Schizophrenia, antipsychotic treatment adherence, and driver responsibility for motor vehicle crash: A population-based retrospective study in British Columbia, Canada

Supplementary appendix

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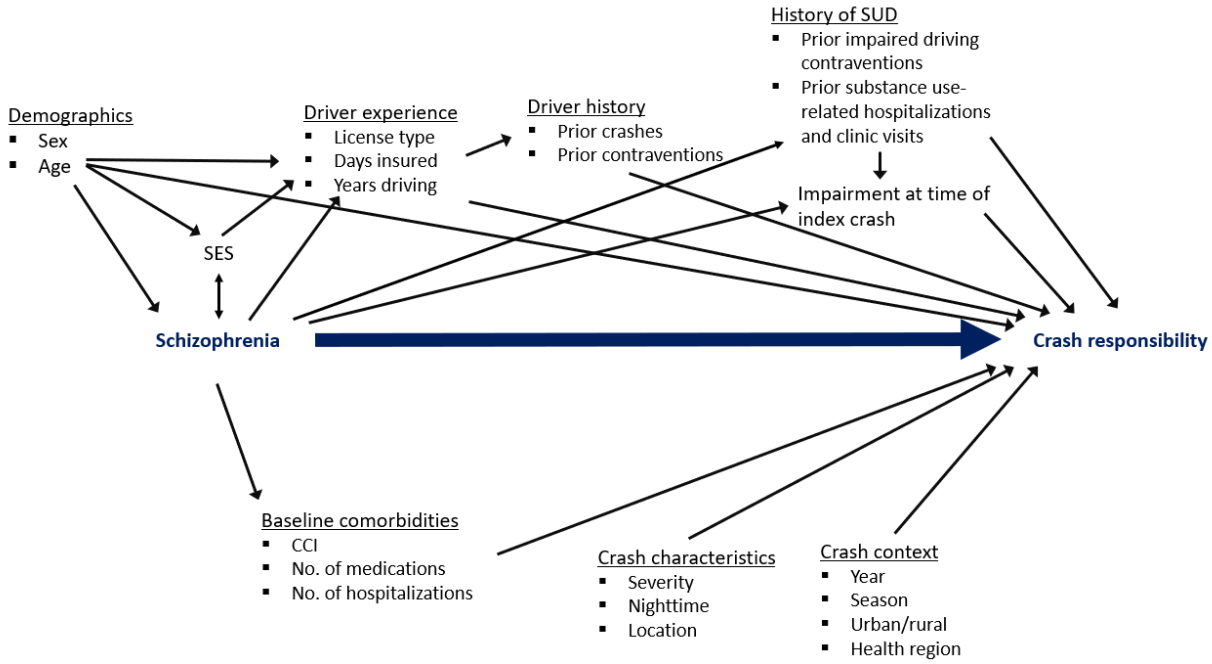
Item S1: Conceptual model of schizophrenia and crash responsibility



Legend. Directed acyclic graph (DAG) depicting relationships between schizophrenia, crash responsibility, and potential confounders. SES = socioeconomic status; SUD = substance use disorder; CCI = Charlson comorbidity index.

Item S2a: Data sources

We accessed health data through Population Data BC, a university-based repository for individual-level longitudinal administrative health data on all BC residents.[1] Probabilistic linkage between driver licence and personal health number (PHN) was based on name, sex, and birthdate and achieved linkage rates ≥95%.[2-4] All BC residents who held a driver license during the study period were eligible for linkage. Our specific data sources included:

- **Discharge Abstract Database**: Canadian Institute for Health Information [creator] (2017): Discharge Abstract Database (Hospital Separations). Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.
- **PharmaNet**: BC Ministry of Health [creator] (2018): PharmaNet. V2. BC Ministry of Health [publisher]. Data Extract. Data Stewardship Committee (2018). http://www.popdata.bc.ca/data.
- **Medical Services Plan**: British Columbia Ministry of Health [creator] (2017): Medical Services Plan (MSP) Payment Information File. Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.
- **Consolidation File**: British Columbia Ministry of Health [creator] (2017): Consolidation File (MSP Registration & Premium Billing). Population Data BC [publisher]. Data Extract. MOH (2017). http://www.popdata.bc.ca/data.
- **BC Vital Statistics Agency** [creator] (2017): Vital Statistics Deaths. V2. Population Data BC [publisher]. Data Extract BC Vital Statistics Agency (2017). http://www.popdata.bc.ca/data.
- **Statistics Canada**, Small Area and Administrative Data Division [creator] (2017): Income Band data file. Population Data BC [publisher]. Data Extract. Statistic Canada (2017). http://www.popdata.bc.ca/data.
- **Income Band**: Statistics Canada [creator]: Statistics Canada Income Band Data. Catalogue Number: 13C0016. V2. Population Data BC [publisher]. Data Extract. Population Data BC (2017). http://www.popdata.bc.ca/data.
- **Driver data**: Insurance Corporation of British Columbia [creator] (2017): Driver Experience, Contraventions, and Exam tables and the Traffic Accident System. Insurance Corporation of British Columbia [publisher]. Data Extract. ICBC (2017). http://www.popdata.bc.ca/data.

All inferences, opinions and conclusions drawn in this manuscript are those of the authors and do not reflect the opinions or policies of the Data Stewards.

Item S2b. Missing data

Study datasets are highly complete for all critical study variables (**Item S2c**):

a) Exposure variables (schizophrenia, antipsychotic adherence) are never missing as they are defined by hospital/clinic visit diagnostic codes and outpatient prescription fills, and these variables are highly complete.[5] Exposure misclassification (e.g., schizophrenia present but no associated hospital/clinic visit/prescription codes in the lookback) is probably uncommon.[6]

b) Outcome (crash responsibility) is almost never missing. Police report factors that contribute to the crash (e.g., animal on road, speeding, defective brakes). The absence of these factors on the report indicates the officer believed these factors did not contribute to the crash (and thus do not

exonerate the driver of responsibility). Less than 2% of TAS police reports are excluded because they are missing data in ≥3 scoring categories.

c) Breath alcohol level is usually not reported because the attending officer may not obtain a breath alcohol level if they do not suspect impairment. There is evidence of impairment (positive breath alcohol level, police suspicion of impairment by alcohol or drugs) in 6.6% of crash-involved drivers (**Item S10**).

d) Missingness in other key variables (e.g., age, sex, number of prior hospitalizations, license type, years of driving experience; **Item S5**) were within acceptable range (<5%) and did not necessitate the use of multiple imputation.[7,8]

