to affect dopamine release as well as neuromodulation which theoretically should be of interest in the treatment of GD although research is still in its infancy[47].

Table 2. Regions studied in relation to gambling disorder and their hypothesized roles in the development and maintenance of gambling disorder.

Brain region or circuit	Hypothesized functions
Striatum[42]	Decision making. Outcome processing.
Prefrontal cortex[48]	Decision making. Reinforcement. Outcome processing.
Frontostriatal circuit[48]	Impulse control. Considering negative outcomes/ loss prediction.
Amygdala[43 44] and hippocampus[44]	Affective decision making.

Socioeconomic Factors in Gambling Disorder

In general, socioeconomic vulnerability appears to increase the risk of GD[49].

An American telephone interview study concluded that belonging to a minority group and having financial difficulties were important factors associated with GD when controlling for psychiatric comorbidity[49]. Indeed a Finnish study provided evidence that individuals with lower income spend a larger proportion on gambling, thus indicating that gambling could augment economic inequality[50]. Further, low education level (<12 years) and a feeling of being lonely as well as being a recipient of social welfare payments (SWP) and receiving sickness compensation appear associated with GD[51 52 53]. It is well known that GD more often affects younger men, and in a recent review, single young men were shown to be at increased risk of GD. Other factors associated with developing GD were being married for less than five years, living alone, poor education and financial difficulties[54].

Availability and Addictive Potential in Games

To develop GD, evidently, gambling opportunities must be present. Further, the design of the games can augment their addictive potential with, for example, visual and auditory cues which simulate winning - "losses disguised as wins" - which stimulates the reward systems and increase the addictive potential[55 56]. Short time from bet to results, possibilities to increase the size of the bet, playing in parallel sessions as well as long gambling sessions and the game creating an illusion that the gambler has control over the game also seem to increase the addictive potential[29 57 58]. Inversely, giving gamblers feedback about their gambling habits and potential over-consumption might be protective, but such measures are by their nature non-profitable to gambling companies and such regulations probably need be mandatory[59]. Further, some games appear to have a greater addictive potential such as electronic gambling machines (EGM)s, casino games, bingo, poker, and online gambling[51 60].

As can be concluded, the reasons for developing PG or GD are many and complex. In spite of this knowledge, Axelius discussed in her paper from 2017 after in-depth literature and ethnographic fieldwork how a number of stake holders in Sweden hold the gambler herself responsible for the harm the gambling has caused[61]. This approach might increase stigma surrounding GD rather than acknowledging the responsibility of gambling providers, policy makers and the like.

Comorbidity in Gambling Disorder

Psychiatric comorbidity appears relatively abundant in GD. A lifetime prevalence of psychiatric comorbidity in individuals with GD has been suggested to be as high as 94 %[62]. In general, anxiety disorder and depressive disorder appear to be the most common comorbid disorders[63], affecting around 7 in 10 of women diagnosed with GD and 5 in 10 of the men[52]. In a Swedish case-control study (utilizing the same data as the fourth article of this thesis) women with GD were more likely to have a psychiatric comorbidity compared with age and gender matched controls from the same municipality than men were[52]. Overall, women were more likely to receive their comorbid psychiatric diagnosis prior to the GD diagnosis, while men were more likely to receive the diagnoses concurrently[52]. Further, women appear more likely to suffer from predominantly affective and anxiety-related comorbidity whilst comorbid SUD appears to effect men and women with GD at similar levels. AUD might be slightly more prevalent in men than women (although not statistically significant)[63]. SUD in general appear more likely to precede GD in both men and women[43], and might indeed increase the risk of GD[52 64].

Suicidality and Self-Harm in Gambling Disorder

When discussing suicidality, several concepts are often used in literature such as the *suicidal process* in which an individual transforms from non-suicidal to *suicidal*. *Suicidality* itself is a concept often used to describe a state of mind in which a person might be at increased risk of suicide. This process can involve *suicidal ideation (thinking of, or planning a suicide)* and *suicide attempts* or could be an impulsive action in which a person commits a fatal *suicide* without a history of *suicidal ideation*. Related to this, an individual might be thinking of *self-harm* and perhaps progress towards self-harming (with the intent of harming oneself without a deadly intention). This can of course similarly be done without previous thoughts of harming oneself but rather be an act of impulse. A suicide is often defined as a fatal suicide attempt, but it is hard to know whether a deceased individual has suffered from fatal self-harm (perhaps without intent to die). Figure 1 describes the complexity and the potential fluctuation between suicidal and self-injurious thoughts and actions.[65]

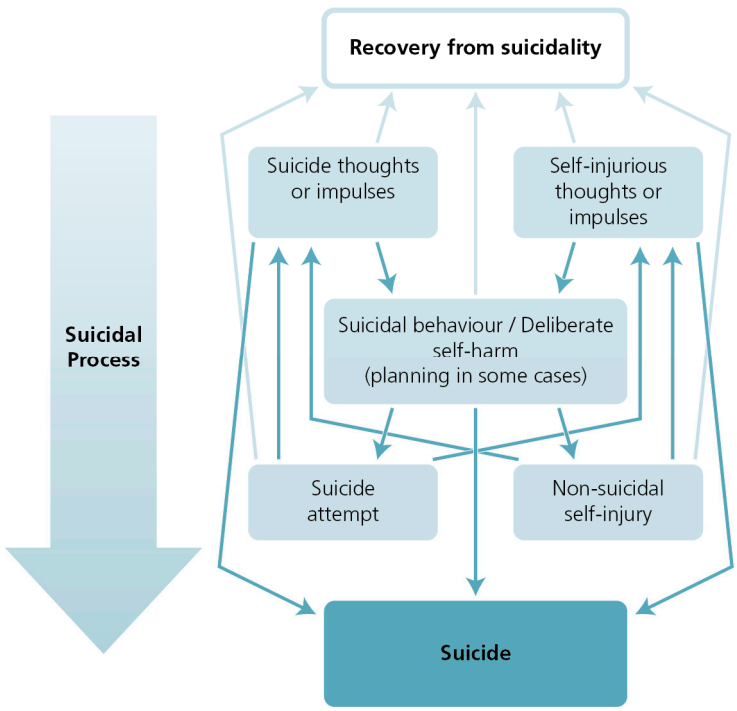


Figure 1. The suicidal process and potential recovery

Suicidality in gambling disorder

Suicidal thoughts are very common at some point in an individual's life affecting approximately nine percent[66], and although common, in a meta-analysis from 2016 suicidal thoughts have been associated with a fourfold increase in risk of suicide death[67]. As many as 60 % of suicide attempters have been described as passing away as a result of their first suicide attempt[68], and among survivors one in fifteen are described as dying from a later suicide attempt within the following nine years[69]. With the severity of the attempt being the most important risk factor within the first five years and psychotic disorder becoming the most important risk factor in the long term[70]. This demonstrates the importance of understanding the suicidal process to hopefully prevent suicide. Individuals with GD appear to suffer from increased levels of suicidality and self-harm. Non-fatal suicidal behaviour is common in GD[71-73], and appears to be more abundant among women with GD[74-77]. A recent study indicates higher risks of suicide attempts within the first year after receiving a GD diagnosis[74].

Several risk factors for suicide attempts in GD have been described, including alcohol use disorders (AUD)[74], depressive disorders[78], anxiety disorders personality disorders[75], being a victim of childhood sexual abuse[79], cluster B personality disorder (as described in DSM-IV)[75], attention deficit/hyperactivity disorder,[81] as well as female gender[75 76]. These risk factors might affect different individuals to varying extents and might be complexly related. For example, being a victim of childhood sexual abuse was described as a risk factors for suicidality in black, but not white, Americans with GD[82].

Psychiatric risk factors thus appear important in the development of suicidality. However, GD often leads to financial hardship and indebtedness which have also been identified as risk factors for suicidality in GD[83]. In a study of male gamblers seeking help in the United Kingdom, of whom roughly one in five reported having made a suicide attempt, having prior suicidal thoughts or depression, being on medication as well as social isolation (loosing relationships to one's family members) and losing one's housing were all associated with having made a suicide attempt[84]. Criminality in general has not been studied much in the GD context but is a known risk factor for suicidality in general[85].

Although many factors associated with suicidality have been identified, little is known about the suicidal process in GD and there are many confounding factors. Does depression increase the risk of GD and do GD and depression together predict suicidality? Such confounding factors are hard to fully correct for statistically.

Marionneau and Nikkinen reviewed qualitative literature on gambling-related suicidality and concluded that the pathways between gambling and suicidality need to be further investigated especially with regards to gender[86]. However, from the twenty

articles included in their review (of which some were case reports) they concluded that unmanageable debt and shame increased suicidality in individuals with PG and GD[86].

Self-harm in gambling disorder

Less is known about self-harm in GD. Self-harm is, however, an important risk factor for suicide in general[87 88], and has been described as being associated with attempts at emotional regulation[89], social communication[89], and self-hatred[90]. Non suicidal self-harm also appears to be predicted by childhood maltreatment[90 91], cluster B personality disorder and feelings of hopelessness[92]. A survey study on youths from Connecticut concluded that self-injurious behaviour was associated with at-risk and PG[93]. Self-harm is common in psychiatric populations, in-fact half of the patients in in-patient and out-patient psychiatric care in Sweden were estimated to have had experiences of self-harm, more often affecting women although men, interestingly, were found likely to have kept their history of self-harm private[94]. Considering this, it might be hypothesized that individuals with GD likely suffer from elevated levels of self-harm.

Suicide Mortality in Individuals with Gambling Disorder

A scoping review published in 2022 on suicide deaths related to PG identified only 18 relevant articles, among which only a handful were original research articles, and concluded that literature on the subject is sparse[95]. Most of the identified studies involved post mortem investigation such as examinations of coroner files or studies based on interviews with people close to the deceased[95]. Findings from these studies will be discussed below.

Blaszczynski and Farell claimed, after investigating 44 coroner files related to gambling, that co-morbid depression, presence of severe financial debt, relationship difficulties, introversion and low self-esteem might be potential risk factors for suicide death among problem gamblers and that the highest risk period may be following a serious loss, disclosure of criminal offenses or gambling-related debts[96].

Bourget et al. hypothesized, after investigating 79 coroner files, that the risk of suicide might be primarily linked to multiple losses as a consequence of the PG itself[97]. A comparative study on 49 individuals deceased from suicide and 41 living individuals, all with at-risk or PG described the deceased individuals as having had more comorbid mental health disorders during their last six months prior to death than the controls, as well as having experienced more financial difficulties during their last ten years[98].

Séguin et al., compared predominantly male suicide victims (>90 % of the suicide victims were of male gender) with and without gambling problems and found

personality disorder to be twice as common in individuals with a history of PG who also were less likely to have been in contact with health care prior to the suicide[99].

Wong and colleagues describe, in an article on 17 suicide victims with GD, that all had unmanageable debts and that none had sought psychiatric health care even though the majority had struggled with depressive disorder[100]. Another study from Wong et al., examining 1201 coroner files indicated a 19 % incidence of prior gambling activities among which 42 % had been put into debt due to gambling[101].

Mortality in Individuals with Gambling Disorder

It appears as if individuals with GD often are burdened by both somatic and psychiatric comorbidity. Indeed, GD is associated with several medical disorders including obesity[102 103], and cardiovascular disorders[104 105]. In a northern-Italian study, mortality was investigated through following 823 individuals diagnosed with GD according to ICD-9 or -10[106]. In the study an increased standardized mortality ratio (SMR) of 1.16 was found, although not statistically significant (95 % CI: 0.85-1.58), highest among those less than 30 years of age[106]. Increased SMRs for suicide were interestingly found for both women and men, although neither were statistically significant[106]. And in a study analysing data from a large bank in the United Kingdom high levels of money spent on gambling was associated with an increased 5-year mortality of about one third for both men and women of all ages[107]. Altogether, although very little is known about the mediators between GD and mortality it appears as if the group suffers from elevated levels of mortality.

Gender in Gambling Disorder

Women are in minority amongst those with GD and tend to develop the addiction secondary to previous psychiatric comorbidity in contrast to men[52]. Furthermore, women appear to be at higher risk of psychiatric comorbidity and socio-economic vulnerability such as receiving sickness activity or rehabilitation compensation[52]. Traumatic life events prior to gambling and sexual abuse have also been described as more common in women with GD[108]. Experiencing intimate partner violence has also been described as increasing gambling among women[109], perhaps in some as a way to escape intimate partner violence physically and psychologically[110]. As such it is important for social workers and clinicians to understand the life context of these women in order to understand their motivations for gambling and also to address current safety with regards to potential ongoing violence.

Thus, women appear more likely to develop GD in line with the "Emotionally vulnerable problem gamblers" pathway in Blazynski and Nower's model[25]. Further, women appear to be older when they start gambling and might progress faster into GD, a phenomenon often referred to as *telescoping*[111].

Men appear more likely to be involved in online gambling and women often appear to gamble on non-strategic types of gambling such as on EGMs or bingo whereas men prefer more strategic games such as poker or sports-betting[108 112 113].

Gambling in Art: Theodore Gericault, A Madwoman and Compulsive Gambler, 1822.

Economic Factors in Gambling

The global gambling market has been growing steadily, exceeding 400,000 million euros in 2019 (measured as the total sum of bets placed minus winnings paid out to gamblers)[114]. In 2017 *The Economist* looked at gambling losses per citizen and concluded that losses were greatest in Australia with Sweden ranking in 12th place[115]. It also appears as if a large portion of revenues are made from individuals with at least PG[116]. As previously described lower socioeconomic status might increase the risk of developing GD, and the uncontrolled gambling itself can then of course cause severe damage to one's personal economy.

Financial difficulties and indebtedness are perhaps not so surprisingly common in individuals with PG and GD[83 117]. Over-indebtedness had been described as being more common among female gamblers in an online gambling setting[112]. It appears as if the higher the percentage of income spent on gambling, the higher the risk of being subject to debt collection by the bailiff[107]. A study on gambling helpline callers concluded that financial difficulties were associated with self-reported suicidality (suicidal thoughts and previous suicide attempts)[118]. Furthermore, over-indebtedness appears to be linked to somatic and psychiatric comorbidity as well as increased mortality[119].

The Swedish Enforcement Authority

When an individual has not repaid his or her debt the claimant or the indebted person can contact the Enforcement Authority who might decide to aid the claimant to collect the debt, a concept refer to as *execution*[120]. This can be done by deducting money from the indebted individual's salary (or other incomes such as sickness or parental benefit or pension) or by selling the possessions of the indebted individual[120].

In a nationwide case-control study Rojas investigated the effect of having experienced action by the Enforcement Authority compared to age and gender matched controls while controlling for socioeconomic and psychiatric comorbidities[121]. The study showed that individuals subject to action by the Enforcement Authority had a 2.4 times increased risk of death from suicide within the first year (self-harm of intentional and of unknown intent, adjusted odds ratio (OR))[121].

The Enforcement Authority can also, in certain cases, provide debt settlement which is intended to make the indebted individual debt-free[120]. A clinical impression is that such aid is rarely granted to individuals with addictive disorders, perhaps due to the long-term risk of relapse.

Treatment

Several studies assessing the effect of different psychiatric medications on GD have been undertaken with varying results[122]. Opioid antagonists and modulators such as naltrexone and nalmefene are being clinically used in several settings and have shown promising results, as has the atypical antipsychotic olanzapine, although further research is needed before the drug might be introduced clinically[122]. Although pharmaceutical therapies such as opioid antagonists and modulators have been shown to have some effect on GD they appear less effective than cognitive behavioural therapy (CBT)[123-126].

