

Association of Schizophrenia Spectrum Disorders and Violence Perpetration in Adults and Adolescents from 15 Countries

A Systematic Review and Meta-Analysis

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[+ Supplemental content](#)

IMPORTANCE Violence perpetration outcomes in individuals with schizophrenia spectrum disorders contribute to morbidity and mortality at a population level, disrupt care, and lead to stigma.

OBJECTIVE To conduct a systematic review and meta-analysis of the risk of perpetrating interpersonal violence in individuals with schizophrenia spectrum disorders compared with general population control individuals.

DATA SOURCES Multiple databases were searched for studies in any language from January 1970 to March 2021 using the terms *violen** or *homicid** and *psychosis* or *psychoses* or *psychotic* or *schizophren** or *schizoaffective* or *delusional* and terms for mental disorders. Bibliographies of included articles were hand searched.

STUDY SELECTION The study included case-control and cohort studies that allowed risks of interpersonal violence perpetration and/or violent criminality in individuals with schizophrenia spectrum disorders to be compared with a general population group without these disorders.

DATA EXTRACTION AND SYNTHESIS The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and the Meta-analyses of Observational Studies in Epidemiology (MOOSE) proposal. Two reviewers extracted data. Quality was assessed using the Newcastle-Ottawa Quality Assessment Scale. Data were pooled using a random-effects model.

MAIN OUTCOMES AND MEASURES The main outcome was violence to others obtained either through official records, self-report and/or collateral-report, or medical file review and included any physical assault, robbery, sexual offenses, illegal threats or intimidation, and arson.

RESULTS The meta-analysis included 24 studies of violence perpetration outcomes in 15 countries over 4 decades (N = 51 309 individuals with schizophrenia spectrum disorders; reported mean age of 21 to 54 years at follow-up; of those studies that reported outcomes separately by sex, there were 19 976 male individuals and 14 275 female individuals). There was an increase in risk of violence perpetration in men with schizophrenia and other psychoses (pooled odds ratio [OR], 4.5; 95% CI, 3.6-5.6) with substantial heterogeneity ($I^2 = 85\%$; 95% CI, 77-91). The risk was also elevated in women (pooled OR, 10.2; 95% CI, 7.1-14.6), with substantial heterogeneity ($I^2 = 66\%$; 95% CI, 31-83). Odds of perpetrating sexual offenses (OR, 5.1; 95% CI, 3.8-6.8) and homicide (OR, 17.7; 95% CI, 13.9-22.6) were also investigated. Three studies found increased relative risks of arson but data were not pooled for this analysis owing to heterogeneity of outcomes. Absolute risks of violence perpetration in register-based studies were less than 1 in 20 in women with schizophrenia spectrum disorders and less than 1 in 4 in men over a 35-year period.

CONCLUSIONS AND RELEVANCE This systematic review and meta-analysis found that the risk of perpetrating violent outcomes was increased in individuals with schizophrenia spectrum disorders compared with community control individuals, which has been confirmed in new population-based longitudinal studies and sibling comparison designs.

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Schizophrenia spectrum disorders are associated with a range of adverse outcomes. These include suicide,¹ premature mortality,² experiencing violence³ and contact with the criminal justice system,⁴ and deficits across broader social domains.⁵ Perpetration of interpersonal violence is also associated with these diagnoses, an outcome with considerable implications for individuals, families, caregivers, those who experience interpersonal violence, and public services. Examining such associations poses particular challenges. Public perceptions around dangerousness in mental illness can contribute to stigma,⁶ and a focus on violence risk may inadvertently increase this. The contribution of mental illness to violent crime is often overstated, such as in media reports on mass shootings,⁷ which can bias public perceptions, and such issues have been integral to the appraisal of epidemiological evidence.⁸ However, failure to acknowledge associations with violence perpetration in turn risks leaving clinical needs unmet in psychiatric services. An accurate and balanced understanding of the nuanced association between mental illness and violence perpetration, development of effective prevention, and balanced communication and contextualization of research evidence may be one approach to reducing stigma.

At a population level, violence is a leading cause of premature mortality and morbidity. Public health approaches to tackling violence focus on prevention and delineating modifiable risk factors, such as mental illness, to inform interventions.⁹ In schizophrenia spectrum disorders, the public health importance of violence perpetration has been reinforced by recent estimates of its economic impact.¹⁰ Updated and precise estimates of violence perpetration risk are needed to inform prevention in health services.

A previous systematic review¹¹ identified 20 primary studies from 11 countries that reported a substantial increase in risk of violence perpetration in individuals with schizophrenia compared with people without schizophrenia, and a doubling of risk with substance misuse comorbidity. However, the search period for this review ended in February 2009. Since then, several large population investigations have been conducted.^{2,12} These newer studies provide improved approaches to examine confounding, test comorbidities, and allow for examination of additional outcomes. Although other systematic reviews have been conducted,^{13,14} to our knowledge, no recent quantitative analyses have integrated these new data. This longer-term perspective provides more precision for risk estimates, subgroup analyses, and meta-regressions. The current study therefore provides an updated systematic review and meta-analysis of the risk of violence perpetration in individuals with schizophrenia spectrum disorders compared with general population control individuals.

Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA)¹⁵ reporting guideline and the Meta-analysis of Observational Studies in Epidemiology (MOOSE)¹⁶ reporting guideline (eTable 1 in the Supplement). The review was registered on PROSPERO

Key Points

Question What are the absolute and relative risks of perpetrating violence toward others in individuals with schizophrenia spectrum disorders compared with the general population?

Findings In this systematic review of 24 studies, the absolute risk of perpetrating violence in a subgroup of register-based studies was less than 1 in 20 in women with schizophrenia spectrum disorders and less than 1 in 4 in men with schizophrenia spectrum disorders over a 35-year period. The elevated relative risk for all violence-perpetration outcomes was higher for women with schizophrenia spectrum disorders than for men with schizophrenia spectrum disorders, but with substantial heterogeneity in the findings.

Meaning Violence perpetration outcomes may be an important target for prevention and to reduce stigma in people with schizophrenia spectrum disorders.