Item S2c. Proportion of missing data for key variables in the study cohort

Full covariate description	Proportion missing	Handling of missing data
Age at time of crash	0%	No data missing.
Sex	<0.1%	Included 3 categories for sex (male, female, missing).
Residential neighbourhood household income quintile	4.1%	Included 6th category for QAIPPE, set as 0 (0 = missing, 1 = first quintile, up to 5).
Residential neighbourhood rurality	2.5%	Included extra category for missing.
Region (Health Authority)	2.7%	Included extra category for missing.
Comorbidities (including prior alcohol or other drug use)	0%	If no physician visits and hospitalizations are present in the data, the comorbidity was deemed absent.
Prior hospitalization for schizophrenia	0%	If no hospitalizations present in the data, assumed count of 0.
Most advanced license type achieved at the time of the crash	0.4%	If no data available for individual prior to crash, assumed did not have license, added category "none".
Years with full license	0%	All drivers without full licenses at crash set to 0.
Number of police-attended crashes in prior 3 years	0%	If no data present assumed no crashes.
Number of contraventions in prior 3 years	0%	If no data present assumed no contraventions.
Year of crash	0%	No data missing.
Season of crash	0%	No data missing.
Crash severity (fatality, injury, property damage only)	0%	No data missing.
Crash location (city streets, rural road, highway)	0%	No data missing.
Any documented impairment by alcohol or drugs at time of crash	0%	If evidence of impairment present in data (i.e., police suspicion of impairment, impairment-related contraventions, nonzero breath or blood alcohol), assume impaired. If no evidence of impairment present, assumed not impaired.
Number of months between schizophrenia onset and crash	0%	No data missing.

Item S3: Diagnostic codes used to identify schizophrenia

Purpose	Database	Description	ICD codes
Identify physician clinic visits for schizophrenia	Medical Services Plan (MSP), ICD-9-CM codes	Schizophrenic disorders	295
		Simple type schizophrenia*	2950
		Disorganized type schizophrenia*	2951
		Catatonic type schizophrenia*	2952
		Paranoid type schizophrenia*	2953
		Schizophreniform disorder*	2954
		Latent schizophrenia*	2955
		Schizophrenic disorders, residual type*	2956
		Schizoaffective disorder, unspecified*	2957
		Other specified types of schizophrenia*	2958
		Unspecified schizophrenia*	2959
		Personal history of schizophrenia	V110
Identify index hospitalization for schizophrenia	Discharge Abstract Database (DAD), ICD-10-CA codes	Schizophrenia	F20
		Paranoid schizophrenia	F200
		Disorganized schizophrenia	F201
		Catatonic schizophrenia	F202
		Undifferentiated schizophrenia	F203
		Post-schizophrenic depression	F204
		Residual schizophrenia	F205
		Simple schizophrenia	F206
		Other schizophrenia (schizophreniform disorder, other)	F208
		Schizophrenia, unspecified	F209
		Schizoaffective disorders (bipolar type, depressive type, other, unspecified)	F250, F251, F252, F258, F259

Legend. Asterisk (*) indicates inclusion of the following subtypes: unspecified, subchronic, chronic, subchronic with acute exacerbation, chronic with acute exacerbation, in remission. ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification. ICD-10-CA = International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Canada.

Item S4: Exposure criteria and other definitions

Exposure	Exposure criteria
Schizophrenia	One hospital admission for schizophrenia (ICD-10-CA codes F20 or F25 or corresponding daughter codes in most responsible diagnosis field of DAD), or three physician visits for schizophrenia within 36 months (ICD-9-CM code 295 or daughter codes in diagnosis field of MSP).[6] We only considered a crash-involved driver to be "exposed" (i.e., to have a diagnosis of schizophrenia) if the schizophrenia "diagnosis date" was before the crash date. This definition was previously validated in Canadian administrative health data (sensitivity, 97%; specificity, 57%); a sensitivity analysis examines an alternate case definition that requires one or more hospitalization for schizophrenia (sensitivity, 82%; specificity, 75%).6 **Diagnosis date:** date of first hospitalization or clinic visit for *schizophrenia*. **Onset date:** date of first hospitalization or clinic visit for *schizophrenia or psychosis* in the 3 years prior to diagnosis date.
Antipsychotic adherence	Quantified using the 'medication possession ratio' (MPR), defined as the number of days of antipsychotic dispensed in or overlapping with the 30-day interval leading up to the crash. It was not possible to determine how days in hospital influenced the MPR numerator because inpatient medications are not available from PharmaNet or any other province-wide data source. However, days in hospital were uncommon in the 30-day interval leading up to the crash (corresponding to ~7% of crash-involved drivers but only ~2% of driver-days in that interval). We performed a sensitivity analysis that excluded all individuals with days in hospital in the pre-crash interval. It yielded results similar to the main analysis suggesting that this source of uncertainty did not substantially bias our results. Antipsychotic medications were identified in PharmaNet outpatient pharmacy dispensing data using standard Anatomical Therapeutic Chemical (ATC) codes:[9] - Antipsychotics: N05A, excluding lithium (N05AN01) - Long-acting injectable antipsychotic ("depot antipsychotics") are injections administered every 2 weeks or more. These were also identified using PharmaNet data. **Near-optimal adherence:** MPR ≥0.8 **Suboptimal adherence:** MPR<0.8 **Complete non-adherence:** MPR=0

Item S5: Variable definitions

Variables	Description
Outcome	
Crash responsibility	Dichotomized as 'responsible' (score ≤13) or 'non-responsible' (score ≥16). Indeterminate scores (14 - 15) are excluded from further analysis.
Exposures	
Schizophrenia	Diagnosis of schizophrenia established any time prior to the crash.
Medication Possession Ratio (MPR)	Calculated as the number of days of medication dispensed in or overlapping with a given interval divided by the number of days in that interval. Dichotomized to 'sub-optimal' (<0.80) versus 'near-optimal' (≥0.80) for the primary analysis.
Potential confounders	
Demographic	
Age	Categorical
Sex	Male; Female; Missing
Residential neighbourhood household income quintile	Ordinal variable (1 = lowest income, 5 = highest income) generated by Population Data BC using census data and residential Forward Sortation Area (FSA is defined by the first three digits of the residential postal code)
Residential rurality	Rural areas and small population centres (towns) vs medium and large population centres (cities), according to population density within residential Forward Sortation Area.
Region (Health Authority)	BC's 5 health authority regions: Vancouver Coastal; Vancouver Island; Fraser; Interior; Northern. Determined according to residential Forward Sortation Area.
Road exposure	
License type	Full license; Novice license; Learner license
Days insured	Number of days insured in the lookback period. Continuous variable.
Driving experience	
Years of driving experience	Crash date minus date of first full license. Continuous variable.
Number of police-attended crashes in 3y lookback period	Continuous variable.
Number of non-impaired contraventions in 3y lookback period	Traffic violations include speeding and distracted driving (but excluding impairment by alcohol or drugs). Continuous variable.
Number of impaired driving contraventions in 3y lookback period	Traffic violations indicating impairment by alcohol or drugs. Continuous variable.
Crash characteristics	
Crash severity	Property damage only; Injury; Fatality
Nighttime crash	Yes if crash occurred between 9pm and 6am.
Crash location type	City street; Highway
Impairment by alcohol or drugs	Any documented impairment by drugs and alcohol (police suspicion of impairment, impairment-related contraventions, positive breath alcohol).
Year of crash	Calendar year
Season of crash	Dec-Feb (Winter); Mar-May (Spring); Jun-Aug (Summer); Sep-Nov (Fall)
Health	
Number of distinct medications	Total number of different classes of medications that are prescribed in a 90-day lookback period.