Therapeutical treatment, especially through CBT appears to have the strongest beneficial effect on GD[124 127]. CBT is sometimes offered in combination with motivational interviewing (MI) which appears to have primarily a short-term positive effect on GD (although clinically valuable in those with comorbid addictions)[124 127]. Both the intended number of sessions of CBT, as well as number of sessions received appear to be positively associated with treatment outcome[128]. Both group [129 130] – and internet-based CBT[131 132] have proved efficient, although CBT provided individually appears to show the best results[133 134]. CBT provided individually should also theoretically improve the opportunity to identify suicidality and increase individual safety during treatment.

Studies on brain modulation such as magnetic stimulation or through creating intracerebral currents might be future treatment options for GD although the research is still rather preliminary[47].

Further studies on individual and combined psychosocial and pharmacological treatments are much needed, potentially addressing different presentations of GD[124 135]. Long-term follow-up studies on both pharmaceutical and therapeutic treatment interventions are also much needed.

It has also been suggested that specific considerations with regards to gender are of importance in research on treatment for GD, with a possible aim at person-centred treatment focusing on increasing self-esteem, self-control and emotion-regulating capacity in women with GD[136].

Finally, some individuals appear to self-recover without any treatment[137]. However, long-term studies are needed to explore self-recovery and treatment outcomes for GD.

Treatment in Sweden

Social services and health care have a shared responsibility for the treatment and care of individuals with addictive disorders and GD was included in this responsibility in

2018[123]. In spite of this, only 600 individuals receive interventions from the social services annually (although this number has been very hard to evaluate) and treatment uptake in health care is also much too low[138]. It is not known who is, or who should be, given treatment by primary care, specialized outpatient care, the social services, private care givers or occupational health care. Knowledge of potential differences in treatment effect and attrition, comparing different treatment providers, is also absent.

In both social services and health care, CBT is the treatment recommended for GD by the Swedish National Board of Health and Welfare[123]. CBT has the strongest evidence for effect on GD but data on long-term follow-up is lacking[123]. For those in need of motivational interventions, MI in combination with CBT is recommended[123], such as for those with comorbid AUD[127]. Identifying suicidality is highlighted as important and should imply involvement with specialized psychiatry as well as identifying and addressing psychiatric comorbidity[123].

Pharmaceutical therapies such as opioid antagonists and modulators are not yet recommended in standard practice in Sweden.

Research Questions

What are the levels of suicide death and intentional self-harm in gambling disorder?

Knowledge about the negative consequences of gambling is on the rise. However, regarding suicidality much research is based on self-reported suicidality often based on a spectrum of individuals with recreational gambling, PG and GD making clinical implication difficult. Suicidality itself can often vary in definition from suicidal thoughts, previous suicide attempts and sometimes self-harm. This is indeed important knowledge; however, it does make suicidality in GD hard to estimate. There is in particular a lack of knowledge on suicide death and its risk factors in individuals with GD.

As such, knowledge on crude suicide rates in GD compared to the general population are needed in order to properly assess suicide risk. As knowledge about risk factors for suicide death is scarce, such associated factors also need further investigation. Further, such knowledge is also needed with regards to intentional self-harm, including suicide attempts without the bias of self-reporting.

Is there an increased mortality in gambling disorder?

Mortality, including somatic mortality is often rather increased in individuals with SUD and with psychiatric diagnoses at large, however, little is known about mortality levels in GD.

Also, much research done on GD involves predominantly (and sometimes only) male subjects making conclusions hard to draw for women. This is especially true for more unusual outcomes such as suicide death in which larger samples are needed to draw conclusions.

What can we learn about the characteristics of suicidal processes in women with gambling disorder?

Finally, although statistical associations have been drawn on GD and factors associated with increased risk of having committed non-fatal suicide attempts - the suicidal process is less well known and of much interest to explore. As GD often comes with psychiatric comorbidity and socioeconomic risk factors, the impact of GD itself on the risk of

suicide mortality, mortality and suicidality is hard to completely adjust for in statistical models. As such, qualitative research is in demand to further understand the suicidal process in GD and how potential risk factors affect this suicidality. Perhaps even more urgently so for women, as women with GD tend to suffer to a greater extent from previous traumatic events, psychiatric comorbidity, and socioeconomic vulnerability.

Aims

This thesis aims to explore the negative consequences for men and women with GD focusing on suicidality, suicide, and mortality.

Study I

To investigate suicide rates and general mortality in GD specifically by investigating SMRs for patients with GD as well as to compare mortality and suicide rates to those in the general population. Furthermore, we aimed to investigate the effects of specific risk factors previously associated with suicidality and suicide among individuals with GD as well as to investigate risk factors in general for mortality.

These were our main hypotheses:

- For suicidality:

  H_0: $SMR_{suicide\ death} \leq 1$

  H_α: $SMR_{suicide\ death} > 1$

- For mortality:

  H_0: $SMR_{mortality} \leq 1$

  H_α: $SMR_{mortality} > 1$

Study II

To further outline the factors associated with intentional self-harm and specifically whether the occurrence of intentional self-harm would demonstrate associations with AUD or DUD, also when controlling for other common psychiatric disorder.

Our main hypothesis was:

H_0: *GD+SUD ≤ prevalence of intentional self-harm compared to only GD*

H_α: *GD+SUD > prevalence of intentional self-harm compared to only GD*

Study III

To investigate risk factors for intentional self-harm, including suicide attempts, in individuals with GD focusing on gender, socio-economic risk factors, primarily SWPs, but also criminality in relation to previously known psychiatric risk factors.

Our main hypothesis was:

H_0: GD+SWP ≤ prevalence of intentional self-harm compared to only GD

H_α: GD+SWP > prevalence of intentional self-harm compared to only GD

Study IV

To compare all-cause mortality, suicide mortality and age of death, between individuals with GD and matched controls. To investigate the association between GD and all-cause and suicide mortality respectively in relation to previously known risk factors, and to compare causes of death between cases and controls.

These were our main hypotheses:

For suicidality:

H_0: GD has a HR ≤ 1 when controlling for known risk factors

H_α: GD has a HR > 1 when controlling for known risk factors

For mortality:

H_0: GD has a HR ≤ 1 when controlling for known risk factors

H_α: GD has a HR > 1 when controlling for known risk factors

Study V

To explore personal experiences of suicidality in women with GD. And to investigate potential pathways from GD to suicidality.

Preconception:

Experiences of trauma, psychiatric comorbidity, shame and stigma and economic and relational difficulties might be important factors in developing suicidality related to GD.

Methods

This thesis is built on quantitative and qualitative research with the aim of answering questions of prevalence and risk of suicidality, suicide, and mortality in GD and to try to understand the suicidal process in women with GD. As such, it was our ambition to include a diversity of study designs to better understand the negative consequences of GD from different angles. Table 3 gives a brief outline of the methodologies used in the five studies included in the thesis.

Table 3. Methodological characteristics of the five studies of the thesis. (N= number of patients in the study, SMR= Standardized mortality ratio). *Same cohort.

Study	Methodology	N		Analyses
I	Quantitative register study	Cohort*	2,099	SMR-calculations Cox-regression Descriptive statistics
II	Quantitative register study	Cohort*	2,099	Chi-square test Logistic regression Descriptive statistics
III	Quantitative register study	Cohort	850	Chi-square test Cox regression Descriptive statistics
IV	Quantitative register study	Case-control	10,792	Cox-regression Descriptive statistics Independent samples T-test
V	Qualitative study	Semi-structured interviews	7	Transcription Coding Theme-building

Sample, Setting and Design

All studies are based on individuals with GD in Sweden. The first four studies are based on register data and contain national cohorts of individuals with a diagnosis of GD in the Swedish national patient register (and in the fourth study a control population as well). Studies I and II are based on the same sample and are an earlier representation of the population, whereas Studies III and IV are based on later retrievals from the registers. The fifth study, being qualitative in nature, will be discussed separately.

Studies I-IV

As can be seen in Table 4, Studies I-IV are based on populations of individuals with GD in the national patient register. The first two studies are based on the same population.

Table 4. Sample and design of studies I-IV. (LISA= Swedish Longitudinal integrated database for health insurance and labour market studies. ICD-10 = International classification of diseases, 10th edition. GD= gambling disorder. SWP= Social welfare payment.)

	Studies I and II	Study III	Study IV
Study inclusion	Date of first GD diagnosis during 2005-2016	Date of first GD diagnosis during 2011-2014	Date of first GD diagnosis during 2005-2019 (same date for controls)
Study censoring	31st December, 2016 or date of death	31st December, 2017 or date of death	31st December, 2019 or date of death
Case vs control	No (However in Study II individuals with substance use diagnoses were compared to those without)	No	Case vs control: 1:2. Matched based on gender, age, and municipality
Average follow-up	4.7 years	4.9 years	4.6 years
N	2,099	848	10,792
ICD-10 codes in Swedish national patient register	Psychiatric diagnosis in detail.		Psychiatric diagnosis in detail. Somatic diagnosis on chapter level
Cause of death register	Information on underlying and contributing psychiatric and somatic causes of death and date of death.		
The LISA register	No	Marital status. SWP Children.	Educational level SWP Unemployment. Sickness, activity, and rehabilitation compensation.
The Swedish National Council for Crime Prevention Register	No	All verdicts during the study period.	No

Registry data and its methodological challenges

The first four studies of the thesis are based on registry data. National registers offer unique research opportunities. In Sweden, at birth, or upon gaining citizenship, a personal identity number (PIN) is created based on birth data i.e., 19920906 (birth year 1992, month of September, followed by the day of the month) and followed by four numbers (0-9). 19920906-XXXX[139 140]. The third of these four last digits is an even number in women (0-8) and uneven in men (1-9)[139]. The fourth number is created based on a calculation of birth-time and date[139]. For those who choose to change their

legal gender a new PIN is allocated[139]. The most common reason for a new PIN number is a discovered fault in the birth data which provides the base of the PIN, which is most common among immigrants[140]. The third and most uncommon reason for a change in PIN is in very severe cases of protected identity[140]. The PIN is the base for all Swedish national registers and unique individuals can, due to the PIN, be linked in several registers.

Since Swedish registry data is quite extensive and of delicate nature it is not accessible to the public. In order to utilize the data for research one must apply to and receive permission from "Etikprövningsnämnden"[c] [141]. Once a permission has been granted, an application to retrieve the data from the authority holding the register of interest can be submitted for internal ethical review within the specific authority. When data is sent to the researcher the PIN is removed and replaced by a number created for research process to ensure privacy. When data from several registers is used, Statistics Sweden is responsible for linking the PIN and creating these fictional identification numbers (ID) linking a unique individual throughout the registers.

This thesis is, as can be seen in Table 3, based on data from several national registers which will be described below, focusing on the national patient register and cause of death register as they are of greatest importance for this thesis.

The Swedish national patient register

The national patient register held by the National board of Health and Welfare contains information on in-patient and out-patient visits to both public and private health care but not primary care[142]. Data is retrieved from the 21 regions and from private caregivers and is updated monthly[142]. The register was externally evaluated in 2011 and was estimated to have a positive predictive value of roughly 90 % and covers 99 % of all hospital discharges and around 80 % of all hospital-based outpatient care[143]. The latter percentage has been suggested to be lower due to missing data from private caregivers and mental health outpatient treatment[144]. However, it is likely that the quality has since improved. In 2006, diagnoses were not reported for as many as 23 % in outpatient psychiatry, but missing data have dwindled to a level of 5 % in outpatient specialist treatment (2021)[145]. In general the quality of the register appears better for inpatient care as well as somatic care, although quality appears to be improving and is estimated to be generally good[145]. However, although the quality of the register appears good, it is built on clinical diagnoses and thus relies on the general quality of the diagnostic process in Swedish healthcare.

[c] in English: the Swedish Ethics Review Authority

The register contains several variables and Table 4 portrays the main variables used in this thesis. Of note is that the register provides not only data on the specific diagnosis but also date about the diagnosis, whether the visit was in in-patient, or out-patient care. The register also holds information on main- and secondary diagnoses classified according to the ICD-10.

What are main and secondary diagnoses in the national patient register?

An individual might be treated for a pneumonia at the primary care unit, while also having a depression and a hypothyroidism. This would, however, not be registered in the national patient register since primary care data is so far not included. However, should the pneumonia get worse, and the individual seek the emergency care unit – then the diagnoses will be registered. The pneumonia will be the main diagnosis and the hypothyroidism and depression will be listed as secondary diagnoses. Should the person instead go to see her psychiatrist while also suffering from pneumonia the psychiatrist will belong to specialized health care and thus diagnoses from this visit will be registered. However, the psychiatrist would perhaps typically diagnose the individual with depression as the main diagnosis and hypothyroidism and pneumonia as secondary diagnoses. As a clinician, uncertainty as to which diagnosis should be registered as "main diagnosis" is common. In this thesis no difference has been made with regards to main and secondary diagnoses since they describe the diagnoses most relevant to that specific contact with health care and not which diagnosis might be most relevant for the individual or the research questions in this thesis.

The Swedish Cause of Death Register

The cause of death register is also held by the National Board of Health and Welfare and contains information according to the International Form of Medical Certificate of Cause of Death[146]. Swedish physicians are obliged to report these data to the National Board of Health and Welfare within 3 weeks from time of death[146], and the register has a coverage of >99 % of deaths in Sweden[147].

If a death is unexpected (such as in a previously healthy individual found dead) or an unnatural cause of death is suspected (such as overdose, homicide or suicide), or a person with a known SUD passes away (irrespective of whether the death was likely due to a somatic disorder), the treating physician does not fill in the cause of death certificate, rather a forensic autopsy is performed[146]. This procedure has been estimated to cover 95 % of the deaths due to suicide[146]. In 90 % of forensic autopsies in Sweden, a comprehensive analysis of alcohols, pharmaceuticals, and illicit drugs is performed[146].

The quality of the cause of death register has been sparsely evaluated externally, but the National Board of Health and Welfare state that the reliability is very high[147]. However,

estimations through comparison to case reports looking at individuals who passed away in the year of 1995 in in-patient care found an agreement of 77% on underlying cause of death with higher accuracy among younger patients (98 % for those <45 years of age and 91 % for those between 45-64)[148].

What are underlying and contributing causes of death?

The Cause of Death register aims to offer an underlying cause of death and often also contains one or several contributing causes of death[147]. Often the treating physician will determine the underlying cause of death. For example, if a primary care doctor is responsible for a home for the elderly and is treating Anna Karlsson 94 years for diabetes and she should fall sick with a stroke and in the days after show symptoms of pneumonia - the general practitioner might, in accordance with his patients wishes, decide not to refer her to the hospital but to treat the pneumonia and palliate her symptoms. Should she die, the general practitioner will do an on-site mandatory post-mortem investigation which includes routine investigations so that no obvious signs of "unnatural death" would be present. Such signs could be physical ones, on the body of the deceased such as knife wounds or a lot of pills in her mouth or obvious signs on the site of death or suspicions evoked from discussion with the staff at the home for the elderly or individuals close to the deceased which might indicate risk of suicide, SUD or murder[149]. In such cases the police must be contacted and decide whether a forensic examination should be performed[149]. If not - the general practitioner will fill in the death certificate as the example in Figure 2.

As can be seen in Figure 2 the doctor chose to state that the terminal cause of death was the pneumonia. She did not state an underlying cause to the pneumonia but rather stated that the stroke and diabetes were contributing causes of death. In this case, another doctor might have made another judgement and stated that the pneumonia was the terminal cause of death but that the stroke was the underlying cause behind the pneumonia and perhaps also that the diabetes was the underlying cause of the stroke.