(CRD42020224942). Risk of bias was assessed using the Newcastle-Ottawa Quality Assessment Scale.¹⁷

Search Strategy

In a previous review,¹¹ MEDLINE, Embase, and PsycInfo databases were searched from January 1970 to February 2009. For the update, we searched PubMed, PsycInfo, and Global Health from March 1, 2009, to March 17, 2021. No limits were imposed on country or age range.

Eligibility Assessment

Identification of schizophrenia spectrum disorders in included studies was from clinical diagnosis or based on diagnostic criteria. See the eMethods in the Supplement for full eligibility criteria. Applying these criteria, 416 relevant articles were identified from updated searches, 25 of which (reporting on 24 studies) met eligibility criteria (eFigure 1 in the Supplement).

Data Extraction

A standardized form was used to extract data on study design, location, last year of follow-up (study period), diagnostic definition, comparison group (including any use of sibling controls), definition and ascertainment of violence, violence perpetration outcomes in individuals with schizophrenia spectrum disorders and control individuals, outcome period, sample size, mean age, and information on comorbid substance misuse, personality disorder, experiencing violence, and treatment. If separate data were available for a range of psychoses, we chose schizophrenia spectrum disorders where possible, including schizophrenia and nonschizophrenia psychoses (ICD-10 codes F20-F29), and excluding affective, drug-induced, and organic psychoses. Where separate data were available for male and female individuals, these were disaggregated for analysis. See the eMethods in the Supplement for details of absolute risk data extraction. Where applicable, authors were contacted for additional data. Two authors extracted data (D.W., G.G.), and discrepancies were resolved by consensus.

Meta-Analysis

We combined eligible studies from this update with data from the original review¹¹ for analysis to ensure that the current review presents the most comprehensive synthesis of available information.^{18,19} To avoid duplication, where studies included overlapping populations or where articles were superseded by updated investigations in the same population, we included the study that used a longitudinal design or the study with the largest sample of individuals with schizophrenia spectrum disorders. Applying these methods, 10 studies were excluded from pooled analyses (eTable 2 in the Supplement).^{3,20-28}

Data for analysis were considered across 4 violence perpetration outcome classifications. First, a broad interpersonal violence perpetration definition (any physical assault, robbery, sexual offenses, illegal threats or intimidation, and arson). Within this classification male, female, and data combined by sex were grouped separately using nonoverlapping samples, and subgroup analyses (not in protocol but added based on reviewer suggestion) were undertaken to examine for sources of heterogeneity (substance misuse comorbidity, geographical region of study, study quality, study type, nature of control group, patient sample, and outcome measure). While data from studies that included homicide, sexual offenses, or arson within their broad violent outcome definition were included within this classification, if a study considered only 1 of those specific offenses in isolation, it was considered separately. Data included within separate classifications for homicide, sexual offenses, and arson were either disaggregated from studies that used a broad definition but also reported separated offenses or from studies that considered only these outcomes (ie, no broad violence category). A total of 12 studies of homicide,^{21,29-32} arson,³³⁻³⁵ and sexual offenses³⁶⁻³⁹ were included in these separate classifications that were not otherwise included in the broader violence perpetration classification owing either to reporting only that specific offense or to issues of population overlap that did not apply within the separate offense classification. Within the arson classification, meta-analysis was not undertaken owing to the clinical heterogeneity of fire-setting definitions.

Statistical Analysis

We generated unadjusted pooled odds ratios (ORs) with 95% CIs for risk of violence perpetration outcomes using random-effects meta-analysis. Heterogeneity was examined using Cochran Q and the I^2 statistic. Analyses were undertaken using R version 3.6.1 (the R Foundation)⁴⁰ and the R package meta.⁴¹ The Mantel-Haenszel method was used to combine odds ratios from 2 × 2 tables, with continuity correction of 0.5 in studies with zero cell frequencies.

Results

Interpersonal Violence Perpetration as Outcome

Twenty-four studies were included (N = 51 309 individuals with schizophrenia spectrum disorders; reported mean age of 21 to 54 years at follow-up; of those studies that reported out-

comes separately by sex, there were 19 976 male individuals and 14 275 female individuals), 16 of which were from the original review (n = 9954 individuals with schizophrenia spectrum disorders [19.4%]), and 8 of which were identified from updated searches (n = 41 355 [80.6%]). Studies were based in 15 countries: 5 from the US,⁴²⁻⁴⁶ 3 from Sweden,^{2,47,48} 2 from Israel reported in 3 publications,⁴⁹⁻⁵¹ 2 from Denmark,^{52,53} 2 from Finland reported in 3 articles,⁵⁴⁻⁵⁶ 1 from Switzerland reported in 3 publications,⁵⁷⁻⁵⁹ and 1 each from Australia,¹² Austria,⁶⁰ Canada,⁶¹ Czech Republic,⁶² Egypt,⁶³ Ethiopia,⁶⁴ Germany,⁶⁵ New Zealand⁶⁶ and the UK.⁶⁷ See the Table for a summary of included studies and eTable 3 in the Supplement for additional details.

Characteristics of Included Studies

For outcomes, 15 studies used register-based measures of violent criminality^{2,12,46-48,51-53,55,56,59-61,65,67} (n = 50 250 [97.9%]) and 9 used self- or informant-report measures (n = 1059 [2.1%]) either solely^{42,44,45,50,62-64} or in combination with register-based data.^{43,66} Ten studies included only individuals with schizophrenia spectrum disorders who had at least 1 inpatient hospitalization^{43,46,47,51-53,59,62,65,67} (n = 11 011 [21.5%]), whereas 14 studies (n = 40 298 [78.5%]) identified individuals with schizophrenia spectrum disorders in the community or who had been in contact with a broader range of inpatient and outpatient care settings.^{2,12,42,44,45,48,50,55,56,60,61,63,64,66} Thirteen reports were considered overall good quality (scoring 7 to 9 of 9 overall and evenly across domains on the Newcastle-Ottawa Quality Assessment Scale),^{2,12,43,45,47,51-53,55,56,61,62,66} and 11 were considered poor to fair (eTable 4 in the Supplement).^{42,44,46,48,50,59,60,63-65,67} The mean (SD; interquartile range) quality score was 7.0 (1.5; 6-8).