Psychiatric hospitalizations in the 3y lookback period	Number of psychiatric hospitalizations in the 3y lookback period excluding hospitalizations for SUDs. Intended to reflect recent stability of psychiatric disease. Continuous variable.
Hospitalization or clinic visits for alcohol or other drug use in the 3y lookback period	Number of hospitalizations or outpatient physician visits for alcohol or other drug use in the 3y lookback period. Continuous variable.
CCI in the 3y lookback period	Dichotomized variable for Charlson Comorbidity Index ≥2 (yes/no)

Legend. Potential confounders were identified using a causal model based on expert knowledge, literature review, and previous experience with the study data (**Item S1**). All models were forced to include confounders with known strong effects: age, sex, license type, number of crashes in 3-year lookback, number of contraventions related to impairment by alcohol or drugs in 3-year lookback, number of non-impairment-related contraventions in 3-year lookback, and documented impairment at the time of index crash. We selected additional confounders for inclusion in each model using recommended procedures:[10]
(i) We identified the initial set of potential confounders ensuring we maintained more than 25 events-per-variable (EPV) in the global model;
(ii) we performed variable selection only on variables not forced into the model because they had no known strong effect;
(iii) we removed variables using backward selection;
(iv) we conducted a stability investigation to understand the impact of variable selection by repeating the variable selection procedure on 200 bootstrap resamples of the dataset. We examined standard stability metrics such as the difference between the mean of the re-sampled coefficient and the global model estimate to assess possible bias, and the root mean squared difference ratio to estimate the extent of variance inflation or deflation induced by model selection.

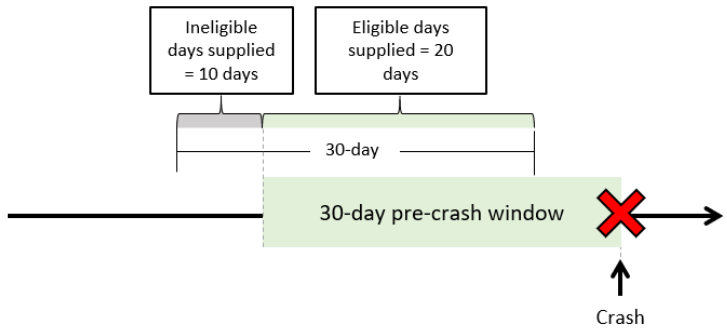
Item S6: Methods used to calculate the medication possession ratio (MPR)

Item S6a: Calculation of MPR. The medication possession ratio (MPR) reflects actual medication consumption and is widely accepted as a valid method to assess adherence.[11-14] We calculated MPR for the 30-day interval prior to each police-attended crash for all crash-involved drivers in the adherence cohort (schizophrenia diagnosis date ≥30 days prior to the crash; ≥1 antipsychotic prescription fill after the diagnosis date; ≥1 antipsychotic prescription fill in the year prior to crash). MPR was calculated as the total number of days of antipsychotic supplied in or overlapping with the 30-day interval prior to crash, divided by 30 days. If a driver was involved in multiple police-attended crashes over the study interval, MPR was calculated independently for each crash.

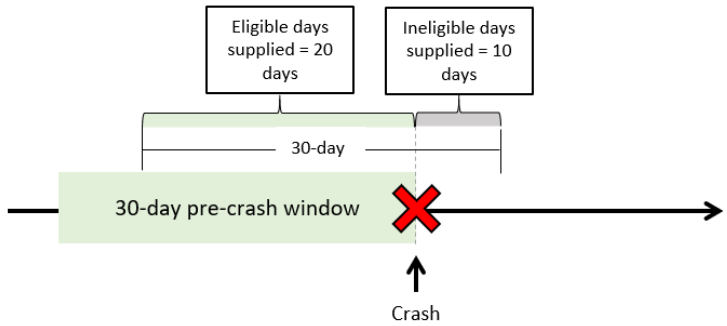
Treatment of prescription fills that overlap with the start or end of the 30-day pre-crash window. We used standard procedures to account for:
i) prescription fills that were dispensed prior to the window but appeared to overlap with the window based on the dispensation date and days supplied;
ii) prescription fills that were dispensed within the window but continued after the crash based on the dispensation date and days supplied.
In both cases, these procedures only included the days supplied that fell within the 30-day pre-crash interval (**Item S6b**). This ensures that all MPR values remain ≤1.0.

Item S6b: Prescription fills overlapping with the bounds of the 30-day pre-crash window

Prescription fill overlaps with the start of the 30-day pre-crash window



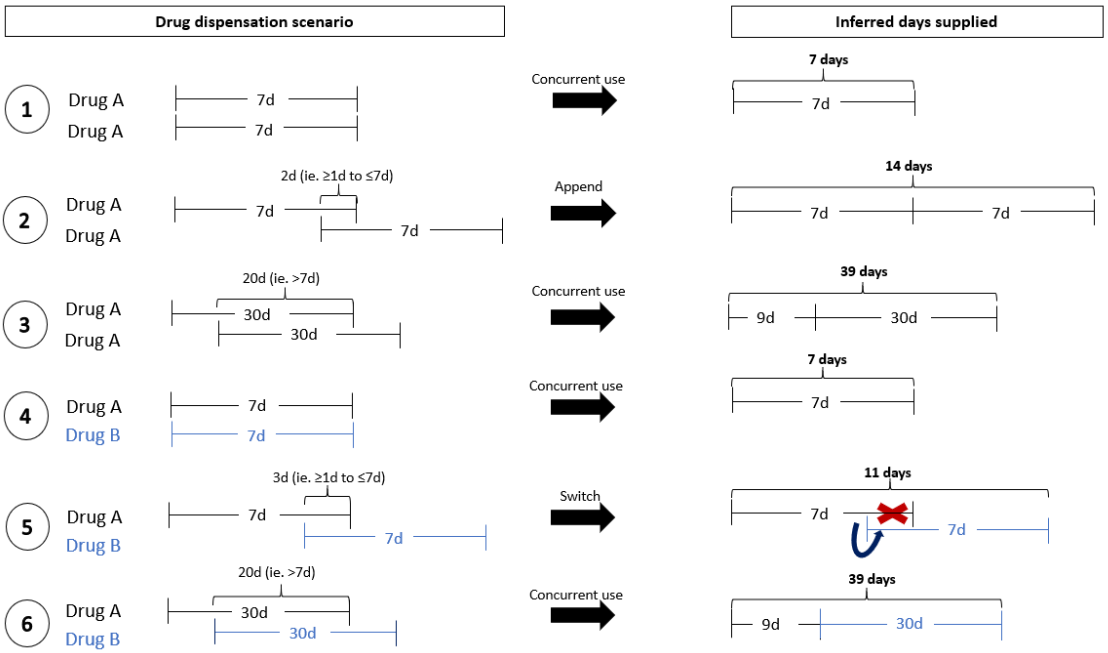
Prescription fill overlaps with the crash date