In fact, deaths among the elderly have been suggested to be the most unreliable data in the cause of death register[149]. Almost 40 % of the deceased received a clinical autopsy in 1969 which dwindled to less than 5 % in 2016 which has been suggested to reduce the validity of the Cause of Death register[150].

However, at the National Board of Health and Welfare, the Cause of Death certificate will be processed and the underlying cause of death will be determined by a routine procedure in accordance with the recommendations from the WHO[147]. The underlying cause of death is stated as the disease (or accident, or intentional harm) that starts the chain of actions ultimately leading to death and should be the factor which – if treated would best prevent death[147].

Rensa Skriv ut

Socialstyrelsen

DÖDSORSAKSINTYG

Till

Socialstyrelsen

☐ Ersätter tidigare utfärdat intyg

Den avlidnes personuppgifter

Personnummer/samordningsnummer (12 siffror)	Födelsedatum (8 siffror) och kön om personnr/samordn.nr saknas			
18920906XXXX	18920906	☒ Kvinna	☐ Man	☐ Går ej att avgöra

Efternamn	Förnamn
Karlsson	Anna

Bostadsadress	Postnummer	Postort
Vilan Ålderdomshem. Storgatan 1	11111	Malmö

Land (om ej stadigvarande bosatt i Sverige)	Identiteten styrkt genom
	Kännedom

Dödsdatum

År mån dag (fyll ut med nollor om exakta uppgifter saknas)			Om dödsdatum ej säkert, anträffad död	År mån dag
19861010	☒ Säkert	☐ Ej säkert		

Dödsplats

Kommun (om okänd dödsplats, kommunen där kroppen påträffades)		
Malmö	☐ Sjukhus	☒ Särskilt boende
	☐ Ordinärt boende	☐ Annan/okänd

Barn som avlidit senast 28 dygn efter födelsen

☐ Dödfött ☐ Avlidet inom 28 dygn efter födelsen

Läkarens utlåtande om dödsorsaken[1]

Sjukdoms- eller skadeförlopp som ledde till den terminala dödsorsaken

	Den terminala dödsorsaken var	Ungefärlig debut (år mån dag)	Akut	Kronisk	Uppgift saknas
A	Lunginflammation	19861007	☒	☐	☐
B	som var en följd av		☐	☐	☐
C	som var en följd av		☐	☐	☐
D	som var en följd av		☐	☐	☐

Andra sjukdomar eller skador som bidragit till dödsfallet	Ungefärlig debut (år mån dag)	Akut	Kronisk	Uppgift saknas
Stroke	19861001	☐	☒	☐
Diabetes Mellitus	19700101	☐	☒	☐
		☐	☐	☐
		☐	☐	☐
		☐	☐	☐
		☐	☐	☐
		☐	☐	☐
		☐	☐	☐

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Den avlidnes personuppgifter

Personnummer/samordningsnummer (12 siffror)	Födelsedatum (8 siffror) om personnr/samordn.nr saknas
18920906XXXX	18920906

Opererad inom fyra veckor före döden

☒ Nej ☐ Uppgift om operation saknas		
☐ Ja	Operationsdatum (år mån dag)	Tillstånd som föranledde ingreppet

Skada/förgiftning

☐ Olycksfall ☐ Självmord		Datum för skada/förgiftning (år mån dag)
☐ Avsiktligt vållad av annan ☐ Oklart om avsikt förelegat		
Kort beskrivning av hur skadan/förgiftningen uppkom (utan att röja eventuellt andra inblandades identiteter)		

Dödsorsaksuppgifterna grundar sig på

☒ Undersökning före döden	☒ Yttre undersökning efter döden	☐ Klinisk obduktion
☐ Rättsmedicinsk obduktion	☐ Rättsmedicinsk likbesiktning	

Underskrift av utfärdande läkare

Ort och datum Malmö 19861010	Läkarens namnteckning	
Läkarens efternamn och förnamn Karlsson, Anna		Befattning ST-läkare i allmänmedicin
Tjänsteställe Vårdcentralen Vilan		
Utdelningsadress Vårdcentralen Vila, Lillgatan 1	Postnummer 111111	Postort Malmö
Telefon (inkl. riktnummer) 0403310000	E-post Karlsson.vilan@skane.se	

❶ Uppgift om dödsorsak

Vid utlåtande om dödsorsaken ska diagnosen specificeras så noggrant som möjligt. Förkortningar och kodnummer ska undvikas.

Ange för diagnoserna

- tumör: malign eller benign samt primärtumörens läge,
- diabetes mellitus: typ och komplikationer, och
- njursjukdomar: komplikationer (t.ex. hypertoni) och etiologi till njursvikt.

Ange det sjukdoms- eller skadeförlopp som haft störst betydelse för dödsfallet. Om förloppet kan beskrivas med en enda diagnos, ska denna anges på den översta raden. Följande rader lämnas då tomma.

Om förloppet måste beskrivas med flera diagnoser, ska den terminala dödsorsaken skrivas på den översta raden. Det eller de tillstånd som ledde fram till den terminala dödsorsaken skrivs på raderna nedanför, så att det bildas en kedja av orsaker och komplikationer från det inledande tillståndet på den nedersta raden upp till den terminala dödsorsaken. En sådan kedja kan vara akuta patologiska förlopp eller ett tidigare tillstånd som har berett vägen för ett senare, t.ex. genom vävnadsskador eller funktionsnedsättning.

För hjärtsvikt och lunginflammation ska eventuella bakomliggande tillstånd anges enligt följande.

Översta raden: hjärtsvikt; följande rad t.ex. lårbensbrott.
Översta raden: lunginflammation; följande rad t.ex. influensa.

Ange tydligt om någon uppgift inte kan lämnas enligt följande.

Översta raden: hjärtsvikt; följande rad t.ex. okänt (patienten avböjde utredning).

Ange under "Andra sjukdomar eller skador som bidragit till dödsfallet" tillstånd som kan ha påskyndat förloppet men som inte ingår i händelsekedjan som beskrivits i "Sjukdoms- eller skadeförlopp som ledde till den terminala dödsorsaken".

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2 (2)

Figure 2. A fictional example of a Swedish Cause of Death certificate illustrating the death of a 94-year-old woman suffering from diabetes, stroke, and pneumonia (in Swedish).

When utilizing data from the Cause of Death Register the process from clinical evaluation to the handling at the Board of Health and Welfare must be considered. Depending on the research question, interest in underlying or contributing causes of death can vary. When looking at general mortality our interest has been in looking at the underlying cause of death. However, when investigating suicide and unnatural death we have included contributing causes as well in Study IV. Should an individual die from pneumonia after suffering a stroke which was the result of a suicide attempt due to hanging – then we have made the decision to include the suicide regardless of whether it was considered the underlying or contributing cause of death. However, in Study I underlying causes of death were used to be able to compare to national statistics.

Challenges in evaluating suicidality and self-harm in registry data

As the Cause of Death and Patient Registers contain information based on ICD-10 it is important to understand some basics of the diagnostic classifications. For most diagnoses, this is rather straightforward, such as for GD (ICD-10 code F63.0). If a patient has been coded in the register as having F63.0, theoretically, the individual should fulfil the diagnostic criteria for GD during that specific time. However, when it comes to diagnosing and classifying suicidality and self-harm it is both a clinical challenge and further complicated by the inability of the ICD system to differentiate between intentional self-harm and suicidal actions, Table 5. Further, there are no diagnostic codes describing suicidal thoughts or plans. Thus, even though such information can and must be recorded in the medical records it cannot be coded in the diagnostic system and will thus never appear in the national registers.

Table 5. Diagnostic codes in the ICD-10 system and fictional examples in the national patient and cause of death registers with comments on difficulties in classification.

ICD-10 code and Diagnosis	Examples in the Patient Register	Examples in the Cause of Death register	Interpretation
X40–49 Accidental poisoning by and exposure to noxious substances	A four-year-old boy has eaten a venomous plant.		Likely accident.
	A person with a substance use disorder has taken an accidental overdose.		Might be an individual who claims the overdose was an accident- but how certain can one be? In some studies on opioid overdose survivors, only 10 % have been classified as of suicidal intent[151], whereas in others about half of the respondents stated suicidal intent to various degrees illustrating the complexity of determining suicidality[152 153].
		An individual with progressed Alzheimer's disease has deceased after taking the wrong medication.	Or did the person intoxicate with a suicidal intention?
X60–X84 Intentional self-harm	A person with a substance use disorder has taken an intentional overdose.		Likely suicidal, however – could it be a call for help?
	A person has cut her wrists to relieve anxiety.		Or was it with suicidal intent?
		A person with a substance use disorder has died from hanging.	High likelihood of suicidal intent.
		A person with newly diagnosed depression has died from a cut to her wrists.	Could it be death from self-injurious behaviour?
Y10–Y34 Event of undetermined intent	A person with a substance use disorder has taken an overdose.		Suicidal intent unclear, might be an act of self-harm, a suicide attempt or none of the above.
		A person with a suspected substance use disorder has died from an overdose.	Suicidal intent unclear, might be an act of self-harm or none of the above.

While working on this project we have further been humbled by the difficulty in investigating suicidality in registry research. We have, however, chosen to define X60-X84 in the Cause of Death register as suicide in line with how it is presented by the Public Health Agency of Sweden[154]. We have tried to broaden and deepen our discussion on

X60-X84 diagnoses with non-fatal outcome to refer to them as events of intentional self-harm, potentially suicidal in nature which is reflected in the third and fourth study. We have chosen never to include events of undetermined intent or accidents in the concepts of suicide, suicidality or intentional self-harm but rather trust the medical profession in their judgement of intent. Björkenstam and colleagues suggested a separation of undetermined and intentional causes of death since several background differences were associated with the death being classified as suicide such as male gender, married status, and not being born abroad[155]. Distinct differences in risk factors between deaths classified as undetermined intent and suicides were also found in a cohort of clients of the criminal justice system with substance use problems[156]. As such, we believe we might underestimate rather than overestimate suicide deaths rates and events of intentional self-harm although it is our believe that this lies closer to the truth.

The LISA register

The Swedish Longitudinal Integrated Database for Health Insurance and Labour Market Studies (LISA) is a register held by Statistics Sweden[157]. The register contains information on educational level, financial support, unemployment, marital status, and potential children.

In the third study, data on SWP, children and marital status was utilized. In this study, the aim was to investigate the effects of economic difficulties on non-lethal suicidality and self-harm. Individuals with SWP are in contact with social services and have apparent financial difficulties. As there is a shared treatment responsibility for GD between health care and social services, we thought SWP would be an interesting factor to evaluate with regards to suicidality/self-harm, hypothesizing that it would be a risk factor for intentional self-harm.

In the fourth study, data on unemployment, SWP, sickness activity and rehabilitation compensation was retrieved and a binary variable on "socioeconomic vulnerability" was constructed as done previously in the research group[52]. This method was chosen since we learned in the third study that individuals with SWP more often had experienced intentional self-harm, although SWP was not statistically associated with the outcome. We thus hypothesized that SWP was too unspecific, and that socioeconomic vulnerability should be assessed differently.

The factor "socioeconomic vulnerability" was defined as any incidence of unemployment, SWP, or receiving sickness/activity/rehabilitation compensation. Sickness compensation requires a permanent inability to work, activity compensation requires an estimated sickness duration of at least one year, and rehabilitation compensation a duration of at least 60 days.

Education level is a category in the register indicating an individual's highest level of education (compulsory school, upper secondary school and education at university level). From this variable we computed a dichotomous variable "elementary school education" dividing the material in two groups:

- those with elementary school (i.e., mandatory education until the 9th grade in Sweden) as their highest educational level and,
- those with high school or higher education as their highest education level.

This division was chosen due to previous findings of an increased suicide risk for men with highest education at elementary level[158].

The Swedish National Council for Crime Prevention Register

The Swedish National Council for Crime Prevention holds a register on Swedish court verdicts, orders of summary punishment as well as a form of "failure to prosecute" where there is no doubt that the suspect has committed the crime, but for various reasons a case cannot be brought to court[159]. The register is estimated to have a high accuracy with only 0.001 % cases missing a PIN in a study on 205,846 violent convictions [160]. In the third study of the thesis, data from this register was utilised, and apart from looking at crime in general, we created variables of violent crime, sexual crime, acquisitive crime, economic crime, and drug crime which were defined through categorizing Swedish law violations as can be seen in Appendix A.

Study V

The fifth study, qualitative in design, was set up in the town of Malmö in the south of Sweden.

The sample was recruited through criterion sampling[161]. The inclusions criteria, which all had to be met were as follows:

- Identifying as a woman
- Having GD
- Having experienced suicidality (thoughts and/or actions)
- Being enrolled at the regional GD treatment clinic situated in Malmö (Triangelmottagningen)[162], the social services based treatment clinic in Malmö (Öppenvårdshuset Gustav)[163], or the patient organization for GD in Malmö (Spelberoendes förening, Malmö)[164].

Information and advertisement were made through:

- Posters, see Figure 3. These were hung on the walls of all three centres as well as digitally distributed through emails at Spelberoendes förening.
- Information brochures, which also were used to obtain written consent were handed out and communicated to women at all three centres by therapists at Triangelmottagningen and Öppenvårdshuset Gustav as well as by the president of Spelberoendes förening Malmö.

Figure 3. Poster for recruitment to study V (in Swedish)

Inclusion ended when the material was considered saturated through continuous evaluation and discussion on the transcribed interviews by authors Anna Karlsson (AK), Anders Håkansson (AH) and Helena Hansson (HH).

The study is based on semi-structured interviews with a first pilot interview-guide which was updated after discussions on the transcription of the first interview and used for the remaining interview (Appendix B). Figure 4 describes the workflow for conducting, transcribing, and discussing interviews until we were reasonably satisfied with the saturation. Before the interviews, the interviewer contacted the study subjects to confirm their willingness to partake in the study, give a short information on the study and answer potential questions.

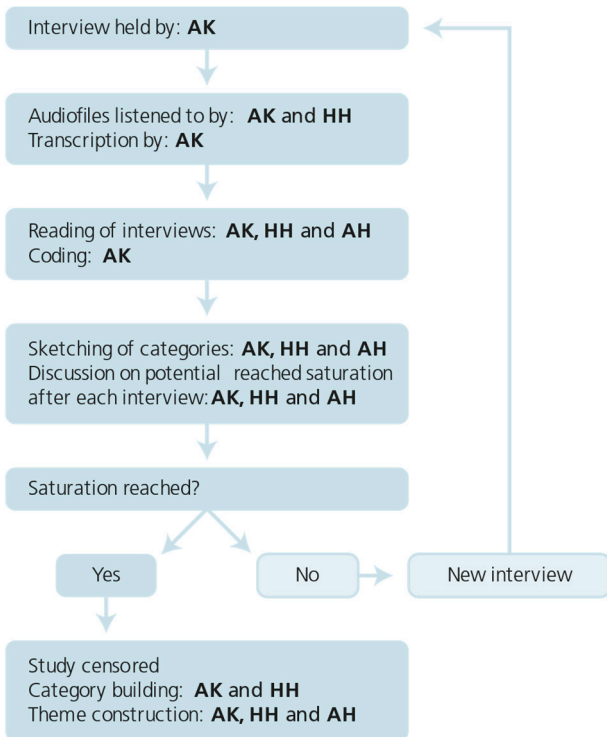

Figure 4. Workflow in interviewing, analysing the content, and determining saturation. (AK= Anna Karlsson, HH= Helena Hansson, AH= Anders Håkansson)

Interviews were conducted at Triangelmottagningen and begun with a brief description of the study and collection of oral and written consent. An audio recorder was then turned on and, with the guidance form the interview guide, a conversation was begun. The study subject and interviewer were situated in two armchairs separated by a coffee-

table. Coffee or tea as well as some form of cake or snack was offered. Napkins were available and the door was closed with a sign not to disturb, the study subject was seated closest to the door which was not locked. The aim was to keep the interviews between one hour and an hour and a half.