Male Data

There were 19 976 male individuals with schizophrenia spectrum disorders. The random-effects pooled OR for the risk of violence perpetration in individuals with schizophrenia spectrum disorders compared with general population control individuals in this group was 4.5 (95% CI, 3.6-5.6), with substantial heterogeneity ($I^2 = 85%$; 95% CI, 77-91) (Figure 1).

Female Data

Among the 14 275 female individuals with schizophrenia spectrum disorders, the random-effects pooled OR for the risk of violence perpetration in individuals with schizophrenia spectrum disorders compared with general population control individuals was 10.2 (95% CI, 7.1-14.6), with substantial heterogeneity ($I^2 = 66%$; 95% CI, 31-83) (Figure 1). Excluding 3 studies of female individuals with schizophrenia^{55,57,67} (n = 256) with no events in either individuals with schizophrenia spectrum disorders or control individuals made no material difference to risk estimates (pooled OR, 10.3; 95% CI, 7.0-15.1).

Studies That Did Not Report Outcomes Separately by Participant Sex

Data from 11 studies with 17 058 individuals with schizophrenia spectrum disorders were not available separately by sex (Figure 1). Risk of violence perpetration was increased

Table. Summary of Studies Reporting Violence Perpetration Outcomes in Individuals With Schizophrenia Spectrum Disorders Compared With General Population Control Individuals Included in Meta-Analyses^a

Source	Sex	No. scz (% viol scz)	Outcome period	Ascertainment of violence	Diagnosis	Nature of clinical contact	Country	Study period	Definition of violence
Sosowsky et al, ⁴⁶ 1980	Male and female ^b	171 (4.7)	≤6.5 y	Register	Schizophrenia	Admitted to and discharged from state hospital	US	1975	Violent crimes
Ortmann et al, ⁵² 1981	Male	86 (2.3)	8 y	Register	Schizophrenia and ICD-8 paranoid states; other psychoses and unspecified psychosis (excluding alcohol use disorder, organic, and affective psychosis)	Psychiatric hospitalization younger than age 26 y	Denmark	1978	Violent offenses (excluding sexual)
Swanson et al, ⁴⁵ 1990	Male	114 (12.7)	1 y	Self-report	Schizophrenia or schizophreniform disorder	Community sample	US	1983	Diagnostic Interview Schedule items indicating self-reported violent behavior
Lindqvist et al, ⁴⁸ 1990	Male	330 (8.5)	15 y	Register	Schizophrenia	Community sample	Sweden	1986	Assault, unlawful deprivation of liberty, unlawful threats
	Female	314 (1.3)							
Modestin et al, ⁵⁹ 1996	Male	282 (5.3)	21 y	Register	Schizophrenia	Hospitalized at least once during study period	Switzerland	1987	Violent crimes (excluding sexual)
Modestin et al, ⁵⁷ 1995	Female	226 (0.4)	26 y	Register	Schizophrenia and other psychoses	All patients hospitalized in 1987	Switzerland	1985 to 1987	Violent crimes (excluding sexual)
Räsänen et al, ⁵⁵ 1998; Tiihonen et al, ⁵⁴ 1997	Male	67 (11.9)	12 y	Register	Schizophrenia, schizophreniform and schizoaffective disorders, paranoid psychosis, and other psychoses (excluding affective and organic)	Birth cohort members with diagnoses on hospital discharge registers (treated in all mental and general hospitals)	Finland	1992	Homicide, assault, robbery, arson, violation of domestic peace
	Female	25 (0)			Schizophrenia				
Stueve et al, ⁵⁰ 1998	Male	51 (25.5)	5 y	Self-report	Psychotic or bipolar disorders	Community-based	Israel	1992	Self-reported measures of fighting and weapon use
	Female	50 (24.0)							
Arseneault et al, ⁶⁶ 2000	Male and female ^b	39 (33.3)	1 y	Register and self-report	Schizophrenia spectrum disorder	Community-based (in year before interview 1.6% of study members overall spent on average 25 d in a psychiatric hospital)	New Zealand	1994	Violent convictions (including illegal threats, presenting an offensive weapon, rape, manual assault, assault, robbery, and homicide), and self-reported violence scale (simple assault, aggravated assault, robbery, rape, and gang fighting)
Brennan et al, ⁵³ 2000	Male	2185 (11.0)	29 y	Register	Schizophrenia and other psychoses (including reactive, paranoid, and unspecified; excluding organic and affective)	Members of a birth cohort hospitalized with schizophrenia	Denmark	1991	Murder, attempted murder, rape, violence against authority, assault, domestic violence, robbery
	Female	2473 (1.7)							
Monahan et al, ⁴³ 2000	Male and female ^b	189 (9.5)	20 wk	Register, collateral, and self-report	Schizophrenia and other psychotic disorders (schizophreniform, schizoaffective, delusional disorder, brief reactive psychosis)	Inpatients postdischarge	US	1995	Acts of battery that resulted in physical injury, sexual assaults, and assaultive acts that involved the use of a weapon or threats made with a weapon in hand
Haller et al, ⁶⁰ 2001	Male and female ^b	1325 (3.9)	12 y	Register	Schizophrenia, schizoaffective and delusional disorders	Previous inpatient or outpatient treatment	Austria	1997	Violent crime

(continued)

Table. Summary of Studies Reporting Violence Perpetration Outcomes in Individuals With Schizophrenia Spectrum Disorders Compared With General Population Control Individuals Included in Meta-Analyses^a (continued)