Item S6c: Treatment of prescription fills that overlap with prior or subsequent prescription fills
As in prior research, we applied consistent rules that aim to reduce underestimation or overestimation of MPR arising from overlapping prescriptions.[15,16,17] Our primary analysis handled overlapping prescriptions using the following rules (**Item S6d**):

1. If two prescriptions of the *same drug* were dispensed on the same date, we assumed concurrent use (DrugA 10mg tabs QD mitte 7 days on day 1 + DrugA 5mg tabs QD mitte 7 days dispensed on day 1 = 7 days supplied);
2. If the overlap between two prescriptions of the *same drug* was ≥1 day and ≤7 days, we assumed that the later prescription was an early refill and that the patient would wait until the previous prescription had run out before starting the next prescription (DrugA 10mg tabs QD mitte 7 days dispensed on day 1 + DrugA 10mg tabs QD mitte 7 days dispensed on day 5 = 14 days supplied);
3. If the overlap between two prescriptions of the *same drug* was >7 days, we assumed concurrent use (DrugA 10mg tabs QD mitte 30 days dispensed on day 1 + DrugA 10mg tabs QD mitte 30 days dispensed on day 10 = 39 days supplied; this might occur if the first set of pills were lost);
4. If two *different drugs* were dispensed on the same date, we assumed concurrent use (DrugA 10mg tabs QD mitte 7 days + DrugB 5mg tabs QD mitte 7 days dispensed on the same date = 7 days supplied);
5. If the overlap between two prescriptions of *different drugs* was between ≥1 and ≤7 days, we assumed that the patient stopped taking the previous drug and switched to the later drug on the day that the later drug was dispensed (DrugA 10mg tabs QD mitte 7 days dispensed on day 1 + DrugB 10mg tabs QD mitte 7 days dispensed on day 5 = 11 days supplied);
6. If the overlap between two prescriptions of *different drugs* was >7 days, we assumed concurrent use (DrugA 10mg tabs QD mitte 30 days dispensed on day 1 + DrugB 10mg tabs QD mitte 30 days dispensed on day 10 = 39 days supplied).

Item S6d: Prescription fills with overlapping days supplied



Legend. The figure depicts scenarios 1 – 6 from **Item S6c**. When we assumed concurrent use, the overlapping days supplied were only counted once. When the patient was assumed to switch from one drug to a different one, the days supplied of the previous prescription was cut off to end the day before the later drug was dispensed. When we assumed an early refill, the date dispensed of the later prescription was shifted to start the day after the previous prescription had ended. In this case, the original days supplied was maintained; however, with an adjusted date dispensed.

Item S7: Baseline patient characteristics at schizophrenia diagnosis date

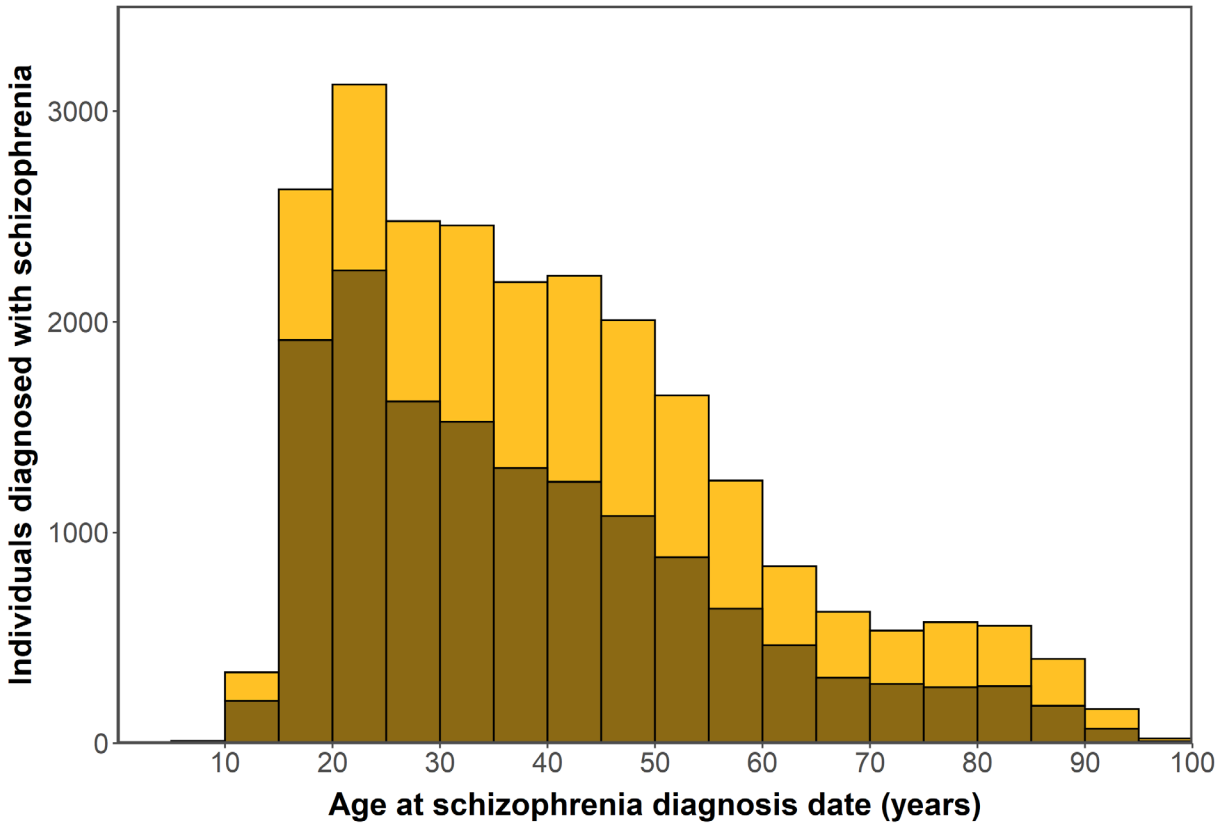
Characteristic	Drivers with schizophrenia, count (%) n = 24,076	Drivers with schizophrenia involved in a crash, count (%) n = 2365	Drivers with schizophrenia, not involved in a crash, count (%) n = 21,711	p-values, crash vs no crash
Median age [Q1, Q3] (years)	38 [25, 52]	32 [22, 43]	39 [26, 53]	<0.001
Age categories				<0.001
. ≤20 years	2979 (12.4%)	427 (18.1%)	2552 (11.8%)	
. 21 to 44 years	12,032 (50%)	1387 (58.6%)	10,645 (49.0%)	
. 45 to 64 years	6039 (25.1%)	477 (20.2%)	5562 (25.6%)	
. ≥65 years	3026 (12.6%)	74 (3.1%)	2952 (13.6%)	
Male sex	14,515 (60.3%)	1553 (65.7%)	12,962 (59.7%)	<0.001
Rural residence	9107 (37.8%)	1048 (44.3%)	8059 (37.1%)	<0.001
Residential neighbourhood household income quintile				0.006
. 1 (lowest income)	6835 (28.4%)	620 (26.2%)	6215 (28.6%)	
. 2	4975 (20.7%)	479 (20.3%)	4496 (20.7%)	
. 3	4207 (17.5%)	427 (18.1%)	3780 (17.4%)	
. 4	3774 (15.7%)	425 (18.0%)	3349 (15.4%)	
. 5 (highest income)	3582 (14.9%)	357 (15.1%)	3225 (14.9%)	
. Missing	703 (2.9%)	57 (2.4%)	646 (3%)	
≥1 hospitalizations in prior year	6683 (27.8%)	665 (28.1%)	6018 (27.7%)	0.698
≥7 physician visits in prior year	3095 (12.9%)	313 (13.2%)	2782 (12.8%)	0.583
Comorbidities				
. Any psychiatric disorder	9059 (37.6%)	924 (39.1%)	8135 (37.5%)	0.133
. Hypertension	1276 (5.3%)	59 (2.5%)	1217 (5.6%)	<0.001
. Alcohol use	1307 (5.4%)	132 (5.6%)	1175 (5.4%)	0.766
. Other drug use	2669 (11.1%)	324 (13.7%)	2345 (10.8%)	<0.001
. Diabetes	710 (2.9%)	29 (1.2%)	681 (3.1%)	<0.001
Active prescriptions at baseline				
. 0 or 1	15,016 (62.4%)	1522 (64.4%)	13,494 (62.2%)	0.038
. ≥2	9060 (37.6%)	843 (35.6%)	8217 (37.8%)	
Medications filled in prior 90 days				
. Quetiapine	3411 (14.2%)	295 (12.5%)	3116 (14.4%)	0.014
. Risperidone	3007 (12.5%)	335 (14.2%)	2672 (12.3%)	0.010
. Olanzapine	1503 (6.2%)	157 (6.6%)	1346 (6.2%)	0.428
. Aripiprazole	310 (1.3%)	14 (0.6%)	296 (1.4%)	0.002
. Clozapine	76 (0.3%)	<5	75 (0.3%)	0.021
. Other antipsychotics	1066 (4.4%)	100 (4.2%)	966 (4.4%)	0.657
. Benzodiazepines	5986 (24.9%)	669 (28.3%)	5317 (24.5%)	<0.001
. Opioids	2688 (11.2%)	295 (12.5%)	2393 (11.0%)	0.036