Saturation was discussed with regards to the emergence of categories and themes. In the last few interviews only similar categories to those already existing emerged and the material was thus considered saturated.

Analyses

As portrayed in Table 3, Studies I-IV were analysed through a range of statistical tests, whilst the fifth study was analysed based on qualitative content analysis. Among the statistical analyses, the regression models, and the SMR calculations are of great importance and these statistical tests are thus discussed separately.

Statistical models of importance for the thesis

The Standardized Mortality Ratio

The SMR is an estimate indicating the ratio of a specific outcome, most often mortality when comparing two groups and has been widely used in epidemiological studies since the 18th century, historically often to evaluate occupational mortality[165].

The SMR is often calculated as follows: (the latter being used in this thesis):

$$SMR = 100\,x\,O/E \; or \; SMR = O/E$$

O *= Observed number of deaths (in the population of interest)*

E *= Expected number of deaths (observed number of deaths per person and year in the control population multiplied by the number of person years in the population of interest)*

In the first study of the thesis, an estimate of mortality among individuals with GD is calculated by means of comparison with official statistics on mortality in Sweden presented by Statistics Sweden and available on their internet site for general mortality[166], and suicide mortality respectively[167].

The SMR has been criticised for its statistical inability to handle deaths of unknown cause[168], but is to this day widely used as an intuitive model for comparing outcomes accompanied by a confidence interval (CI).

Regression models

Regression models are statistical tools in identifying relationships among different factors and are widely used in clinical research as they can identify and quantify potential risk factors[169]. The most common regression models in medical research are linear, logistic, Cox, and Poisson Regressions[169], of which logistic regression and Cox regression are of special importance in this thesis. Both the logistic regression and the Cox regression were introduced by statistician sir David Roxbee Cox (1924-2022)[170].

The two regression models can be utilized to analyse potential risk factors for a binary outcome such as death or not. If the outcome is defined as death, then those who die are defined as having a "failure" and those who remain alive are defined as "being censored". Table 6 gives an outline of the specific characteristics of the two models. Both models are commonly used in both univariable and multivariable analyses. In multivariable analysing, potential risk factors are analysed whilst corrected for each other – a delicate matter where potential correlation must be considered. When testing multiple variables, a correction model can be utilized in order to further correct the significance level as the risk of achieving statistically significant results by random increases when testing several variables (type I error)[171].

Table 6. Characteristics of logistic regression and Cox regression[170 172 173].

Regression Model	Study	Outcome variable	Depends on	Some important assumptions
Logistic Regression	II	Odds Ratio	Number of individuals with failure* and number of censored** individuals	i) Linearity between variables and logarithmic outcomes ii) Absence of multicollinearity (variables should not be too correlated)
Cox Regression	I III IV	Hazard Ratio (Age/time-specific failure rate)	Time until censoring or time until failure	i) Assumption of proportional hazards ii) Censoring in the data is random or noninformative (cannot be tested statistically but demands a large sample)

*Failure is a statistical term evolving a dichotomous variable where those classified as "1" have had the outcome of interest, such as e.g., suicide death (suicide would be the failure) and those with "0" have not.
**Censoring is a term describing when an individual is lost to follow-up. If we are investigating suicide death and an individual dies from stroke before follow-up, then he or she will be censored when dying from the stroke. Censoring can also be at the end of follow-up for those who have not had a failure or premature censoring.

Study I

SMRs with 95 % CI were calculated for general mortality and suicide mortality for individuals with GD (see Table 4 for specifics on the population) as compared to the general Swedish population[166]. SMRs were stratified on gender and age in accordance with the age intervals displayed by Statistics Sweden[166]. Age intervals were chosen as 20-74 years as the material consisted of individuals 18-83 years of age, mean: 36.5 years, standard deviation (SD) 11.9, these intervals excluded outliers with regards to age. The age interval was also split in the middle creating two groups: 20-49 years of age and 50-74 years age, large enough to potentially detect a statistical difference.

Somatic and psychiatric comorbidity as well as underlying causes of death were described as crude numbers and in percentages of the study population.

Separate multivariable Cox regression models with 95 % CI were then conducted investigating suicide and general mortality.

To minimize the risk of random significant results, the variables were kept relatively low yet included:

- Age at inclusion
- Gender
- The most common categories of psychiatric comorbidity (depression, SUD and anxiety disorder)
- The most common somatic comorbidities which were also most common as underlying causes of death (malignant disease and cardiovascular disease)

With regards to suicide mortality, outcomes were fewer and thus two models were created to cut down the number of variables in each model:

i. with psychiatric comorbidity, as described above, gender and age, and

ii. with somatic comorbidity, as described above, gender, and age.

From these two models a stepwise procedure was utilized creating a common model with the significant factors from models: i) and ii).

SMR calculations were done in Microsoft Excel and all other analysis in SPSS version 24.0 (Armonk, NY, USA).

Study II

Intentional self-harm (including suicidal and self-injurious behaviour) was reported descriptively for the population (the population is described in Table 3) as well as for those: i) with comorbid AUD (and no DUD), ii) with comorbid DUD (but no AUD), and iii) for those with both a comorbid alcohol and drug use diagnosis.

Individuals with and without diagnosis of intentional self-harm were then compared through chi-square tests on age at baseline, gender and potential comorbidity with AUD, DUD, psychotic, depressive, and anxiety disorder.

Finally, a logistic variable with intentional self-harm as outcome was created including abovementioned variables and presented as OR with a 95 % CI.

Analyses were carried out using the IBM SPSS statistical software, version 25.0 (Armonk, NY, USA).

Study III

Table 4 displays the population characteristics. Age was presented in median and interquartile ranges. Pearson chi-square tests were performed comparing male and female gender and recipients and non-recipients of SWP with regards to psychiatric comorbidity and socioeconomic factors.

In the gender analysis we hypothesised that female gender would be associated with receiving SWP and increased psychiatric comorbidity. The factors analysed were:

- **self-harm** (with separate factors for intentional self-harm and self-harm of unknown intent as well as with and without fatal outcome).
- **psychiatric comorbidity** at large and divided per diagnostic group (bipolar disorder, anxiety, depressive disorders, other depressive disorders, psychotic disorder, personality disorder (all personality disorders excluding antisocial personality disorder which was treated as an independent factor), and antisocial personality disorder.
- **SUD** at large and divided per substance.

As several factors were analysed a Bonferroni correction was utilized to diminish the risk for type I error[174]. We chose to consider the variables as three groups: self-harm (n=4), substance use disorders (SUD) (n=11), and psychiatric comorbidities (n=8). For each group, the Bonferroni procedure was used to test the significant results (with the significance level of alfa <0.05). Of note is that a typographical error incorrectly

describes the procedure as the Bonferroni-Holm in the published article. See Appendix C for our letter to the editor on this mistake.

In the analysis comparing recipients and non-recipients of SWP the following factors were analysed:

- **non-lethal intentional self-harm**
- **SUD** divided by AUD and DUD
- **psychiatric comorbidity** at large and specifically (psychotic, bipolar, anxiety, depressive, and personality disorder)
- **criminality**

Criminality was added in this analysis as individuals with a history of criminal activity are often in contact with the social services and hypothesized to more often receive SWP.

A separate chi-square test was performed investigating distribution of criminal convictions during follow-up at large and categorized as violent crime, sexual crime, property crime, drunk driving, drug crime, economic crime, and other criminal convictions. The details on the criminal categories can be found in Appendix A. The significance levels of this analysis were also corrected with the Bonferroni procedure.

Finally, a stepwise Cox regression with 95 % CI was built to investigate potential risk factors for intentional, non-fatal self-harm. Previously known risk factors (with references in Figure 5) for suicide, though not previously investigated in relation to GD for non-lethal intentional self-harm and receiving SWP which we hypothesized would increase risk of intentional self-harm, were investigated in the model as can be seen in Figure 5.

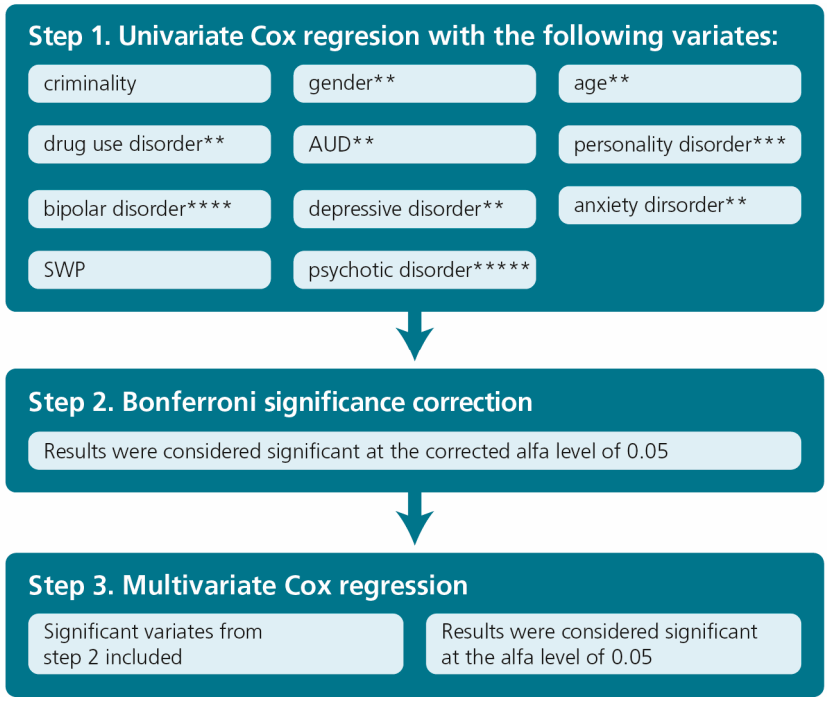

Figure 5 depicting the stepwise procedure of the Cox regression on previously known risk factors for non-lethal intentional self-harm as well as criminality and social welfare recipiency, Study III. Citations: *[85], **, *** [175], ****[176],*****[177]. SWP= social welfare payment. AUD = Alcohol use disorder

Analyses were carried out using the IBM SPSS statistical software, version 26.0 (Armonk, NY, USA).

Study IV

Table 4 gives a brief outline of the study population and design. Age distribution was presented as means with standard errors. Numbers and percentages of comorbid diagnoses and underlying causes of death were calculated for cases and controls separately. For cases the same procedure was performed for men and women separately. Chi-square tests were utilized to investigate potential differences. Chi-square test and Fischer's test were also used to compare death and suicide death among cases and controls. This was followed by a Benjamini-Hochberg correction to correct significance level due to multiple testing[171].

The independent samples t-test was used to compare potential age differences between cases and controls for death and suicide death, followed by separate analyses for men and women.

Two Cox regression models were then built for i) general mortality and ii) suicide mortality as binary outcomes. In building the models we tested the assumption of proportional hazards for each outcome by Kaplan Meyers curves and log(-log) plots for categorical variables. For age the Scale Schoenfeld Residual test was used[178]. Gender did not fit in the model as no proportional hazard was observed and the two analyses thus had to be stratified on gender. This required renewed testing for proportional hazard and the inclusion of fewer variables in the Cox regression for women due to their lower numbers in the study.

In the multivariable Cox regression model for men on general mortality the following factors were included:

- case vs control
- age
- respiratory disease
- cardiac disease
- malignant disease
- SUD
- previous intentional self-harm
- depressive disorders
- anxiety-related disorders
- socioeconomic status
- elementary school education

In the mortality analyses the leading underlying causes of death were chosen (respiratory, cardiac, and malignant disorder and previous intentional self-harm (including suicide attempt) were chosen, since these diagnoses were the leading causes of death in the study population. Diagnoses of SUD, depression and anxiety-related disorders were included due to their high prevalence among cases, and previous knowledge of their impact on mortality. Socioeconomic status and educational level were also included due to their previously known impact on mortality[179].

For women, fewer co-variabels could be included due to the smaller size of the group and the following co-variables were thus included:

- case vs control
- age
- somatic comorbidity (with respiratory, cardiac, or malignant disease computed into a dichotomous yes/no co-variable)

- psychiatric comorbidity in general (ICD chapter F-diagnosis excluding F63.0, GD)
- socioeconomic status

With regards to suicide mortality, a separate model was built stratified for gender. Variables were chosen due to their known effect on the risk of suicide death.

For men, the following co-variables were included:

- case/control,
- SUD
- previous intentional self-harm,
- depressive disorder,
- anxiety-related disorders
- age, and
- education

For women, again, a much smaller model had to be constructed due to the lower numbers of suicide death, including the following factors:

- case vs control,
- age,
- psychiatric comorbidity in general

Analyses were carried out using the IBM SPSS statistical software, version 28.0 (Armonk, NY, USA).

Study V

The analysis of the material was based on qualitative content analysis as described by Graneheim and Lundman[180]. An inductive approach was used whilst still focusing on the research questions by systematically searching for patterns and similarities in different episodes of the interviews, as well as across the interviews[181].

Interviews were transcribed verbatim in Microsoft Word by author AK. Transcripts and audio files were then imported to the software program NVivo version 1.6.1 which was utilized to analyse the material.

In NVivo stop words in Swedish were utilized to exclude non important words from the analysis such as mmm, hmm, and so forth. A word cloud was synthesized to give a picture of the raw data in the material.

AK coded the material into small unit codes in NVivo which were discussed with her supervisors, AH and HH. AK, AH and HH then constructed categories based on codes and interpretations of the written interviews. To ensure accuracy, HH also listened through the audio files. AK, AH and HH then constructed themes of factors mediating suicidality based on the categories. Categories and themes were discussed back and forth. Categories were built simultaneously with the first few interviews whilst themes started to build up during the later interviews. Although analysis of the material continued parallel to the interview process.

In creating codes, themes and categories authors AK, AH and HH had a shared preunderstanding which is likely to have impacted analysis and interviews. These preunderstandings were based on experiences of treating individuals with GD as a psychiatrist in a GD clinic (AH), previous research on GD-related suicidality (AK, AH and HH) and research on suicidality in general (AH, HH). These preunderstandings were discussed openly and involved a belief that monetary effects and indebtedness as well as psychiatric comorbidity, social isolation, gambling-related lies, relational difficulties as well as previous life traumas would be important mediators for suicidality.

Ethical considerations

Conformity with laws and international agreements

The research was carried out in accordance with the Declaration of Helsinki[182], although in the registry-based studies, Studies I-IV, the requirement of informed consent was not applicable due to the study design (national registers). In Study III, containing very sensitive information on criminal history, attempts to inform the public and offer the opportunity to opt out were made through information at the Lund University platform "LUPOP" on 02052019[183]. Further, Studies I-IV were ethically reviewed and received approval from the Regional Ethics Board Lund (File numbers: Studies I and II: 2016/1104, Study III: 2018/147[d] and Study IV: 2019-01559). Study V was instead reviewed and approved by the Swedish Ethical Review Authority (Ethical approval number: 2021-02747). This was because of a change in organization moving responsibility of ethical revision from regional to national level[184]. In Study V the requirement of informed consent was met, and study subjects received written and oral information and were given the opportunity to ask questions on an occasion prior to the interview as well as at the interview[182]. Oral and written consent was obtained.

[d] In the published article, incorrectly referred to as 2018/3, which was actually the protocol number of the meeting in which approval of the ethical application was decided.