Source	Sex	No. scz (% viol scz)	Outcome period	Ascertainment of violence	Diagnosis	Nature of clinical contact	Country	Study period	Definition of violence
Corrigan et al, ⁴⁴ 2005	Male and female ^b	42 (11.9)	1 y	Self-report	Nonaffective psychosis	Community sample	US	1992	Serious trouble with the law or physical fight resulting in injury
Hodgins et al, ⁶⁷ 2007	Male Female	10 (35.0) 5 (11.8)	31 y	Register	Schizophrenia and other psychoses	Inpatients	UK	2005	Violence against another person, sexual offenses (excluding prostitution-related offenses), and robbery
Elonheimo et al, ⁵⁶ 2007	Male	14 (7.1)	4 y	Register	Psychotic disorder (including schizophrenia and schizophreniform psychosis)	Community sample (assessed at military call-up)	Finland	2004	Assault ("various kinds"), battery, robbery
Soyka et al, ⁶⁵ 2007	Male and female ^b	1662 (3.7)	7-12 y	Register	Schizophrenia	Postdischarge former inpatients	Germany	2002	Physical assault, aggravated assault or battery, threatening or invasion of privacy, sexual abuse of a child, robbery, illegal restraint, manslaughter (including attempted and involuntary), murder, sexual assault, rape, holding someone at gunpoint
Elbogen et al, ⁴² 2009	Male and female ^b	294 (9.2)	3 y	Self-report	Schizophrenia and other psychoses	Community sample	US	2005	Self-reported violence, including using weapons in a fight, arson, forcible sex, substance-related violence, domestic violence
Eriksson et al, ⁴⁷ 2011	Male	377 (24.7)	35 y	Register	Schizophrenia	Discharged at least once from hospital	Sweden	2005	Serious violent conviction (homicide, manslaughter, assault, robbery, assaulting or threatening an officer, forcible confinement, and sexual assault [excluding attempts])
Short et al, ¹² 2013	Male and female ^b	4168 (10.0)	35 y	Register-based	Schizophrenia disorder (including schizoaffective disorder, paraphrenia, shared psychotic disorder, delusional disorders, unspecified nonorganic psychosis)	All persons diagnosed with psychosis in public mental health system	Australia	2005	Guilty of a violent offense, including all contact sex offenses and any physical assaults involving force or causing harm
Fazel et al, ² 2014	Male Female	14 621 (3.5) (6.0) and (10.7) (16.6) 9676 (0.8), (1.5), (2.7) (5.4)	1, 2, and 5 y Postdiagnosis Mean 9.5 y 1, 2, and 5 y Postdiagnosis Mean 9.5 y	Register	Schizophrenia and other nonaffective psychosis	National patient register identifying any hospital admission 1972 and later; outpatient appointments 2001 and later	Sweden	2009	Violent conviction (homicide, attempted homicide, aggravated assault, common assault, robbery, arson, any sexual offense [rape, sexual coercion, child molestation, sexual harassment], illegal threats or intimidation)

(continued)

compared with general population control individuals (random-effects pooled OR, 4.6; 95% CI, 3.7-5.7), with substantial heterogeneity ($I^2 = 72\%$; 95% CI, 48-85).

Register-Based Outcomes and Study Quality

When restricting analysis to studies that used exclusively register-based violence perpetration outcomes ($n = 50\ 250$)

Table. Summary of Studies Reporting Violence Perpetration Outcomes in Individuals With Schizophrenia Spectrum Disorders Compared With General Population Control Individuals Included in Meta-Analyses^a (continued)

Source	Sex	No. scz (% viol scz)	Outcome period	Ascertainment of violence	Diagnosis	Nature of clinical contact	Country	Study period	Definition of violence
Fleischman et al, ⁵¹ 2014	Male	1746 (23.9)	13.6 y	Register (court records)	Schizophrenia	Persons admitted to psychiatric hospitals, day hospitals, or psychiatric units in general hospitals	Israel	NR	Violent crimes (murder, attempted murder, assault, rape, threats, and robbery) for which convicted (control individuals), or either convicted or deemed mentally incompetent to stand trial
	Female	1441 (4.3)							
Tsigebrhan et al, ⁶⁴ 2014	Male and female ^b	92 (27.2)	1 y	Self-report	Schizophrenia and schizoaffective disorder	Community sample	Ethiopia	2011	MacArthur interview for past-year violence against others (used a weapon, hit someone hard, purposely set a fire, forced sexual intercourse, fought when drinking alcohol or chewing khat, involved in a fight that came to blows, started a fight)
Refaat et al, ⁶³ 2015	Male and female ^b	30 (86.7)	1 wk	Self-report	Schizophrenia	Outpatients either experiencing short-term relapse or receiving maintenance antipsychotic treatment and coming in for follow-up	Egypt	NR	Physical violence grade 3-5 on Modified Overt Aggression Scale (stroked, pushed, scratched, or pulled hair of others without injury; attacked others causing mild injury or serious injury)
Černý et al, ⁶² 2018	Male	93 (41.9)	6 mo	Self-report, collateral, and file review	Schizophrenia, delusional disorder, acute polymorphic psychotic disorder, schizoaffective disorder	Inpatients hospitalized >3 d	Czech Republic	2009	MacArthur Community Violence Interview for past 6-mo moderate violence (simple assault without injury or weapon use) and serious violence (any assault with a lethal weapon, any threat with a lethal weapon in hand, any sexual assault)
	Female	65 (38.5)							
Casiano et al, ⁶¹ 2020	Male and female ^b	9046 (3.4)	1 y	Register	Psychotic disorder (including schizophrenia, delusional disorders, acute and transient psychotic disorders, schizoaffective disorder, drug-induced psychosis, and other and nonspecified psychosis)	Community-based sample (diagnoses coded on inpatient or outpatient health care contact)	Canada	2012	Violent charges laid down by police and tracked by a Manitoba Justice database; violence inclusive of assault, sexual, and other violent crimes (Canadian criminal codes listed in study appendix)

Abbreviations: NR, not reported; Scz, individuals with schizophrenia spectrum disorders; viol scz, individuals with schizophrenia spectrum disorders who developed at least one violence perpetration outcome.