Item S7: Baseline patient characteristics at schizophrenia diagnosis date (continued)

Characteristic	Drivers with schizophrenia, count (%) n = 24,076	Drivers with schizophrenia involved in a crash, count (%) n = 2365	Drivers with schizophrenia, not involved in a crash, count (%) n = 21,711	p-values, crash vs no crash
Driver licence type				<0.001
. Learner	2420 (10.1%)	139 (5.9%)	2281 (10.5%)	
. Novice	2510 (10.4%)	348 (14.7%)	2162 (10.0%)	
. Full	16,985 (70.5%)	1682 (71.1%)	15,303 (70.5%)	
. No license	2161 (9.0%)	196 (8.3%)	1965 (9.1%)	
Active license in prior 3 years	19,375 (80.5%)	2103 (88.9%)	17,272 (79.6%)	<0.001
Median years with full license	10	8	10	<0.001
Police-attended crash in prior 3 years	1561 (6.5%)	263 (11.1%)	1298 (6.0%)	<0.001
Any contravention in prior 3 years	7040 (29.2%)	1128 (47.7%)	5912 (27.2%)	<0.001
. Alcohol contravention	1287 (5.3%)	239 (10.1%)	1048 (4.8%)	<0.001
. Speed contravention	3178 (13.2%)	609 (25.8%)	2569 (11.8%)	<0.001
. Distraction contravention	231 (1.0%)	17 (0.7%)	214 (1.0%)	0.249

Legend. From a total of 24,076 individuals with a diagnosis of schizophrenia, 2365 (9.8%) were involved in a police-attended crash over a median follow-up of 3.3 years. Notably, although all cohort members had an active license at some point in our study interval, 19% of individuals with schizophrenia had a follow-up time of zero because they did not hold an active license at any point after the schizophrenia diagnosis date plus 30 days. Most drivers with schizophrenia were male, were between the ages 21 and 44 years, and held an active driver license in the past 3 years. Drivers with schizophrenia were overrepresented in lower-income residential neighbourhoods. About 40% crash-involved drivers had a psychiatric disorder at baseline (i.e., ≥1 hospitalization or ≥2 physician visits with a diagnosis code corresponding to a psychiatric disorder), with a quarter of them on benzodiazepines. Compared to drivers with schizophrenia who were not involved in a crash, drivers with schizophrenia who were involved in a crash were younger, more likely to be male, more likely to have prior medical visits for drug use, more likely to have a Novice license, and more likely to have a prior contravention for alcohol or speed. The large sample size in our study can result in p-values <0.001 even when the difference between groups may not be clinically meaningful.

Item S8: Age at schizophrenia diagnosis in the study cohort



Legend. Stacked histogram of the number of drivers in our study cohort by age at schizophrenia diagnosis date. Darker brown (lower portion of bars) indicates number of males; brighter yellow (upper portion of bars) indicates number of females. In our cohort of individuals who also held a driver license during the study interval, the median age at schizophrenia diagnosis date was 38 years. In a meta-analysis of 36 studies, Solmi *et al* report that the median age at schizophrenia onset was 25 years.[18]

There are two principal reasons why the median age at schizophrenia diagnosis for our cohort of drivers is higher than the reported median age at symptom onset among all individuals eventually diagnosed with schizophrenia:

1. Our cohort only includes individuals with schizophrenia who held a driver license in the study interval. Solmi *et al* report that 12% of schizophrenia occurs prior to 18 years of age.[18] Individuals with adolescent-onset schizophrenia may be disproportionately excluded from our cohort as they are less likely than unaffected peers to go on to acquire a driver license. Maglione *et al* report that 20-29% of schizophrenia has an age of onset over 40 years.[19] Individuals with late onset schizophrenia may be overrepresented in our cohort as they had several decades to acquire a driver license before the onset of schizophrenia.