Stigma and integrity

In registry research, no PIN are handed to the researcher but are kept at Statistics Sweden who have a key linking the constructed IDs for research purpose to the actual PINs. This is to enable the integrity of the study subjects. However, since the registry data contains a multitude of information, a hypothetical possibility for known individuals to be identified by the researcher does exist. As such, handling of the data was carried out with care. We chose not to investigate nor present specific sensitive information in rare situations, such as method of suicide or criminal history among women with GD who passed away to suicide in order to avoid the public identifying the study subjects and to diminish the risk of indirect identification of the study individuals.

Further, we tried to present the research in a respectful manner as our aim has always been to improve knowledge on these delicate matters so as hopefully to better prevent mortality, morbidity, and suicidality in individuals with GD. In line with this we tried to use inclusive language and avoid stigmatizing phrases such as gambling disordered or problem gamblers, rather we considered individuals to be suffering from GD or PG[185]. It has been our understanding that individuals with GD experience stigmatization[186], and as we describe private and delicate information on mental and physical health as well as criminality and suicidality, we have been careful to conduct and present the research respectfully vis-à-vis the study population.

The fifth study, in which research was done in a small sample, of a group who described stigmatization due to gender, GD, and suicidality, questions of integrity and stigma were very present. However, whilst performing the study we got the impression that the women in the study believed such research might decrease stigma. As these brave women shared their stories with us, we felt a need to express the knowledge gained in a truthful manner whilst balancing this with integrity and confidentiality. This was not easy and was a point thoroughly discussed within the research project. To reduce the risk of identification of study subjects citations were slightly altered to become more unspecific and we avoided linking interviews to citations in presenting the results at the cost of decreased interval validity.

In the studies on individuals with GD it was our conviction that the research projects were justified as the results will hopefully benefit the group. However, in Study IV, a control group was included. On an ethical note, this could be problematic since the results might not directly benefit the control group. However, as GD is very prevalent, many of us have someone in our proximity who suffers from it. Further, the societal benefits from potentially decreasing mortality, suicidality, and morbidity in individuals with GD could benefit us all.

Economic compensation

In the fifth study, a gift voucher valid at a shopping mall in Malmö, Sweden was given to the study subjects after the interview. The value was set at 500 SEK (roughly 50 USD). The gift card could not be used to buy gambling products or alcohol and was given with a couple of days delay after the interview. This procedure was decided upon after a conversation with a Swedish network for researchers within the gambling field, "the gambling addiction research network" (GARN)[187]. In general, the network was positive towards financial compensation, some had given monetary compensation, some had given gift vouchers for shopping malls and some cinema tickets. The network shared our ambivalence on economic compensation. On the one hand financial compensation might trigger gambling itself, on the other hand individuals giving their time and energy for the purpose of the study should be compensated just as rightfully as in any other research.

Thus, our conclusion was that a gift voucher without possibility to gamble, given with a few days delay, would be the best way to balance the risks of a monetary reward whilst still respecting the time and effort put in by the study subjects.

Safety

In the four initial studies of the thesis no intervention or contact was made directly with the study subjects and thus no direct harm should have been caused to the study population. In the fifth study, conversations on traumatic and personal life circumstances as well as suicidality were held. To minimize the risk of harm to the study subjects the interviews were held at the regional treatment centre for GD in proximity to experienced psychiatric nurses, therapists, and psychiatrists, lest an acute suicidal situation occur. Further, audio uptakes and transcripts were continuously evaluated among the three authors, thus assuring that interviews were carried out in a respectful way regarding the study subjects. The aim was to treat the study subjects in a professional and empathic manner, validating their experiences. In doing so our aim was to rather decrease suicidality through hopefully diminishing the stigma surrounding it.

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the funders had any role in study design, data collection, data analysis, data interpretation, or writing of the reports.

AB Svenska Spel is a state owned-company with a responsibility towards its clients as well as towards gambling-research. Nonetheless, it is a company providing gambling opportunities and as such we reflected upon the ethical dimensions of receiving this grant. AB Svenska Spel has previously been criticised for failing to own responsibility for their role as gambling provider in the development of PG[61]. However, we have concluded, since it is state-owned and since AB Svenska Spel did not interfere with the research conducted, that it is more beneficial to conduct research with their funding than not.

Main Results

Table 4 contains information on study samples and follow-ups for Studies I-IV. Main results will be presented for each of the five studies below.

Study I

In this study 77 % of the population were men and age at inclusion varied between 18–83 years of age (mean: 36.5 years, SD: 11.9). Psychiatric comorbidity was abundant with anxiety disorder (60 %), depressive disorder (51 %) and SUD (41 %) being most prevalent. During follow-up, 19 % had a diagnosis of intentional self-harm and 21 individuals (31 %) had suicide (intentional self-harm) as underlying cause of death which indeed was the leading cause of death in the population followed by neoplasms (16 %) and diseases of the circulatory system (12 %). Table 7 presents the SMR of the population with regards to suicide death and general mortality[e].

Table 7. Standardized mortality ratio (SMR) for suicide and mortality stratified for gender and age presented with 95% confidence intervals in brackets.

	Gender	SMR 20-74 years of age	SMR 20-49 years of age	SMR 50-74 years of age
General mortality	All	1.8* [1.4–2.2]	6.2* [4.1–8.4]	1.3 [0.9–1.8]
	Men	1.5* [1.1–1.9]	4.6* [2.7–6.5]	1.2 [0.8–1.7]
	Women	2.1* [1.0–3.3]	10.5* [2.7–18.2]	1.3 [0.3–2.3]
Suicide mortality	All	15.1* [8.7-21.6]	19.3* [9.8-28.7]	9.6* [1.2–18.0]
	Men	12.1* [6.5-17.7]	14.3* [6.5-22.0]	9.5* [1.2-17.8]
	Women	16.1* [6.5-33.5]	30.1* [12.2-62.6]	No suicides

*Significant at the alfa level of 0.05

In the multivariable Cox regression analysis, general mortality was predicted by older age (HR: 1.04, CI: 1.02–1.07) and cardiovascular comorbidity (HR: 2.32, 95 % CI: 1.33–4.02). The multivariable Cox regression on suicide mortality with somatic

[e] The 95 % CI for women 20-74 and 20-49 years of age differ from those originally published due to a mistake in the CI calculations. A correction (Appendix D) has been published.

comorbidity did not find any statistically significant factors. However, in the model with psychiatric comorbidity, gender and age, suicide death was predicted by depressive comorbidity (HR: 5.45 95 % CI: 1.57–18.93).

Study II

In the cohort, 417 individuals had either had an episode of non-fatal intentional self-harm or were deceased due to suicide[f]. Women were significantly older p<0.001. No prevalence difference in AUD (30 % of men and 29 % of women p=0.68) or DUD disorders (23 % of men and 25 € of women, p=0.41) were seen between men and women. Among those without SUD, 10 % had an incident of intentional self-injury, compared to 50 % of those with both AUD and DUD, 36 % of those with DUD and 20 % of those with only AUD. In the multivariable logistic regression, female gender (OR: 2.13 95 % CI: 1.63–2.78), depressive disorder (OR: 2.65, 95 % CI: 2.00–3.50), anxiety disorder (OR: 1.78, 95 % CI: 1.34–2.35), AUD (OR:1.95, 95 % CI: 1.51–2.51) and DUD (3.60 2.76–4.69) were all statistically associated with intentional self-harm.

Study III

Age at inclusion ranged between 18-84 years (median 37, IQR: 28-47), 19.5 % of the population were women. Seven individuals (all men) passed away to suicide and two more deceased due to self-harm of unknown intent. Among the women 37.9 % were parents compared to 29.6 % of the men, p=0.039. Women were also more often married, 13.6 % compared to 12.8 % of the men (p< 0.001) and roughly one in five had been divorced.

In this population 12.6 % of the study subjects had a diagnosis of intentional self-harm (fatal or non-fatal, more abundant in women, p=0.005) and as many as 86.2 % had a concomitant psychiatric comorbid diagnosis, which was more abundant in women (p<0.001). In the population 45.5 % had received SWPs during follow-up (slightly more abundant in women).

Among recipients, psychiatric comorbidity in general (p<0.001) as well as depressive disorder (p=0.043), anxiety disorder (p<0.001), personality disorders (p<0.001), AUD

[f] In the published study, the abstract incorrectly states that 10 individuals passed away due to suicide. The correct number is 21. This is likely an error based on a subtraction between (those who had a fatal or non-fatal self-injury in the NPR) – (those who had a non-fatal self-injury in the cause of death register). However, some individuals have both.

(p=0.031) and DUD (<0.001) were more common. Psychiatric comorbidity was abundant, Table 8. Criminal conviction (p<0.001) and non-lethal self-harm (p=0.042) were also more abundant. Roughly one in four had been found guilty of an illegal act during follow-up, more often men (p=0.004).

In the stepwise Cox regression, SUD (HR: 2.4, 95 % CI: 1.6–3.7), anxiety disorder (HR: 1.9, 95 % CI: 1.2–3.2), depressive disorders (HR: 2.4, 95 % CI: 1.5–3.7), and personality disorders (2.2 1.4–3.3) were associated with intentional self-harm.

Table 8. Prevalence of social welfare payment and psychiatric comorbidity in men and women with gambling disorder. Significant prevalence difference after Bonferroni correction marked with *. ICD= International classification of diseases. DUD= drug use disorder.

Variable, ICD 10 code	Men n (%)	Women n (%)	All n (%)
Social welfare payment	301 (44.3)	85 (50.3)	386 (45. 5)
Death from suicide, X60–X84	7 (1)	0 (0)	7 (0.8)
Death from self-harm of unknown intent, Y10–Y34	2 (0.3)	0 (0)	2 (0.2)
Non-lethal intentional self-harm, X60–X84	71 (10.5)	31 (18.3)	102 (12)
Non-lethal self-harm of unknown intent Y10–Y34	16 (2.4)	6 (3.6)	22 (2.6)
Psychiatric comorbidity, chapter F (excluding F63.0)*	572 (84.2)	159 (94.1)	731 (86.2)
Alcohol, F10	188 (27.7)	45 (26.6)	233 (27.5)
DUD, F11–F19	154 (22.7)	41 (24.3)	195 (23.0)
Opioids, F11	21 (3.1)	6 (3.6)	27 (3.2)
Cannabinoids, F12	34 (5.0)	7 (4.1)	41 (4.8)
Sedatives, F13	39 (5.7)	18 (10.7)	57 (6.7)
Cocaine, F14	5 (0.7)	1 (0.6)	6 (0.7)
Other stimulants, F15	18 (2.7)	1 (0.6)	19 (2.2)
Hallucinogens, F16	4 (0.6)	2 (1.2)	6 (0.7)
Tobacco, F17	17 (2.5)	7 (4.1)	24 (2.8)
Volatile solvents, F18	1 (0.1)	0 (0.0)	1 (0.1)
Multiple drug use and psychoactive substances, F19	88 (13)	24 (14.2)	112 (13.2)
Bipolar disorder, F30–F31*	69 (10.2)	35 (20.7)	104 (12.3)
Anxiety disorder, F40–F48*	352 (51.0)	113 (66.9)	465 (54.8)
Depressive disorders, F32–F33*	280 (41.2)	370 (43.6)	379 (43.6)
Other depressive disorder, F34–F39	23 (3.4)	9 (5.3)	32 (3.8)
Psychotic disorder, F20–F29	61 (9.0)	7 (4.1)	68 (8.0)
Personality disorder, F60–F62 excluding antisocial personality disorder (F602)*	80 (11.8)	53 (31.4)	133 (15.7)
Antisocial personality disorder, F602	13 (1.9)	1 (0.6)	15 (1.7)

Study IV

In this cohort, age at inclusion ranged from 18 to 93 years of age (mean: 36.3, standard error 0.11), again with women being older. There were no differences between cases and controls with regards to age at inclusion, or the proportion of women, indicative of a successful matching.

The number of deaths during follow-up was 132 among cases (3.8 %), and 94 among controls (1.3 %, $p<0.001$), the difference being significant for both men and women, separately ($p<0.001$ for both comparisons). Cases were also younger when they deceased (mean age of death for cases: 50.5 years, standard error 1.27, compared to controls: mean age: 57.7 years, standard error 1.61, $p<0.001$). This difference was seen among men ($p<0.001$) and women ($p=0.035$) separately.

In total, 63 individuals passed away from suicide as either contributing or underlying cause of death among whom 41 (1.2 %) were cases, and 22 (0.3 %) controls ($p<0.001$). This difference was statistically significant for men ($p<0.001$) but not for women ($p=0.165$). No significant age differences for those who died from suicide were seen for men or women. Suicide death (adjusted $p<0.001$), death of unknown intent (adjusted $p<0.001$) and death from respiratory disease (adjusted $p=0.005$) were all more common in cases.

Suicide was the most prevalent underlying cause of death (n=41, 30.9%) followed by neoplasms and diseases of the circulatory system. For controls however, neoplasms were the most prevalent underlying cause of death (n=25, 27.8 %) followed by diseases of the circulatory system and then suicide.

In male cases suicide was also the most common cause of death (n=36, 34.6 %) but not among females (n=5, 17.2 %), for whom death from neoplastic disorders was most prevalent (n=7, 24.1 %).

Psychiatric and somatic comorbidity was abundant among cases. Depressive disorders were common, with 38 % of the cases having a depressive comorbidity, (4.2 % of controls). AUD and DUD were also common with a prevalence of 22.8 % and 23.1 % (in controls only 2.8 % and 2.5 % respectively).

The multifactor Cox regression model did not show a statistical association for cases vs controls with respect to suicide nor general mortality, for men or women. Interestingly, for men, low educational level was the factor with strongest effect on both suicide and all-cause mortality. Suicide mortality in men was associated with SUD (including AUD), HR: 2.3, 95 % CI:1.2-4.5 and low education level, HR: 16.0, 95 % CI: 2.2-116. General mortality in men was associated with increasing age, HR 1.0, 95% CI: 1.0-1.0, neoplastic disorders, HR: 1.8, 95 % CI:1.3-2.6, diseases of the respiratory

system, HR: 1.6, 95 % CI: 1.1-2.2, intentional self-harm, HR: 2.2, 95 % CI: 1.4-3.3, SUD (including AUD), HR: 2.4, 95 % CI: 1.6-3.5, and low educational level HR: 7.9, 95 % CI: 3.5-17.8.

For women, increasing age, HR: 1.1, 95 % CI: 1.1-1.1, and the combined variable: respiratory, cardiac, or neoplastic disorder, HR: 11.2, 95 % CI: 2.5-50.2, were the factors most strongly associated with all-cause mortality, whereas no significantly associated factors were found with respect to suicide death.

Study V

Two women opted out after having shown initial interest in partaking in the study due to current unstable mental health and chaotic life circumstances. Nevertheless, seven women were interviewed, producing recordings of between 63 and 79 minutes resulting in 65,972 transcribed words. From listening to and reading through the transcripts it could be concluded that all women qualified for a GD diagnosis according to the DSM-5 and ICD-11 criteria[13 18].

Four individuals were recruited from the regional health care clinic and three from social services. No women were recruited from the patient organization and the head of the organization later stated that no women with GD had been active in the organization during the study period. The women were of different ages and socioeconomic and cultural backgrounds, had different sexual orientations and some had been born abroad. All the women had faced severe financial disadvantages as a result of their GD. One woman was facing action by the enforcement authority, three were awaiting a decision and one woman was fearing a possible involvement. Some had committed illegal acts due to their gambling and some had borrowed from close friends, partners or relatives. Five of the women described having psychiatric comorbidities such as anxiety, depression or SUD and four of the women talked about growing up with parents with mental health disorders such as GD, SUD and more. Many had grown up in families with strong gambling cultures. Some women had experienced sexual or physical abuse including intimate partner violence both growing up and later in life.