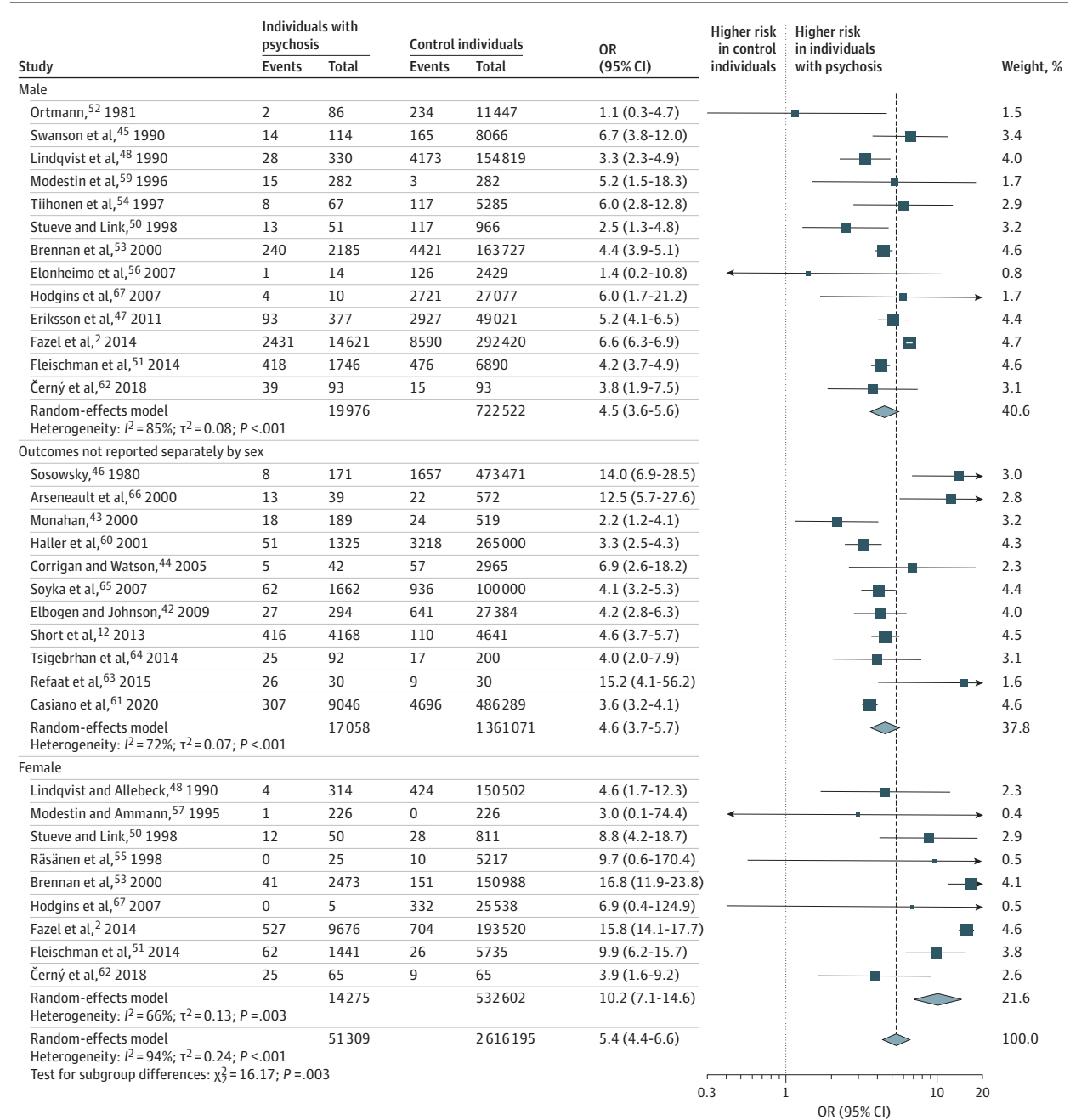
^a For additional study details, see eTable 3 in the [Supplement](#).

^b Data required for pooled analyses were not reported separately by sex.

(eFigure 2 in the [Supplement](#)), the pooled OR for violence perpetration in male individuals was 4.6 (95% CI, 3.6-5.9; $I^2 = 88%$; 95% CI, 79-93); in female individuals, the OR was 12.8 (95% CI, 9.5-17.4; $I^2 = 48%$; 95% CI, 0-78); and in studies where sex was not reported separately, it was 4.3 (95% CI, 3.4-5.4; $I^2 = 78%$; 95% CI, 47-91). When studies were grouped by quality, pooled OR

for studies rated good (n = 46 425) was 5.7 (95% CI, 4.3-7.5; $I^2 = 96%$; 95% CI, 95-97) and for studies rated poor to fair (n = 4884) was 4.6 (95% CI, 3.7-5.9; $I^2 = 48%$; 95% CI, 6-71) (eFigure 3 in the [Supplement](#)). Subgroup analysis by study design showed that findings were comparable (eFigure 4 in the [Supplement](#)).

Figure 1. Forest Plot of Association Between Schizophrenia Spectrum Disorders and Violence Perpetration



Odds ratio (OR) of violence perpetration outcomes in individuals with schizophrenia spectrum disorders compared with general population control individuals.

Absolute Risks

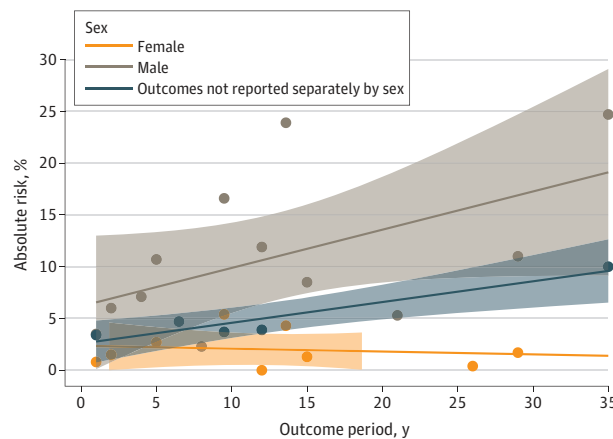
Absolute rates of violence perpetration in included studies of register-based violent outcomes ranged from 2.3% to 24.7% in men with schizophrenia spectrum disorders and from 0% to 5.4% in women with schizophrenia spectrum disorders, over outcome periods that ranged from 1 year to lifetime measures spanning up to 35 years (Table; Figure 2).