2. We derive diagnosis date from hospitalization and clinic visits. These healthcare system contacts are much more likely to occur with first episode of psychosis than to occur with the first onset of negative symptoms. First episode psychosis typically occurs several years after the onset of symptoms: Hafner *et al* report that the mean age of the first signs of schizophrenia is 25 years, while the mean age of the first episode (maximum psychiatric symptoms) is 30 years.[21,20]

Despite these differences, the histogram of age at diagnosis date that we present is strikingly similar to the age distribution of schizophrenia onset presented in other studies, including a peak age at diagnosis in the early 20s and a longer tail that lasts into later life (see Solmi *et al*'s Figure 4[18]; Hafner *et al*'s Figure 7.1[21]; Sham *et* al*'s* Figure 1a[22]; and Hilker *et al*'s Figure 1[23]). Our cohort also reflects the real-world population for whom clinicians are asked to make fitness-to-drive decisions.

Item S9: Responsibility score components among responsible and non-responsible drivers (exposure: schizophrenia)

Characteristic	Drivers deemed responsible for crash, count (%) n = 434,119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Road Type				
Traffic flow				<0.001
. One-way	33,547 (7.7%)	18,349 (4.9%)	9772 (7.7%)	
. Two-way	388,593 (89.5%)	353,493 (94.4%)	110,990 (87.3%)	
. Other/unknown	11,979 (2.8%)	2471 (0.7%)	6333 (5.0%)	
Road class				<0.001
. Single lane	18,056 (4.2%)	13,718 (3.7%)	5083 (4.0%)	
. Single lane, ramp	1827 (0.4%)	1102 (0.3%)	332 (0.3%)	
. Multi-lane	344,479 (79.4%)	323,251 (86.4%)	102,559 (80.7%)	
. Multi-lane, ramp	1049 (0.2%)	890 (0.2%)	328 (0.3%)	
. Not applicable	43,164 (9.9%)	12,317 (3.3%)	6068 (4.8%)	
. Other/unknown	25,544 (5.9%)	23,035 (6.2%)	12,725 (10.0%)	
Crash location				<0.001
. At intersection	193,756 (44.6%)	196,620 (52.5%)	69,759 (54.9%)	
. Between intersection	168,568 (38.8%)	142,948 (38.2%)	40,579 (31.9%)	
. Parking lot	31,084 (7.2%)	6511 (1.7%)	4300 (3.4%)	
. Other/unknown	40,711 (9.4%)	28,234 (7.5%)	12,457 (9.8%)	
Roadside hazard/design listed as contributory factor	2124 (0.5%)	5416 (1.4%)	999 (0.8%)	<0.001

Item S9: Responsibility score components among responsible and non-responsible drivers (exposure: schizophrenia) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 434,119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Driving Conditions				
Road condition				<0.001
. Dry	284,250 (65.5%)	205,106 (54.8%)	90,330 (71.1%)	
. Wet	112,325 (25.9%)	117,257 (31.3%)	27,595 (21.7%)	
. Snow/slush/ice/mud	33,361 (7.7%)	49,662 (13.3%)	5466 (4.3%)	
. Other/unknown	4183 (1.0%)	2288 (0.6%)	3704 (2.9%)	
Road surface				<0.001
. Asphalt/concrete	421,282 (97.0%)	366,189 (97.8%)	121,013 (95.2%)	
. Stone/gravel/earth/wood	11,450 (2.6%)	7153 (1.9%)	2755 (2.2%)	
. Other/unknown	1387 (0.3%)	971 (0.3%)	3327 (2.6%)	
Weather				<0.001
. Clear/cloudy	347,730 (80.1%)	271,954 (72.7%)	104,458 (82.2%)	
. Rain/strong wind	64,545 (14.9%)	73,329 (19.6%)	16,215 (12.8%)	
. Fog/smoke/smog	2987 (0.7%)	4187 (1.1%)	663 (0.5%)	
. Snow/sleet/hail	14,119 (3.3%)	22,331 (6.0%)	1996 (1.6%)	
. Other/unknown	4738 (1.1%)	2512 (0.7%)	3763 (3%)	
Lighting				<0.001
. Daylight	290,948 (67%)	245,838 (65.7%)	88,422 (69.6%)	
. Dusk/dawn	25,863 (6.0%)	24,568 (6.6%)	7222 (5.7%)	
. Dark with full illumination	33,473 (7.7%)	26,915 (7.2%)	10,287 (8.1%)	
. Dark with no/some illumination	80,688 (18.6%)	75,191 (20.1%)	17,925 (14.1%)	
. Other/unknown	3147 (0.7%)	1801 (0.5%)	3239 (2.5%)	
Weather/visibility listed as contributory factor	26,926 (6.2%)	29,007 (7.7%)	1569 (1.2%)	<0.001
Vehicle Condition				<0.001
. Vehicle condition listed as contributory factor	2929 (0.7%)	12,103 (3.2%)	1460 (1.1%)	
. Vehicle condition not listed as contributory factor	431,190 (99.3%)	362,210 (96.8%)	125,635 (98.9%)	

Item S9: Responsibility score components among responsible and non-responsible drivers (exposure: schizophrenia) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 434,119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Unsafe Driving Actions				<0.001
. Index driver driving safely, obeying road laws	74,569 (17.2%)	372,404 (99.5%)	123,902 (97.5%)	
. Index driver not driving safely or disobeying road laws	359,550 (82.8%)	1909 (0.5%)	3193 (2.5%)	
Contribution Other Parties				<0.001
. Yes	0 (0.0%)	238,240 (63.6%)	1649 (1.3%)	
. No/index driver driving unsafely	434,119 (100%)	136,073 (36.4%)	125,446 (98.7%)	
Crash Type				
Number of vehicles involved				<0.001
. Single vehicle	125,752 (29%)	63,318 (16.9%)	19,120 (15.0%)	
. Two vehicles	265,481 (61.2%)	235,298 (62.9%)	88,928 (70.0%)	
. Three or more vehicles	42,886 (9.9%)	75,697 (20.2%)	19,047 (15.0%)	
Diagram description				<0.001
. Intersection - right angle	56,624 (13.0%)	61,477 (16.4%)	22,054 (17.4%)	
. Head on	12,060 (2.8%)	15,917 (4.3%)	4839 (3.8%)	
. Rear end	92,074 (21.2%)	124,656 (33.3%)	23,035 (18.1%)	
. Backing	21,052 (4.8%)	5963 (1.6%)	3478 (2.7%)	
. Turn	65,017 (15.0%)	53,633 (14.3%)	26,452 (20.8%)	
. Overtaking	11,162 (2.6%)	7593 (2.0%)	4436 (3.5%)	
. Off road	83,361 (19.2%)	33,581 (9.0%)	8832 (6.9%)	
. Other/unknown	92,769 (21.4%)	71,493 (19.1%)	33,969 (26.7%)	
Damage location				<0.001
. Front	195,777 (45.1%)	125,346 (33.5%)	53,952 (42.5%)	
. Front/rear	6995 (1.6%)	15,282 (4.1%)	3696 (2.9%)	
. Front/side	29,080 (6.7%)	19,920 (5.3%)	8504 (6.7%)	
. Rear	30,065 (6.9%)	90,214 (24.1%)	13,277 (10.4%)	
. Rear/side	3655 (0.8%)	5857 (1.6%)	1137 (0.9%)	
. Side	52,845 (12.2%)	49,941 (13.3%)	15,050 (11.8%)	
. Tires/undercarriage/ windshield/roof	3368 (0.8%)	2597 (0.7%)	1141 (0.9%)	
. Whole vehicle	55,102 (12.7%)	29,140 (7.8%)	10,385 (8.2%)	
. None	26,590 (6.1%)	14,178 (3.8%)	8703 (6.8%)	
. Other/unknown	30,642 (7.1%)	21,838 (5.8%)	11,250 (8.9%)	