Several women wondered why they had developed GD. Some blamed themselves entirely. Others blamed specific gambling providers as well as individuals who had caused them harm previously. Table 9 displays some background information on the sample.

Table 9. Sample characteristics. N=7.

Descriptive information	N
Age	
20-40	3
41-65	3
>65**	1
In a relationship	4
Has children	4
Education level:	
Elementary school (9 years)	1
Upper secondary school (12 years)	3
University	2
Unknown	1
Current employment status:	
Employed (and for some, part time sick leave)	3
Unemployed and/or full time sick leave	3
Retired	1
Gambling form:	
Slot machines	3
Online casino	7
Online roulette	1
Offline casino	2
Online poker	2
Offline poker	3
Sports betting	1
Lottery	0
Bingo	2
Previous suicide attempts	4
Gambling disorder-related suicidality:	6
Ideation (thoughts or planning)	6
Attempts	2

From the interviews three main themes of factors mediating the relationship between GD and suicidality were constructed:

Guilt, shame, and self-stigmatization

…which was built on the following categories:

- Shame about not being able to repay debt
- Guilt and shame about financial situation
- Feeling of being a burden
- Shame about lying to or stealing from others
- Disgust with one-self
- Guilt and shame about not being able to control one-self / continued gambling
- Feeling of failure

Loss of control / chaotic life circumstances

…which was built on the following categories:

- Fear of homelessness or unstable living conditions
- Fear of criminal vindication
- Fear of economic consequences
- Not being able to control chaotic gambling
- Fear of being subject to action by the enforcement authorities

Social consequences / fear of guilt and shame from others

…which was built on the following categories:

- Feeling of not fitting in with an "Instagram life[g]"
- Fear of being outed to family/friends/work – expecting or receiving a negative reaction
- Feeling that you have broken the expectations on you as a woman through gambling
- Not being or feeling accepted

Of note is that one woman described having suicidal experiences feelings only due to other circumstances in her life and not connected to GD itself. However, she felt that should the GD affect her in her work, which was crucial for her well-being, then she

[g] A description from one of the interviews of a "picture perfect" life where everyone seems to be happy and everything seems picture perfect or at least that it is important that everyone seems happy and everything appears perfect.

feared she would not know how to be able to live on. Indeed, several women had experienced feelings of suicidality related to other difficulties which were not related to GD such as being a victim of intimate partner violence, sexual harassment, SUD, and difficult circumstances in relationships and during their childhood. Other women had no previous experiences of suicidality nor psychiatric comorbidity and described happy upbringings – and had suicidality solely due to the consequences of their GD.

Further, several women described how having a therapist was helpful with decreasing suicidality and some even described how they might not have been alive if it was not for their therapist. Some described negative experiences from group treatment which several women finally had opted out of. The women who had been to group therapy had been the only woman there and described a strong feeling of not fitting in. Some described how they had felt like they were "mothering" the younger men in group therapy, and others had received unwanted invitations or sexual harassment.

Also, coming clean to near ones was described as very stressful and as augmenting suicidality. However, for those who had felt accepted, this was very helpful in decreasing suicidality and was experienced as extremely relieving. This situation was similar to the experiences with the Enforcement Authority as well. Many described increased suicidality in awaiting decision from the enforcement authority, but once such a decision had been made and the control of the affected women's finances was no longer in their own hands, some experienced a sense of relieve.

As can be noted amongst the categories above, financial consequences were commonly brought up in relation to suicidality. However, in some the financial consequences spurred a sense of loss of control, in others a strong sense of shame and having broken their expectations of themselves and letting others down, mourning how they would leave nothing behind for their children or not being able to pay their debts.

For others, the financial consequences had led to anger and disappointment from close friends, partners and relatives which caused suicidality. As such, the economic difficulties could influence suicidality in several different ways. And finally, a few of the women wanted to particularly explain how they no longer cared about "having money, or being wealthy" as long as they had enough to manage. They explained how relieved they were to feel that way. Sometimes, however, this appeared difficult for close friends, partners, and relatives to understand or accept.

Discussion

Methodological considerations

In the Methods section a discussion on registry research including its validity and which analytical methods were used was presented. We are therefore focusing this discussion on external and internal validity, including the risk of type I and type II errors, bias, and confounding as well as trustworthiness in qualitative research.

Validity can be defined as whether a concept is accurately measured in a quantitative study[188], and is often divided into:

- external validity, which refers to whether a relationship can be generalized to a different population[189], and
- internal validity, if the relationship or concept is correctly measured in the studied population[188].

Validity can be affected by bias, systematic errors that effect the results of the study[190].

Who are we studying?

To understand whether the results from this thesis can be generalized to other settings, i.e., the external validity, one must consider the context in which the studies were undertaken. Approximately 0.23 % of the population, globally, have sought help for PG during the last year or at some point in their life[191]. Despite this relatively high percentage of people seeking help on a global level, few individuals with GD appear to receive treatment within specialized psychiatric care and within the social services[63 138]. A recent Finnish study on treatment uptake found similarly low levels of treatment uptake in health care even though data from both specialized and primary health care were investigated[192]. It appears as if individuals who seek help for problematic gambling do so from a variety of services including helplines, posting on online forums, attending support groups and reaching out to family members[193]. Thus, it appears as if a minority receive treatment or support from healthcare or social services. As the four initial studies are based on individuals diagnosed with GD in specialized health care, it is important

to keep in mind that they constitute a minority of those with PG in Sweden and not even everyone with GD.

This being said, Studies I-IV are indeed based on nationwide samples and can thus tell us a lot about a clinical population of individuals with GD. The studies have shown that this group suffers from psychiatric comorbidity including AUD and DUD. Further, these individuals suffer from increased mortality, intentional self-harm, and suicide death. Thus, it appears evident that the doors to specialized health care need to be open to individuals with GD.

In the fifth study, the sample is also based on individuals receiving treatment for GD as only women with ongoing therapeutic contacts within the social services or regional health care participated. As such, we do not know if women, should there have been any, from the GD peer support group would have presented a different picture of the development of GD-related suicidality. Nor do we know if women who did not seek help for their GD would have differed. Although, it can be noted that some of the suicidality and suicide attempts took place before the individual reached out to communal or regional treatment centres.

A strength in this thesis with regards to internal validity is that the material is based on specialized health care data (Studies I-IV), hopefully improving the quality of psychiatric diagnoses as these are very likely to have been made in specialized psychiatric health care. And in the fifth study we have, as clinicians, made our own assessment of the status of GD.

However, we have chosen not to include individuals below the age of 18 due to the risk of a mix-up with the diagnosis of *gaming disorder*, a behavioural addiction in which the subject is addicted to gaming rather than gambling. Gaming disorder is likely much more prominent among youth and adolescents[194] than GD (in the first two studies of this thesis only 3 % were less than 18 years of age).

The Swedish term for GD, "spelberoende" linguistically might refer to either of the two addictions and a clinical impression is that many medical doctors not in the field of psychiatry are unaware of the difference between GD and gaming disorder and we thus feared that a risk of misclassification might result in diagnosing youths with gaming disorder with GD. Although the reverse could also happen (an adult with gaming disorder being diagnosed with GD) we believe it is less extensive. As such, this thesis relies on data from an adult population. However, the relationship between gaming and gambling, especially in youths is one that demands further attention with features of gambling-like scenarios in online games, potentially increasing the risk of developing PG in adolescents[195].

Further, the studies in this thesis rely on Swedish data which should be kept in mind as the combination of legislation, health care system, taxation systems, gambling culture and much more of importance for developing GD and potentially experiencing comorbidity, suicidality and impacting mortality are unique to each country.

Who are the controls?

The results on mortality and suicide mortality differ in the first and fourth study. Results from the fourth study lie within the confidence intervals presented in the first study, whereas the results from the first study give an impression of a much greater risk of suicide as compared to the controls. As the fourth study is based on later register data it could be argued that the population diagnosed with GD has changed. However, this is more likely due to using different controls.

In the first study, mortality and suicidality is compared to the overall Swedish population with gender and wide age matching. Due to suicide being a relatively uncommon event statistically, age matching had to be done in rather wide age groups which makes comparison hard, as suicidality varies with age (and gender, but this was matched on)[196]. These comparisons based on age groups compared to the general population did not consider the age distributions within the age groups making the estimates quite rough. Thus, the fourth study, being matched on gender and age, deals with this issue in a more precise manner and the results ought probably to be closer to the truth. Further, the controls in the fourth study are also matched by municipality, a factor associated with suicide deaths in men particulary[197], and mortality in general[198].

As control groups differ, they tell us different information about mortality and suicide death in GD. The first study tells us about suicide and general mortality compared to the general Swedish population, whereas the fourth study rather aims to investigate the effect of GD on suicide and general mortality.

Type I and type II errors

In statistical testing, two opposing hypotheses are tested, e.g.: is there an increased risk of suicide in GD - the alpha hypothesis (H_α). Or is there not – the null hypothesis (H_0). If there truly is an increased risk – the alpha hypothesis should reach statistical significance and the null hypothesis should be rejected.

However, type I and type II errors are statistical terms describing distinct phenomenon where statistical testing can lead us to:

- in type I errors: reject the null hypothesis, when in fact the null hypothesis is true, and

- in type II errors: reject the alpha hypothesis, when in fact the alpha hypothesis is true[199].

In this thesis we have considered the risk of type I errors mainly by:

- choosing variables carefully in regression models (i.e. minimum of 5 but aiming for 10 events per predictor variable[200]) and using a stepwise procedure to reduce the number of variables in the models.
- correct significance levels through Bonferroni[174] and Benjamini Hochberg procedures in multiple testing[171].

And the risk of type II errors mainly by:

- creating larger age intervals in SMR calculations in Study I as to not lose power
- utilizing nationwide samples in Studies I-IV to reach as good power as possible

Although efforts to reduce risk of type I and type II errors were made, they cannot entirely be compensated for. In this thesis, the main error of concern is that we could not detect whether GD is an independent risk factor for suicide and mortality. The risk of type II error is, in our opinion, too big, and further studies, in larger settings need to examine this relationship.

Confounding

Confounding is a delicate matter in statistical analysis and needs to be considered carefully. It implies that the effect of the exposure variable is mixed with the effects of another, or several other variables, or "confounders"[201]. A confounder has an impact on the exposure factor as well as the outcome but cannot mediate the effect between the exposure and outcome. Dealing with a confounder statistically is often referred to as "controlling for".

Multivariable analyses, such as those used in Studies I-IV, can in fact deal with confounding factors, but caution must be taken so that the confounding factor is not in fact a mediator, or a collider, in such cases when one controls for the mediating factor – results can become erroneous due to colliding bias[190].

Sometimes confounders are easily detectable, although in psychiatric research it can be difficult to correctly identify confounding factors. Figure 6 depicts possible interactions between GD, depression and suicidality and the image could be further complicated: could suicidality lead to depression or GD, perhaps in some cases. We have, in situations of doubt, opted to control for factors of great importance to the outcome although there might be a mediating potential in the factor as well. This procedure was chosen since observational studies are the only ethical option to investigate these

relations and since, in this case, controlling for depression would rather decrease the effect of GD on suicidality.

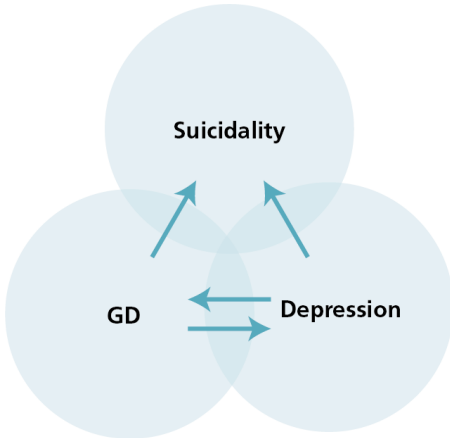

Figure 6. Relationship between gambling disorder (GD), depression, and suicidality in which depression effects both GD and suicidality and perhaps mediates the effect of GD on suicidality.

In Study IV, matching by age and gender as well as municipality was done to prevent confounding[202].

Trustworthiness

Qualitative research differs from quantitatice and the quality of the methodology in the fifth study is measured differently. In qualitative research trustworthiness refers to whether the findings can be trusted[203]. Some key terms in assessing trustworthiness in qualitative research are credibility, transferability, and dependability.

Credibility refers to whether the findings and interpretations represent information drawn from the original data as well as the intended focus[180 203]. In our studies, attempts to increase credibility were made through:

- finding agreements on interpretation between authors,
- interpreting material on women of different ages and backgrounds ensuring a diverse data,
- prolonged engagement through ongoing interviews and previous research on the topic as well as prior clinical experience

Further interviews and method triangulation (such as using a complementing methodology – such as reading diaries or therapist-interviews) might have further increased credibility[180 204].

Transferability is similar to external validity and demands a thick description of study methodology and settings so that transferability can be judged[180 203]. Dependability deals with the extent to which data change over time and how the researchers evolve or make different judgements during the analysis process[180 203]. In this thesis dependability was discussed within the research group and interviews were listened to and read with this question in mind. The semi-structured methodology was used so as to not drift to much from the original interviews.

A potential bias in our fifth study is that we chose to interview those who were fluent Swedish speakers in order to increase safety. Although the material consisted of individuals from different European regions, all spoke fluent Swedish and might not be fully representative of the general Swedish population or of Malmö, a multi-ethnic town of individuals with different geographical and cultural backgorunds[205]. However, a clinical impression is that very few non-Swedish speaking individuals are enrolled at health care or social services with regards to GD and this group needs further attention clinically as well as in research on GD.

Interpretation of Main Findings

Elevated Mortality in Gambling Disorder

Results from the first and fourth studies strengthen the notion that individuals with GD suffer from increased levels of mortality. Men and women decease at earlier ages than controls as well as at an increased rate compared to both controls and the general population. Not surprisingly, this was predicted by age and cardio-vascular diseases in the first study.

In the fourth study GD did not at a statistically significant level explain the increased mortality, but increasing age, low education level (i.e., only elementary schooling), previous episodes of intentional self-harm, respiratory diseases, and SUD (including AUD) were instead associated with mortality in men, and having respiratory, cardiac, or neoplastic disorder in women in the combined cohort of cases and controls.

A study from northern Italy found insignificantly increased SMR for mortality in gamblers receiving treatment in health care, although rates were lower than we found in the first study[106]. This difference might be due to several factors, one being the much longer follow-up in the Italian study (up to 27 years) and another that the authors found that the increased mortality was greatest the year after diagnosis. Another

important difference possibly explaining the lower mortality was the less frequent psychiatric comorbidity in the Italian study population[106].

When comparing mortality levels from the first study they were similar to cohorts of individuals with comorbid psychiatric comorbidity[206-208]. It has been suggested that this might be due to the inability of health care to effectively identify and treat somatic comorbidity in these patients[209]. Drinking alcohol and smoking tobacco have both been associated with gambling[210], and such comorbid patterns of substance use or SUD might also explain part of the increased mortality, especially with regards to respiratory, neoplastic, and cardiovascular disorders.

An intricate pattern of socioeconomic, psychiatric, and somatic risk factors is probably important in understanding the increased mortality in GD. However, efforts to better address and treat somatic comorbidity are much needed.

Increased Suicide Death in Gambling Disorder

The first and fourth studies found increased suicide levels in men with GD compared to the general population and matched controls respectively. The first study also provided evidence of increased suicide levels in women with GD compared to the population at large, although no calculations could be done in women aged 50-74 due to no deaths in this group. This could not be replicated in the fourth study where the difference did not reach statistical significance.