Substance Misuse and Other Comorbidity

Seventeen studies^{2,12,42-45,47,50,51,53-55,59,61-65} included data on substance comorbidity among individuals with schizophrenia

spectrum disorders, either under a broad substance misuse definition^{12,42,43,45,50,51,53,61,63,65} or separately for drug use^{2,44,47,59,62,64} and alcohol use.^{2,44,47,54,55,59,62,64} A variety of descriptors were used to define the comorbidity; in studies that described misuse (without or without dependence),^{42-45,50,51,53-55,59} or use disorders,^{2,12,61} prevalence ranges were reported for men and women (eTable 3 in the Supplement). In 13 studies,^{12,42-45,50,51,53,54,59,63,65} data allowed violence perpetration in individuals with schizophrenia spectrum disorders with or without substance misuse comorbidity to be compared with general population groups

Figure 2. Absolute Risks of Violence Perpetration in Individuals With Schizophrenia Spectrum Disorders



Outcome period and absolute risk of violence perpetration in individuals with schizophrenia spectrum disorders in studies included in meta-analyses reporting register-based violent outcomes. Data using self- and collateral-report measures were excluded from comparison owing to lower severity threshold. Linear regression lines with 95% CIs are presented by sex.

separately. The pooled odds of violence perpetration in individuals with schizophrenia spectrum disorders without substance misuse comorbidity ($n = 11\,079$) was 3.5 (95% CI, 2.6-4.6; $I^2 = 81\%$; 95% CI, 68-89) (eFigure 5 in the Supplement), and in individuals with schizophrenia spectrum disorders with substance misuse comorbidity ($n = 3586$), it was 9.9 (95% CI, 7.2-13.5; $I^2 = 82\%$; 95% CI, 69-89) (eFigure 6 in the Supplement).

Information on other comorbidities was limited. One study reported on comorbid antisocial personality disorder.⁶² No included studies provided treatment information.

Geographical Region

Subgroup analyses were undertaken for studies undertaken in Europe ($n = 33\,836$), North America ($n = 9856$), Australia and New Zealand ($n = 4207$), and Africa ($n = 122$). Relative risk estimates for violence perpetration among individuals with schizophrenia spectrum disorders compared with general population control individuals did not significantly vary by region (eFigure 7 in the Supplement).

Familial Confounding

Two included studies, conducted in Sweden² and Israel,⁵¹ used population registers to examine risk of violence perpetration in individuals with schizophrenia spectrum disorders and their unaffected siblings ($n = 33\,892$ unaffected siblings) in addition to comparing individuals with schizophrenia spectrum disorders with general population control individuals. Both studies found relative risks of violence perpetration in unaffected siblings remained significantly increased compared with population control individuals, but to a lesser degree than in the corresponding patient samples (eFigure 8 in the Supplement), indicating familial confounding. When comparing violence perpetration in individuals with schizophrenia spectrum disorders with their unaffected siblings, the study in Sweden²

reported a ratio of ORs of 4.2 (95% CI, 3.8-4.5) and the study in Israel⁵¹ an OR of 2.8 (95% CI, 2.5-3.3).

Inpatient and Community Samples

When data were grouped according to samples identified by a history of psychiatric hospital admission or using a wider definition of outpatient or inpatient psychiatric settings, there were no significant differences in relative risk estimates (inpatient pooled OR, 5.4; 95% CI, 4.1-7.0; combined community and inpatient pooled OR, 5.5; 95% CI, 4.0-7.4) (eFigure 9 in the Supplement).

Homicide Perpetration as Outcome

Eight studies were identified with homicide perpetration as an outcome (Figure 3; eTable 5 in the Supplement). All used official sources for outcomes. There was an increase in risk of homicide perpetration in individuals with schizophrenia spectrum disorders compared with those without (Figure 3), leading to a random-effects pooled OR of 17.7 (95% CI, 13.9-22.6) with substantial heterogeneity ($I^2 = 70\%$; 95% CI, 39-85). Excluding 1 study ($n = 282$ [0.4%])⁵⁹ with no events in the control group did not materially change the pooled risk estimate (OR, 17.9; 95% CI, 14.1-22.8). Four studies were rated good quality^{21,29,30,51} and 4 were rated poor to fair^{31,32,59,60} (eTable 4 in the Supplement).

Sexual Offense Perpetration as Outcome

Nine studies^{22,36-39,51,52,59,64} were included in a meta-analysis of sexual offense perpetration outcomes (Figure 4; eTables 4 and 6 in the Supplement). All but 2 studies^{38,64} used a register-based outcome. Risk was increased in individuals with schizophrenia spectrum disorders compared with control individuals, with a random-effects pooled OR of 5.1 (95% CI, 3.8-6.8) with moderate heterogeneity ($I^2 = 54\%$; 95% CI, 7-78) (Figure 4).