Item S9: Responsibility score components among responsible and non-responsible drivers (exposure: schizophrenia) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 43,4119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Task Involved				
. Avoidance manoeuvre listed as contributory factor	3114 (0.7%)	8474 (2.3%)	227 (0.2%)	<0.001
Pre-collision action				<0.001
. Straight	234,398 (54%)	244,304 (65.3%)	80,846 (63.6%)	
. Backing	26,414 (6.1%)	2376 (0.6%)	2499 (2.0%)	
. Turning	100,296 (23.1%)	38,213 (10.2%)	27,180 (21.4%)	
. Changing lanes/merging	9320 (2.1%)	2413 (0.6%)	1926 (1.5%)	
. Loss of control	10,205 (2.4%)	4331 (1.2%)	768 (0.6%)	
. Stopped/parked	8534 (2.0%)	57,956 (15.5%)	814 (0.6%)	
. Other/unknown	44,952 (10.4%)	24,720 (6.6%)	13062 (10.3%)	

Legend. Relative to drivers deemed non-responsible for their crash, drivers deemed responsible for their crashes were far more likely to be disobeying road laws or not driving safely and to be involved in a single vehicle crash. Drivers deemed non-responsible were far more likely to have other drivers contribute to their crash, more likely to be stopped/parked at the time of crash, and more likely to be rear-ended. These findings are direct manifestations of the responsibility scoring tool that assigns responsibility based on these factors. They are also plausible and intuitively appealing contributors to crash responsibility. Drivers with indeterminate responsibility were not included in analyses and are presented here for descriptive purposes only. P-values compare responsible drivers to non-responsible drivers. The large sample size in our study may produce p-values <0.001 even in the absence of a clinically meaningful difference between groups.

Item S10: Other crash characteristics among responsible and non-responsible drivers (exposure: schizophrenia)

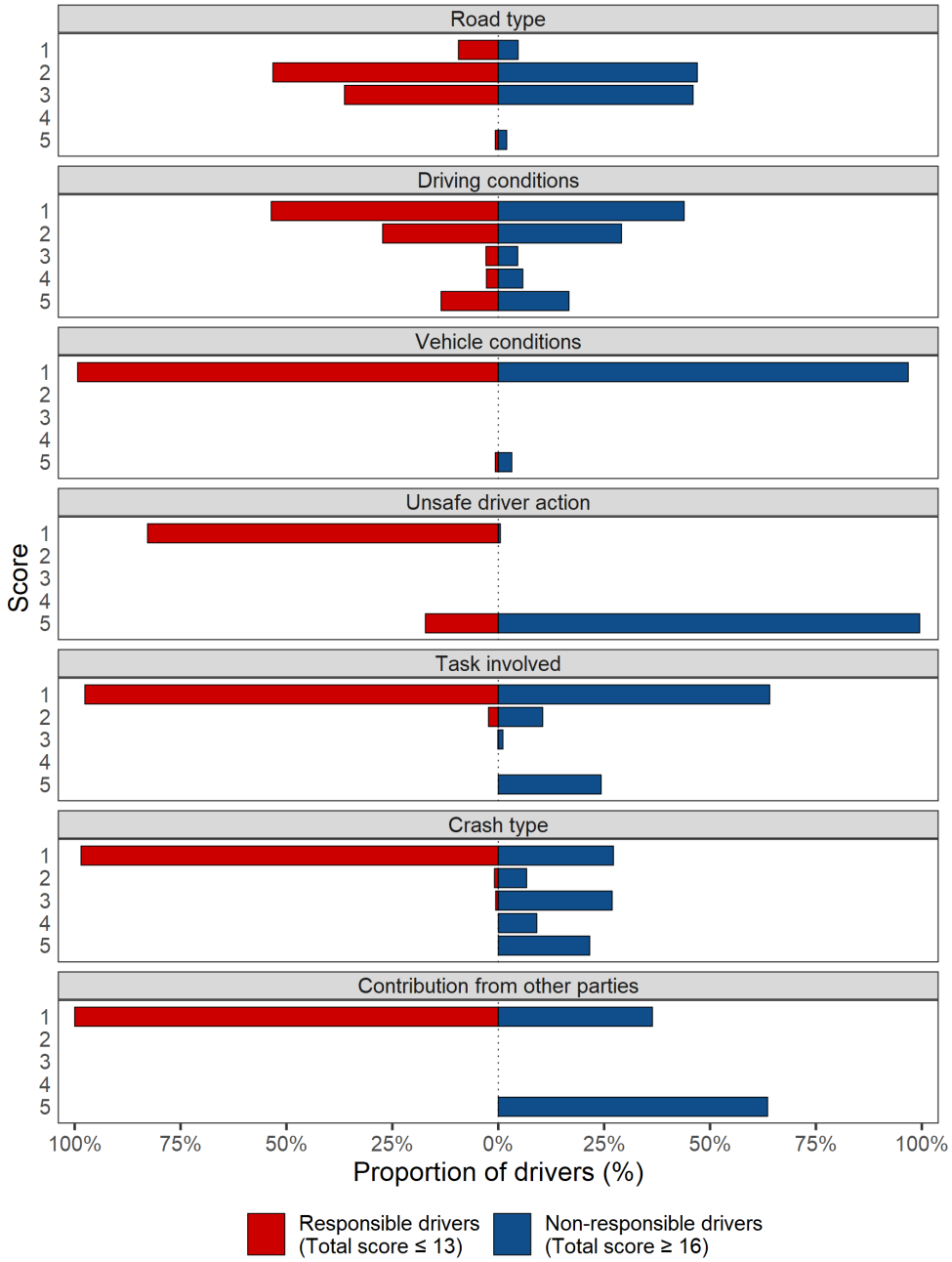
Characteristic	Drivers deemed responsible for crash, count (%) n = 434,119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Human conditions				
. Alcohol	43,001 (9.9%)	6662 (1.8%)	4897 (3.9%)	<0.001
. Medications	1135 (0.3%)	182 (0.0%)	146 (0.1%)	<0.001
. Drugs	4472 (1.0%)	714 (0.2%)	472 (0.4%)	<0.001
. Illness/fatigue	7576 (1.7%)	1306 (0.3%)	942 (0.7%)	<0.001
. Distracted/inattentive	119,900 (27.6%)	33,269 (8.9%)	10,692 (8.4%)	<0.001
. Pre-existing physical disability	1271 (0.3%)	258 (0.1%)	158 (0.1%)	<0.001
Breath alcohol positive				<0.001
. Yes	6986 (1.6%)	1515 (0.4%)	1113 (0.9%)	
. No evidence	427,133 (98.4%)	372,798 (99.6%)	125,982 (99.1%)	
Impaired by alcohol or drugs				<0.001
. Yes	47,821 (11%)	8108 (2.2%)	5805 (4.6%)	
. No evidence	386,298 (89.0%)	366,205 (97.8%)	121,290 (95.4%)	
Crash severity				<0.001
. Casualty (fatal or injury)	201,754 (46.5%)	180,496 (48.2%)	62,074 (48.8%)	
. Property damage	232,365 (53.5%)	193,817 (51.8%)	65,021 (51.2%)	
Road location				<0.001
. Rural road	20,618 (4.7%)	13,728 (3.7%)	3792 (3%)	
. Provincial highway	113,897 (26.2%)	112,324 (30.0%)	28,514 (22.4%)	
. City street	299,604 (69.0%)	248,261 (66.3%)	94,789 (74.6%)	
Speed zone				<0.001
. <50 km/h	25,904 (6.0%)	13,886 (3.7%)	5390 (4.2%)	
. 50 km/h	233,730 (53.8%)	207,172 (55.3%)	74,894 (58.9%)	
. 60-70 km/h	57,248 (13.2%)	55,170 (14.7%)	15,830 (12.5%)	
. ≥80 km/h	69,688 (16.1%)	72,818 (19.5%)	15,503 (12.2%)	
. Other/unknown	47,549 (11.0%)	25,267 (6.8%)	15,478 (12.2%)	
Vehicle damage severity				<0.001
. Light	92,846 (21.4%)	107,851 (28.8%)	32,631 (25.7%)	
. Moderate	121,158 (27.9%)	11,9778 (32.0%)	37,154 (29.2%)	
. Severe	112,460 (25.9%)	82,358 (22.0%)	27,971 (22.0%)	
. Demolished	49,383 (11.4%)	25,449 (6.8%)	8709 (6.9%)	
. None	26,590 (6.1%)	14,178 (3.8%)	8703 (6.8%)	
. Other/unknown	31,682 (7.3%)	24,699 (6.6%)	11,927 (9.4%)	