Depression appears to be a risk factor for increased suicide death in those with GD (Study I). Interestingly, a study on American in-patient registers comparing individuals with major depression and no GD to individuals with major depression and a secondary diagnosis of GD concluded that suicidal ideation and suicide attempts were strongly associated with having GD as well[211]. As such, it can be hypothesized that the combination of depression and GD increases the risk of suicidality.

In the fourth study the suicide risk was not however, significantly associated with GD, but rather SUD (including AUD) and low education level in the combined cohort of cases and controls. However, for men especially, the association was close to significant at the 0.05 alfa level and for women there was also a tendency towards a risk increase in the multivariable analysis. Such noisy estimates could be due to correlations between confounding factors and a meta-analytic methodology might be needed to draw conclusions on the independent effect of GD on suicidality and intentional self-harm[212 213].

Together these findings indicate that there is an evident increase in risk of suicide death in men and women with GD and that depressive disorder might increase the risk of

suicide death. Socioeconomic vulnerability and psychiatric comorbidity might be important and explain part of this risk increase, but further studies are needed to assess whether GD is an independent risk factor for suicide death in GD which could not be concluded in our case-control study.

Future meta-analyses could potentially aggregate the data from our studies and potential future studies in different settings to investigate the question of whether GD is an independent risk factor for suicide death. Interestingly, the only other study to our knowledge investigating suicide death in individuals with GD found markedly higher suicide levels in women with GD compared to the population as a whole but could not identify a difference in men with and without GD[106].

High prevalence of Intentional Self-Harm in Gambling Disorder

Suicide attempts and intentional self-harm without a fatal outcome cannot be differentiated in register research but appear abundant in GD, especially so in women. The prevalence was found to be of 12 % and 19 % in Studies I, II and III (with varying follow-up and slightly varying populations). Interestingly, in a study from the 80s in the United States similar levels of suicide attempts were found in a clinical sample of individuals with GD[214].

The results from this thesis show that intentional self-harm is even more abundant in socio-economically vulnerable individuals, i.e., recipients of SWP and in individuals with psychiatric comorbidity, especially those with comorbid AUD and DUD. Although intentional self-harm was more abundant in recipients of SWP it did not appear to be an independent risk factor for suicidality, instead previously known risk factors for intentional self-harm in GD were confirmed as potential risk factors in Studies II and III (i.e., AUD, DUD, anxiety, depressive, and personality disorders appeared associated with intentional self-harm).

A potential bias in our self-harm rates is that the very suicide attempt or self-harm episode which we evaluate could be what made an individual seek health care and what eventually led to the GD-diagnosis being registered. This might increase the risk of over-estimating the self-harm rates. Yet, the rates describe the actual rates of diagnosed self-harm in a clinical sample and it could also be argued that not all episodes of intentional self-harm have been diagnosed.

A study from South Korea examined associations between diagnostics according to DSM-5 criteria for GD and suicidal ideation and self-harm among individuals with a GD diagnosis[215]. Interestingly, they found that individuals who gambled to escape negative emotions and who became irritable when refraining from gambling were more

likely to have made a suicide attempt and that relational difficulties due to gambling as well as depending on others economically were associated with suicidal ideation. The latter two criteria closely relate to conclusions from our fifth study in which relational consequences and financial crisis appeared important in mediating suicidality. They could also conclude that roughly one in four answered that they currently were thinking about suicide, although only 8.5 % reported previous suicide attempts[215].

Several previous estimates of suicide attempts describe similar prevalence to those found in this thesis[216 217], or even higher[218 219]. The correlation between relational difficulties and the findings from our interview study of the importance of acceptance and support from close friends, partners and family might be in line with findings of a statistical association between divorce rates and history of suicide attempts and suicidality in individuals with GD[219]. Further, increased rates of suicide attempts have also been found in relatives of individuals with GD compared to controls[219].

In a recent twin-study, unique in its kind, the relationship between suicidal thoughts and GD appeared to be mediated by common environmental and genetic factors especially in women[220]. In contrast to this GD also appeared to be associated with suicide attempts after taking into account environmental and genetic factors, especially in men[220]. They also concluded that psychiatric comorbidity appeared to account for 70 % of the relationship between GD and suicidality (suicidal thought, plans and previous attempts) but less so with regards to suicidal plans and suicide attempts[220].

In the fifth study the women had varying degrees of presence of the factors found to be associated with suicidality in the second and third study. Indeed, there were women with comorbid DUD, AUD, anxiety, depressive and perhaps personality disorders. However – there were also women who had experienced suicidality related to GD with the presence of none of the abovementioned risk factors. This proves the complexity of suicidality and the individuality in its development. Personal vulnerability such as from psychiatric comorbidity or trauma, stigma and loss of control are likely to form a complex relationship from which suicidality can arise.

However, in the fifth study an idea that the consequences of GD can lead to suicidality in previously healthy and resilient women was strengthened. Interestingly, many women blamed themselves entirely for the development of GD, in line with previous Swedish ethnographic research in which several stakeholders including the national organization for individuals with GD considered the affected individual primarily responsible for retracting an addiction as opposed to acknowledging the role of the gambling providers[61]. The concept of blaming only the individual who has suffered from GD is likely to cause increased stigmatization.

It has been suggested after conducting online surveys on Australian gamblers that 'debt stress' might mediate psychological distress, depression, and consequences for one's family among problem gamblers, after controlling for sociodemographic factors and psychiatric history[221]. Such stress was common and burdensome for many of the women in the fifth study. Themes of internal and external stigma and chaos appeared to mediate suicidality in the fifth study. In the study, women described fear of eviction, and in a recent study a strong association to suicide death was found among evicted individuals when controlling for known psychiatric and socioeconomic risk factors[222].

Further, case-control studies could bring valuable insight on the strength of GD as a potential risk factor for intentional self-harm. A recent meta-analysis on PG found significant positive associations with regards to suicidal ideation and suicide attempts but concluded that longitudinal studies are needed to investigate causality[213].

But how does one recover from suicidality and prevent suicide death? The answers to that question might be many. In the fifth study three main themes of meditating factors for suicidality were suggested in women with GD. In Figure 7, a map of the relationship between GD, suicidality and potential recovery from suicidality is drawn. A further hypothesis not depicted in this map is whether decreased suicidality could be beneficial in recovery from GD.

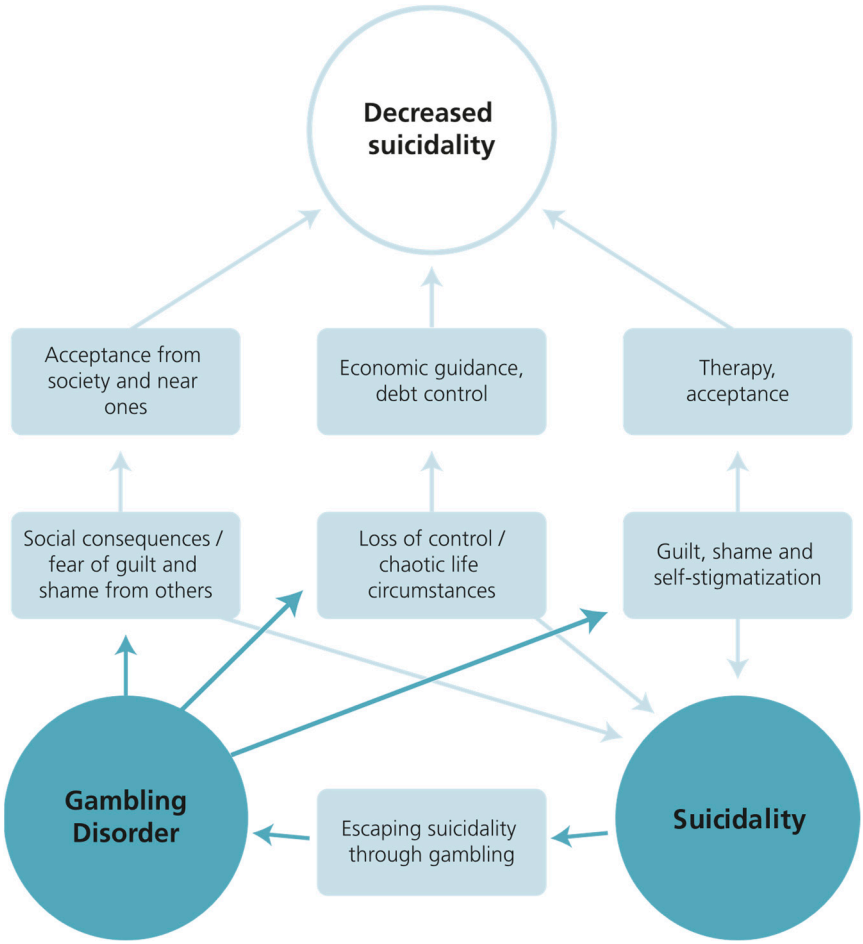

Figure 7. Depicting the relationship between mediating factors between gambling disorder and suicidality and potential paths to recovering from suicidality.

Other important factors in decreasing suicidality related to GD should theoretically lie in treating comorbid disorders as these appear strongly associated with intentional self-harm in Studies II&III.

Comorbidity – a Cause for Concern in Gambling Disorder

In the third study, we found an 84.6 % prevalence of any psychiatric comorbid diagnosis during follow-up with a significantly higher proportion of women with comorbid disorders. It thus appears as if psychiatric comorbidity is the rule rather than the exception in individuals with a GD diagnosis in Swedish healthcare. A previous Swedish register

study on comorbidity in GD found lower ratings of psychiatric comorbidity, in which 73 % had any occurrence of psychiatric comorbidity[63]. However, the studies differ in follow-up. The high prevalence of psychiatric comorbidity was also seen in a German case-control study from a non-clinical sample[62]. This is interesting since there might be a risk in our clinical population studies that the high comorbidity rates might be what the study subjects actually sought health-care for and the GD has then later been diagnosed, thus creating a biased population of individuals with more psychiatric comorbidity. All in all, psychiatric comorbidity appears abundant in clinical and non-clinical samples of individuals with GD, especially so in women.

In PG, a longitudinal case-control study concluded that suffering from anxiety or depression increased the risk of developing PG in women but not men and that comorbidity developed prior to PG in women but not men[223]. In men, on the contrary, PG appeared to be the first condition with later onset of psychiatric comorbidity and suicidality[223].

Although some individuals appear to develop GD and perhaps suicidality without any comorbid disorders, it is evident that psychiatric comorbidity is abundant in GD and can increase the risk of both suicidality and suicide. Psychiatric comorbidity can in some individuals develop prior to, and in some subsequent to GD. It is plausible to think that some of the genetic factors, social factors and personal experiences that might mediate the development of GD could increase the risk of other addictive disorders and mental health problems, as suggested by Slutske et al[220].

Economic difficulties and Criminality in Gambling Disorder

Results from the third study indicated a high prevalence of economic difficulties in individuals with GD as nearly half of the population had received SWP. These high levels were later confirmed in a case-control study in which it could also be concluded that GD often was diagnosed subsequent to receiving SWP[52]. This evokes questions of causality and there appears to be a reciprocal relationship between economic difficulties and GD[49]. Further, growing up in families with lower social class and economic difficulties appear to increase the risk of developing PG[224]. Although receiving SWP was not an independent risk factor at a statistically significant level for intentional self-harm, it is evident that intentional self-harm was more abundant among recipients.

Criminal convictions were also abundant in individuals with GD and could of course be due to several factors. Slutske and colleagues also found a large prevalence of criminal convictions in problem gamblers and saw common genetic factors for anti-social personality disorder and GD possibly mediated through low self-control in childhood[32 224 225].

General Conclusions

From the five studies in this thesis, we have learned that, in a clinical population, gambling disorder is associated with somatic and psychiatric comorbidity, socioeconomic vulnerability, suicidality, and self-harm as well as increased suicide and mortality levels. We have also learned from the descriptions of women with gambling disorder that experiences of stigma and chaotic life circumstances caused by gambling disorder can lead to suicidality in some.

Suicidality:

- Intentional self-harm including suicide attempts is common in individuals diagnosed with gambling disorder.
- Intentional self-harm is even more common in women, those with comorbid substance use disorders and financially disadvantaged individuals such as recipients of social welfare payments.
- Potential risk factors identified in these studies were psychiatric comorbid diagnoses, namely: alcohol use disorder, drug use disorder, anxiety, depressive, and personality disorders.
- Women with gambling disorder have described experiences of internal and external stigmatization and shame as well as chaotic life circumstances which might increase suicidality.

Suicide

- Suicide is more common amongst men with gambling disorder.
- For women, there were mixed results as to whether suicide death was more common in individuals with gambling disorder.
- Gambling disorder was not an independent risk factor for suicide, although further research is needed.
- Comorbid depression appears to increase the risk of suicide death in gambling disorder.

Mortality:

- Mortality levels are increased for men and women with gambling disorder.
- Among those with gambling disorder, older age and cardiovascular disease were associated with an increase in mortality.
- Gambling disorder did not at a statistically significant level explain the increased mortality when controlling for age, psychiatric and socioeconomic factors.

Comorbidity

- Psychiatric comorbidity is the rule rather than the exception in individuals with a gambling disorder diagnosis in Swedish healthcare, especially among women.
- Psychiatric comorbidities appear to increase the risk of suicidality and depression appears to increase the risk of suicide death in gambling disorder.
- Although psychiatric comorbidity was abundant, women both with and without psychiatric comorbidity shared experiences of suicidality in the qualitative interview study.

Together, these findings portray difficulties for individuals with gambling disorder in several areas. Economic difficulties, low socioeconomic status, psychiatric and somatic comorbidity, and the gambling disorder itself probably affect quality of life. Further, increased mortality and suicide levels should demonstrate the need for adequate care, treatment and preventive actions from several key stakeholders in society including health care, social services and also with regards to regulation and general awareness in society.

Implications

It is evident that too few individuals with GD receive evidence-based treatment or are clinically diagnosed. Societal awareness of GD and the right to treatment might increase treatment uptake. Education in primary care and social services could be one way to address this.

Screening for and treating somatic and psychiatric comorbidity in individuals with GD could potentially decrease mortality and suicidality in GD. Of special interest should be screening for and treating factors associated with cardiovascular disease such as smoking, SUD, obesity, and hypertension to possibly prevent increased mortality. In the same way, screening for and offering treatment for SUD, anxiety, depressive and personality disorders might decrease suicidality.

Addressing internal and external stigmatization might be of importance in the rehabilitation of women with GD as well as addressing financial difficulties and potential crises such as risk of losing one's home or being subject to debt collection by the bailiff.

Further, experiences of intimate partner violence need to be addressed to ensure a safe environment for women with GD and their potential children.

The high risks of suicidality and the increased risk of suicide and mortality in GD should call for regulatory actions. Such regulations might directly target gambling providers regulating the games but perhaps might also target payday loans and gambling advertisement – more clearly describing the mortality and suicidality common in individuals who develop GD. Information campaigns aimed at decreasing stigma surrounding GD, psychiatric disorders in general as well as over-indebtedness might be helpful.

Finally, the need to address and discuss suicidality with individuals with GD in social services and health care is evident. Structured suicide risk assessments should be included in standard practice and should include questions about financial circumstances.

Ideas for Future Research

We have now learned that GD in a clinical adult population is associated with somatic and psychiatric comorbidity, socioeconomic vulnerability, suicidality, and self-harm as well as increased suicide and mortality levels. As such, targeting comorbidity is probably of importance in preventing suicidality and suicide death as well as mortality.

Hence, studies examining interventions to increase quality of life and decrease suicide and mortality levels should be of great interest.