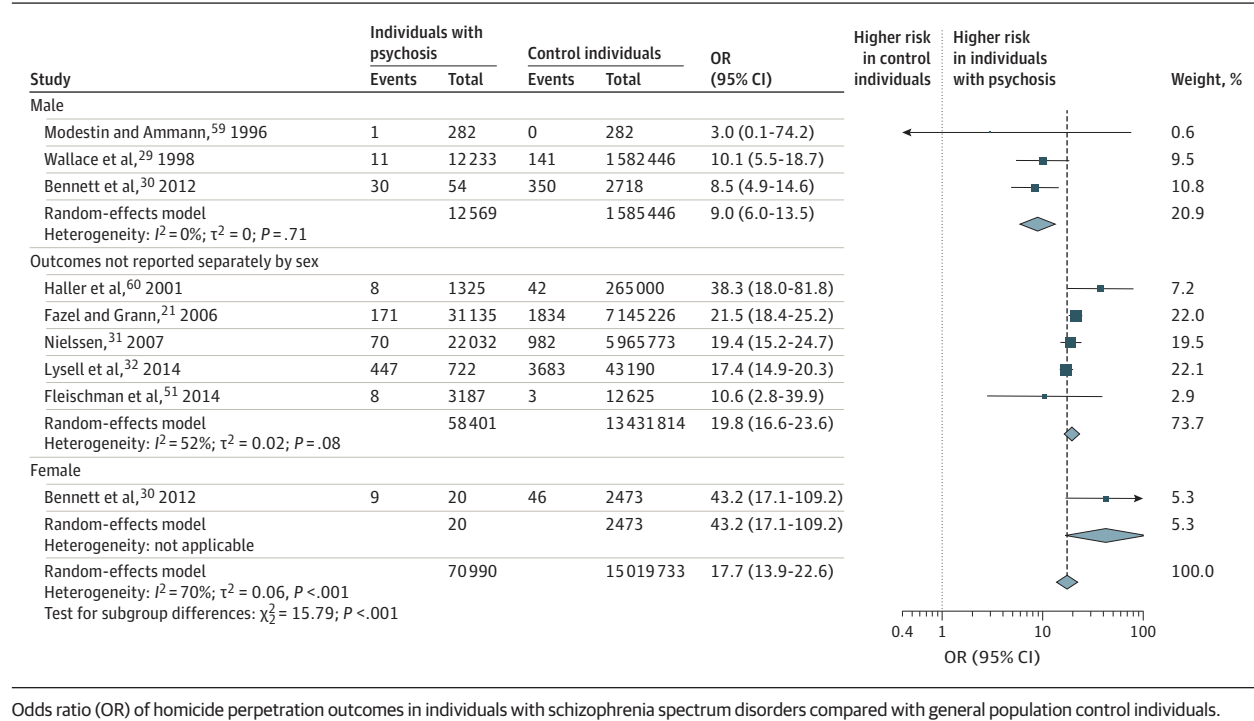
Arson as Outcome

Four studies presented data on risk of arson. Findings ranged from no association between schizophrenia and self-reported fire-setting in 1 study⁶⁴ to 2 register-based studies of arson and related convictions that showed a significant positive association with schizophrenia spectrum disorder diagnosis, with ORs of 18 (95% CI, 12-26) in male individuals and 23 (95% CI, 13-41) in female individuals in a study in Sweden,³³ and 7 (95% CI, 4-13) in a study in Australia that did not report outcomes separately by sex of participants³⁴ (eResults in the Supplement). Meta-analysis was not considered owing to the heterogeneity of arson outcomes.

Discussion

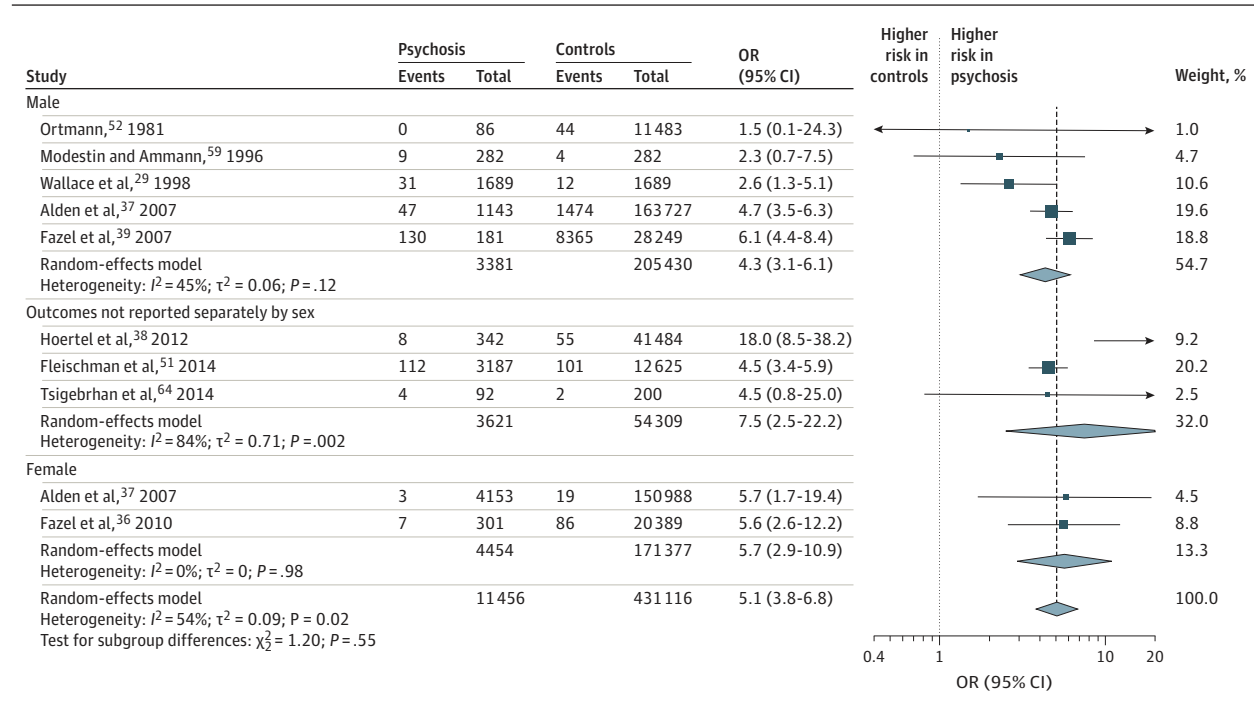
This systematic review and meta-analysis included 51 309 individuals with schizophrenia spectrum disorders from 24 studies in 15 countries over 4 decades and investigated risk of violence perpetration outcomes. Additionally, we examined data on homicide perpetration and studies reporting sexual offense perpetration and arson as outcomes. Our

Figure 3. Forest Plot of Association Between Schizophrenia Spectrum Disorders and Homicide Perpetration



Odds ratio (OR) of homicide perpetration outcomes in individuals with schizophrenia spectrum disorders compared with general population control individuals.

Figure 4. Forest Plot of Association Between Schizophrenia Spectrum Disorders and Sexual Offense Perpetration



Odds ratio (OR) of sexual offense perpetration outcomes in individuals with schizophrenia spectrum disorders compared with general population control individuals.

findings update and extend a previous meta-analysis¹¹ in 4 main ways.

First, the study included more than double the number of individuals with schizophrenia spectrum disorders in the meta-

analysis of violence perpetration outcomes than the previous meta-analysis. This is despite deploying strict exclusion criteria to avoid double-counting of individuals in pooled analyses that excluded otherwise eligible studies. The improved

precision of the current study is principally owing to the inclusion of 4 large, high-quality register-based studies conducted since the previous review.^{2,12,51,61} Despite studies from the last decade contributing most of the data, estimates for the relative risk of violence perpetration have remained broadly stable based on visual inspection of the forest plots (Figure 1).

Second, we pooled risks of sexual offense perpetration. Primary studies varied as to whether they included sexual offenses in an overall definition of violent offending or provided separate data on these offenses. Although there have been descriptive reviews of associations with sexual offending,⁶⁸ to our knowledge this is the first quantitative synthesis. Data on arson and fire-setting were more limited, although 2 register-based studies reported a significant increased association with schizophrenia spectrum disorders.

Third, we summarized information on absolute risks of violent crime perpetration and on the time period over which these outcomes occurred. Time periods ranged from 1 to 35 years in register-based studies, and absolute risks varied considerably over time and between sexes. Absolute risks were less than 1 in 20 (or 5%) in female individuals with schizophrenia spectrum disorders and less than 1 in 4 men.

Fourth, large register-based studies undertaken since the original review¹¹ provided more power to investigate confounding. We replicated in pooled analyses the finding that violence perpetration risk was reduced but remained increased relative to control samples when individuals with substance misuse comorbidity were excluded.^{12,51} In individuals with schizophrenia spectrum disorders and substance misuse comorbidity, there was increased odds of around 10-fold compared with general population control individuals, whereas in individuals with noncomorbid schizophrenia spectrum disorders, this was around 3-fold compared with general population control individuals. Additionally, the contribution of familial factors has now been estimated in studies that have compared risks of violence perpetration in individuals with schizophrenia spectrum disorders, their unaffected siblings, and general population control individuals. These investigations reported residual risk among unaffected siblings and therefore some familial confounding, but risk remains elevated among affected individuals compared with their unaffected siblings.^{2,51} The latter finding further confirms the independent association between schizophrenia and violence perpetration.

There are several implications of our findings for clinical services and future research. In clinical settings, risks in absolute terms, particularly in young men, are typically high enough to be considered of routine clinical importance to prevent. This is reflected to a limited extent in clinical guidelines, but guidance on assessing and managing risk could be improved.⁶⁹ Likewise, the importance of comorbid substance misuse has been further highlighted, reinforcing the need to prioritize the assessment and treatment of comorbid substance misuse disorders in clinical services. The applicability of findings to a particular clinical setting is a limitation of pooling data from individuals at different stages of illness and treatment in a variety of geographical and health care settings. However, the amount of data included has allowed for

exploration of some relevant factors, such as variation by region, patient samples, and substance misuse comorbidity. This improves the ability of clinicians to consider the extent to which findings may apply to their practice.

This replication of relative risk estimates for violence perpetration with the inclusion of larger data sets suggests that further small studies of the relative risk of violence in schizophrenia are not priorities. Future epidemiological research could focus on specific offenses or outcomes, such as sexual offenses and arson. Violence perpetration as an outcome is necessarily broad, but there may be important differences in clinical and risk profiles between more specific violence perpetration outcomes.

This meta-analysis found robust associations between schizophrenia spectrum disorders and violence perpetration, but did not answer the question of the nature of causal pathways and whether they are present. Empirical studies have suggested that symptoms such as persecutory delusions may be causally linked to violence.⁷⁰ The current study found that the association between schizophrenia spectrum disorders and violence perpetration remained, albeit with reduced estimates, after adjusting for substance misuse and familial confounders, which can exist on the causal pathway and explain a proportion of the association. However, other background, psychiatric, and socioeconomic factors unaccounted for in these pooled analyses can contribute to this pathway, and there is research in support of early conduct problems,⁷¹ adverse childhood experiences,⁷² and economic disadvantage.⁷³ Large prospective studies are needed to further evaluate causality.⁷⁴ For clinicians, the multifactorial association means that a key priority should be to refine approaches to individualized risk assessment and management. Scalable prediction tools offer one way to translate contemporary knowledge on risk factors (including sociodemographic, familial, and treatment factors) into clinical practice and achieve a more stratified approach to assessing and managing clinical needs around violence risk.⁷⁵

There was little information on treatment effects. There is evidence from pharmacoepidemiological studies that antipsychotics can reduce violence perpetration outcomes.⁷⁶⁻⁷⁹ This needs confirmation in randomized trials, and violence perpetration should be a routine outcome in effectiveness trials of pharmacological and nonpharmacological interventions. One question is how risk of violence perpetration in individuals with schizophrenia spectrum disorders treated with antipsychotic medication compares with that risk in general population samples. One population study in Sweden found rates of violent offenses of 33 per 1000 person-years during treatment with olanzapine compared with 96 offenses per 1000 person-years prior to treatment.⁷⁷ To what extent these treatment effects bring rates of violence perpetration down toward baseline population levels requires comparison with matched groups.

Limitations

This study has limitations. Most data in pooled analyses used register-based violence perpetration outcomes, which offer advantages over self- or informant-rated measures in that they objectively cross a severity threshold for clinical relevance and

resource implications, do not rely on ongoing contact with health services, and avoid interrater variability and recall bias. A limitation is to what extent these measures may be confounded by differential treatment of individuals with mental disorders by the justice system. However, a study examining the Dunedin cohort found that associations with mental disorders were similar when using self- or informant-report and official court records, suggesting that the degree of underreporting is similar in individuals with schizophrenia spectrum disorders and control individuals when using either outcome.⁶⁶ In terms of other limitations, only 3 studies presented information on experiencing interpersonal violence^{61,62,64} and 1 on the contribution of childhood trauma.⁶² The importance of the overlap between risk of experiencing violence and perpetrating violence is increasingly recognized.^{3,61,80} Further, although analyses did not reveal significant differences in risk estimates when studies were grouped by quality, variation between studies in the level of matching of comparison groups is an additional consideration to explain heterogeneity, as this was only partially captured by the quality rating. A study of

more than half a million individuals using population registers in Denmark replicated findings of increased risk of violence perpetration in individuals with schizophrenia spectrum disorders (with incident rate ratios of 6 in men and 18 in women),⁸¹ but could not be included in pooled analyses because the study lacked the necessary tabular data.

Conclusions

This review has quantitatively summarized the association between schizophrenia spectrum disorders and violence perpetration outcomes. Prevention of violence perpetration should be a target for clinical services that assess and treat individuals with these disorders. New work should consider preventive approaches, including the improvement of the clinical assessment of risk and targeted resource allocation to treat modifiable factors. Violence perpetration outcomes should be routinely collected in studies of the effectiveness of clinical services and therapeutic interventions.

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