- Would screening for and treating obesity, smoking, SUD and hypertension in those seeking treatment for GD diminish excess mortality?
- Does CBT for GD prevent suicidality and suicide in the long and short term?
- Could drugs such as nalmefene or naltrexone influence suicidality or suicide death?
- What interventions could prevent suicide or treat suicidality in GD?
- How should individuals with GD and psychiatric comorbidity best be managed?
- How does treatment outcome differ in social services and the health care sector and who should be treated where?
- What are the potential mediators for suicidality in men and what are their experiences of GD-related suicidality?
- How can a larger proportion of individuals with GD be identified and given treatment?
- What are suicide and mortality levels in youths <18 years of age with GD?
- Evaluate the knowledge of GD and its treatment in primary care and social services.
- Evaluate educative efforts aimed at social services and primary health care with regards to GD.

These questions and many more remain unanswered with regards to GD and its negative effects.

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Appendix A

Criminal categories were derived utilizing statistics from the national criminal records registry held by The Swedish National Council for Crime Prevention. Seven different categories were created: violent crime, sexual crime, property crime, drug crime, financial crime, drunk driving, and a category containing other crimes. The register contains information on court verdicts, orders of summary punishment and a form of "failure to prosecute" which in Sweden implies that there is no doubt that the suspect has committed the crime, but it will not be brought to court due to circumstances such as the crime being irrelevant in comparison to the other crimes for which the individual faces charges.

Categories of crime were determined after investigating previous studies utilizing Swedish criminal statistics and by examining the Swedish law and including crimes in relevant categories as well as investigating the categories of crime defined by the Swedish National Crime Council. We chose an approach where violent sexual crimes would be included in both the categories 'sexual crime' and 'violent crime'.

Below is a list of specific laws utilized to create the categories in Swedish.

FINANCIAL CRIME: EKONOMISK BROTTSLIGHET, BIDRAGSBROTTSLIGHET & BEDRÄGERI

Bidragsbrottslagen (2007:612)

BRB 9 kap. Bedrägeri och annan oredlighet

RB 10 kap. Förskingring, annan trolöshet och mutbrott:

BRB 11 kap. Borgenärsbrott

Skattebrott brott mot skattebrottslagen

Brott mot insiderlagen (Lag om straff för marknadsmissbruk på värdepappersmarknaden f.om 1 feb 2017, dessförinnan lagen om straff för marknadsmissbruk vid handel med finansiella instrument (2005:377)
Aktiebolagslagen

Lagen om näringsförbud (1986:436 Lag om näringsförbud, Lagen upphörde att gälla 2 augusti 2014, då lagen (2014:836) om näringsförbud trädde i kraft.

DRUG CRIME: NARKOTIKABROTT

Narkotikastrafflagen (1968:64)

Lag om straff för smuggling (2000:1225) (obs endast 6 §)

Narkotikasmuggling (6 §)

DRUNK DRIVING: RATTFYLLERI

Brott mot trafikbrottslagen (1951:649)

Obs endast paragraf 4, rattfylleri (alkohol & narkotika) och grovt rattfylleri (4a §)

SEXUAL CRIME: SEXUALBROTT

BRB 6 kap. Sexualbrott

(8 Redovisningen avser brott såväl mot den nya sexualbrottslagstiftningen (som trädde i kraft den 1 april 2005) som mot tidigare gällande lagstiftning.)

Våldtäkt (1 §)

Grov våldtäkt (1 §)

Sexuellt tvång (2 §)

"Sexuellt utnyttjande av person i beroendeställning (3 §) (Inklusive den tidigare lydelsen sexuellt utnyttjande resp. grovt sexuellt utnyttjande (3 §).

Våldtäkt mot barn (4 §) (Inklusive den tidigare lydelsen sexuellt utnyttjande resp. grovt sexuellt utnyttjande av underåriga (4 §).)

Grov våldtäkt mot barn (4 §)(11 Inklusive den tidigare lydelsen sexuellt utnyttjande resp. grovt sexuellt utnyttjande av underåriga (4 §).)

Sexuellt utnyttjande av barn (5 §)

Sexuellt övergrepp mot barn (6 §) (12 Inklusive den tidigare lydelsen sexuellt umgänge med barn (6 §).)

Samlag med avkomling/syskon (7 §)(13 Inklusive den tidigare lydelsen sexuellt umgänge med avkomling resp. med syskon (6 §).)

Utnyttjande av barn för sexuell posering (8 §)

Köp av sexuell handling av barn (9 §)1 14 (Inklusive den tidigare lydelsen förförelse av ungdom (10 §).)

Kontakt med barn i sexuellt syfte (10a §) (15 Paragrafen trädde i kraft 1 juli 2009.)

Sexuellt ofredande (10 §) (16 Inklusive den tidigare lydelsen sexuellt ofredande (7 §).)

Köp av sexuell tjänst (11 §) 17 Paragrafen trädde i kraft 1 april 2005. Redovisningen kan även omfatta brott mot lagen (1998:408) om förbud mot köp av sexuella tjänster.

Koppleri (12 §)(18 Inklusive de tidigare lydelserna koppleri (8 §) och grovt koppleri (9 §).)

Grovt koppleri (12 §)

PROPERTY CRIME: TILLGREPPSBROTT

BRB 8 kap. Tillgreppsbrott

Stöld (1 §)

Ringa stöld (2 §)19

Grov stöld (4 §)

Tillgrepp av fortskaffningsmedel (7 §)

Grovt tillgrepp av fortskaffningsmedel (7 §)

Egenmäktigt förfarande (8 §)

Självtäkt (9 §)

Olovlig energiavledning (10 §)20

Brott mot 8 kap. (11 §)

Brott mot 8 kap. (12 §) För försök eller förberedelse till stöld, grov stöld, rån, grovt rån, tillgrepp av fortskaffningsmedel, grovt tillgrepp av fortskaffningsmedel, olovlig energiavledning eller grov olovlig energiavledning

Brott mot 8 kap. (13 §) Har annat i detta kapitel angivet brott än grov stöld, rån eller grovt rån förövats mot

1. någon som inte endast tillfälligt sammanbodde med gärningsmannen,

2. make, den som är i rätt upp- eller nedstigande släktskap eller svågerlag, syskon, svåger eller svägerska eller

3. någon annan som på liknande sätt är närstående till gärningsmannen, får åklagaren väcka åtal endast om målsäganden har angett brottet till åtal eller åtal är påkallat ur allmän synpunkt.

VIOLENT CRIME: VÅLDSBROTT

BRB

3 kap. Brott mot liv och hälsa:

Fullbordat mord, dråp eller misshandel med dödlig utgång

Misshandel inkl. grov

därav mot barn 0-6 år

mot barn 7-14 år

mot barn 15-17 år

mot kvinna 18 år eller äldre

mot man 18 år eller äldre

Övriga brott mot 3 kap.

4 kap. Brott mot frihet och frid

Människorov (1)

Människohandel (1a)

Olaga frihetsberövande (2)

därav grov fridskränkning (4a)

grov kvinnofridskränkning (4a)

olaga förföljelse (4b)

ofredande (7)

6 kap. Sexualbrott

1 § Våldtäkt

1 § Grov våldtäkt

2 § Sexuellt tvång

2 § Grovt sexuellt tvång

4 § Våldtäkt mot barn

4 § Grov våldtäkt mot barn

Delar av 8 kap. Stöld, rån m.m.

Rån (inkl. grovt) (5§)

därav bankrån (6§)

13 kap. Allmänfarliga brott

16 kap. Brott mot allmän ordning: 1-8 §

17 kap. Brott mot allmän verksamhet därav våld mot tjänsteman: §1-5 & 10

Appendix B

Intervjuguide version 2 (in Swedish with an English translation below)

Personal Experiences of Suicidality in Women with Gambling Disorder – a Qualitative Interview Study.

Karlsson, A; Håkansson, A & Hansson, H

1. Välkomnande och introduktion av studie och av mig själv (AK).
2. Information om kort journalföring.
3. Förklaring kring ljudinspelning och transkription sam möjlighet till avbrytande av studie eller om man senare önskar ångra sitt deltagande.
4. Göra en diagnostisk skattning av spelberoende innan intervjun om diagnos ej finns.
5. Diktafon sätts på.

1) Berätta varför du tackade ja till att delta i studien.
2) Berätta lite om dig själv, vem är du?
    a. Partner – sexuell orientering
    b. Barn
    c. Relationer och ensamhet
    d. Arbete
    e. Ekonomi
    f. Trosuppfattning
    g. Livshändelser
    h. Utsatthet för brott
    i. Psykisk ohälsa
    j. Alkohol och drogvanor.
3) Berätta om hur ditt spelande började.

4) Hur är ditt spelande idag / när det var som värst.
5) Berätta om hur spelandet fått dig att må.
6) Berätta om när du har mått som sämst.
    a. Hade du några suicidtankar då?
    b. Gjorde du något självmordsförsök?
    c. Vad ledde upp till dina suicidtankar/ditt suicidförsök?
    d. Varför tror du att du mådde så dåligt just då / riskfaktorer
        - spelandets betydelse
        - trauman
        - livshändelser
        - ekonomi
        - andra faktorer?
    e. Berättade du för någon att du mådde så dåligt?
    f. Sökte du vård under den här tiden?
    g. Fick du någon hjälp som var bra eller dålig?
    h. Vad har fått dig att orka härefter/skyddsfaktorer?

7) BERÄTTA HUR DU SER PÅ SPELET /SUICIDTANKARNA
8) Vilka är de 2-3 största skillnaderna mellan spelet och suicidtankarna?
9) Berätta om senaste gången du spelat.
10) Vilka råd skulle du ge till någon som är i en liknande situation?
11) Hur tror du att en idealisk vårdkontakt ser ut?
    - Använd en bild för att beskriva det.
12) Berätta hur din behandling ser ut en vanlig dag.
13) Kan vården bli bättre?
14) Spel suicid socialt nätverk vård och våld.
15) Berätta vad du tror hjälper dig i vården
    a) Tillgänglighet
    b) Personkemin
    c) Metod.
16) Berätta lite om dig själv idag och hur du ser på din framtid.
17) Stort tack!

English translation:

1. Welcoming and introduction to the study and to me (AK).
2. Information on short medical record entry.
3. Explaining audio recording, transcription, and possibility to withdraw study consent.
4. Making a diagnostic evaluation should the gambling disorder diagnosis not be present in the medical journal.
5. Dictaphone is switched on.

1) Tell me why you chose to accept the invitation to partake in the study.
2) Tell me a bit about yourself, who are you?
    a. Partner – sexual orientation
    b. Children
    c. Relations and loneliness
    d. Work
    e. Economy
    f. Belief system
    g. Life events
    h. Criminal victimization
    i. Mental unhealth
    j. Substance use
3) Tell me about how your gambling begun.
4) How is your gambling today / when was it at its worst?
5) Tell me how the gambling makes you feel.
6) Tell me about when you felt at your worst.
    a. Did you have any suicidal thoughts at that time?
    b. Did you make any suicide attempt?
    c. What led up to your thoughts of suicide/ your suicide attempt?
    d. Why do you think you felt so unwell at that time /risk factors
        - the impact of gambling
        - trauma
        - life events

- finances
- other factors.

e. Did you share the fact that you were feeling so unwell with anyone?
f. Did you seek professional help during this time?
g. Did you receive any help that was good or bad?
h. What gave you strength to carry on with life after this time/ protective factors?

7) TELL ME HOW YOU VIEW YOUR GAMBLING/ THE SUICIDAL THOUGHTS
8) Which are the 2-3 biggest differences between the gambling and the suicidal thoughts?
9) Tell me about the last time you gambled.
10) What advice would you give someone else in a similar situation?
11) How do you think an ideal treatment contact should be
    i. Use a picture to describe it.
12) Tell me about what your treatment is like on a normal day.
13) Can treatment improve?
14) Gambling, suicide, social network, and violence.
15) Tell me what you think helps you in your treatment:
    1. Availability
    2. Personal chemistry
    3. Methodology?
16) Tell me about yourself today and how you view your future.
17) Thank you very much!

Appendix C

Letter to editor

Dear editor Sharon Collard,

We are addressing you since we have found an unfortunate error in our published article "Psychiatric Comorbidity and Economic Hardship as Risk Factors for Intentional Self-Harm in Gambling Disorder—A Nationwide Register Study, October 2021 | Volume 12 | Article 688285".

In the review process a Bonferroni-Holm correction or Bonferroni correction was suggested to reduce the risk of bias due to multiple testing. However, there was a mix-up between the Bonferroni-Holm and Bonferroni correction. The article and procedure were done using the Bonferroni correction but due to a mistake - the Bonferroni-Holm model was presented and published. This implies that the "Bonferroni-Holm significance level" column in table 1 and 4 should instead be the "Bonferroni significance level" and in table 1 the new Bonferroni significance level should be all p-values <0.002 and in table 4 all p-values <0.005. This does not change the main results of the article, however, as it is presented now it is not quite correct. "Non-lethal intentional self-harm X60–X84" should not be marked with an asterix in Table 1. If you would like us to, we would be happy to publish a supplement with the corrected tables or if you prefer, we could update the article so that it is correct. Further, "the Bonferroni-Holm correction" should of course be interchanged for "the Bonferroni correction" throughout the text.

We are very sorry to have made this mistake and for the inconvenience.

Best regards
Anna Karlsson and co-authors.

Appendix D

AKADÉMIAI KIADÓ

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CORRIGENDUM

Corrigendum to: Gambling disorder, increased mortality, suicidality, and associated comorbidity: A longitudinal nationwide register study

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The above paper should be modified as follows:

The original version of this article unfortunately contains a mistake. The corrected details are given below.

1. On page 1093, under heading **Results**, in the fifth paragraph the following sentences

"For men alone, the overall increase was 12.1 times (14.3 times for those 20–49 years of age and 9.5 for those 50–74 years of age). For women, no significant results were obtained (Table 4)."

should read as

"For men, the overall increase was 12.1 times (14.3 times for those 20–49 years of age and 9.5 for those 50–74 years of age) and for women, 16.1 (30.1 times for those 20–49) and no suicide deaths were observed in those 50–74 years of age (Table 4)."

2. Table 4 is incorrect with regards to the confidence intervals for women 20–74 and 20–49 years of age and is presented with correct confidence intervals below.

Table 4. (corrected) SMR for suicide stratified for different sex and age categories presented with a 95% confidence interval

	SMR 95% [CI]	SMR 95% [CI]	SMR 95% [CI]
Age group	20–74 years old	20–49 years old	50–74 years old
Men and women	15.1* [8.7 to 21.6]	19.3* [9.8 to 28.7]	9.6* [1.2–18.0]
Men	12.1* [6.5 to 17.7]	14.3* [6.5 to 22.0]	9.5* [1.2–17.8]
Women	16.1* [6.5–33.5]	30.1* [12.2–62.6]	**

Note: Swedish individuals with gambling disorder compared to the Swedish general population in 2016. CI: confidence interval, SMR: standardized mortality ratio. *Significant result. **No documented suicides in this category.

We apologize for the mistake.

The Authors

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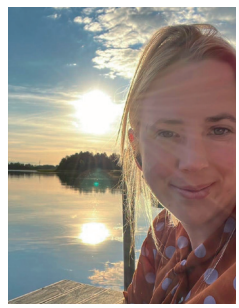
GAMBLING DISORDER IS increasingly being recognized as an addictive disorder with a number of negative consequences. In this thesis comorbidity, suicidality, mortality, and suicide amongst individuals with gambling disorder are explored, with a focus on gender and socioeconomic factors.

Individuals with gambling disorder appear to suffer from increased suicide and mortality rates, psychiatric comorbidity, and suicidality. Efforts regarding primary prevention as well as treatment, suicide risk assessment and somatic health care should be given focus in order to decrease the negative consequences of gambling disorder.



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