Item S10: Other crash characteristics among responsible and non-responsible drivers (exposure: schizophrenia) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 434,119	Drivers deemed non-responsible for crash, count (%) n = 374,313	Drivers with indeterminate responsibility, count (%) n = 127,095	p-values, responsible vs non-responsible
Crash year				<0.001
. 2000-2004	154,334 (35.6%)	120,253 (32.1%)	41,909 (33.0%)	
. 2005-2010	158,889 (36.6%)	138,030 (36.9%)	44,688 (35.2%)	
. 2011-2016	120,896 (27.8%)	116,030 (31.0%)	40,498 (31.9%)	
Crash season				<0.001
. Winter (Dec-Feb)	105,160 (24.2%)	107,549 (28.7%)	28,711 (22.6%)	
. Spring (Mar-May)	102,907 (23.7%)	81,603 (21.8%)	30,759 (24.2%)	
. Summer (Jun-Aug)	114,229 (26.3%)	83,253 (22.2%)	34,529 (27.2%)	
. Fall (Sep-Nov)	111,823 (25.8%)	101,908 (27.2%)	33,096 (26.0%)	
Day of week				<0.001
. Weekday (Mon-Thurs)	245,233 (56.5%)	219,121 (58.5%)	74,249 (58.4%)	
. Weekend (Fri-Sun)	188,886 (43.5%)	155,192 (41.5%)	52,846 (41.6%)	
Time of day				<0.001
. Morning (6:01-12:00)	109,269 (25.2%)	99,185 (26.5%)	31,980 (25.2%)	
. Afternoon (12:01-18:00)	184,254 (42.4%)	162,618 (43.4%)	57,326 (45.1%)	
. Evening (18:01-24:00)	93,636 (21.6%)	83,669 (22.4%)	26,708 (21.0%)	
. Night (0:01-6:00)	37,896 (8.7%)	21,502 (5.7%)	8066 (6.3%)	
. Other/unknown	9064 (2.1%)	7339 (2.0%)	3015 (2.4%)	

Legend. Relative to drivers deemed non-responsible for their crash, drivers deemed responsible for their crash were far more likely to have alcohol (unadjusted odds ratio (OR), 6.07; 95%CI, 5.91-6.23; p<0.001), drugs (OR, 5.45; 95%CI, 5.03-5.9; p<0.001), fatigue/illness (OR, 5.07; 95%CI, 4.78-5.38; p<0.001), and distraction/inattention (OR, 3.91; 95%CI, 3.86-3.96; p<0.001) listed by the attending police officer as contributors to the crash. They were also far more likely to be impaired by alcohol (OR, 5.59; 95%CI, 5.46-5.73; p<0.001). These are widely recognized risk factors for motor vehicle crash. They do not directly contribute to the calculation of the responsibility score, and the fact that they are nevertheless strongly associated with crash responsibility supports the face validity of responsibility analysis for identifying risk factors for crash. Drivers with indeterminate responsibility were not included in analyses and are presented here for descriptive purposes only. P-values compare responsible drivers to non-responsible drivers. The large sample size in our study may produce p-values <0.001 even in the absence of a clinically meaningful difference between groups.

Item S11: Mirrored histograms of responsibility score components among responsible and non-responsible drivers (exposure: schizophrenia)



Legend. Mirrored histograms comparing scores between responsible and non-responsible drivers for each of the seven components of the responsibility score. The actions of the driver (through unsafe actions, task involved, and crash type) and the contributions from other drivers involved in the crash are the primary determinants of driver responsibility for crash.

Item S12: Results for the main analysis of schizophrenia and crash responsibility

Variable	Adjusted odds ratio (95%CI); p-value
Intercept	0.98 (0.95, 1.00); 0.045
Schizophrenia diagnosis prior to crash (exposure of interest)	**1.67 (1.53, 1.82); <0.001**
Crash-involved driver aged ≤20 years (referent: 21-44 years)	1.43 (1.40, 1.46); <0.001
Crash-involved driver aged 45-64 years (referent: 21-44 years)	1.02 (1.00, 1.03); 0.009
Crash driver aged ≥65 years (referent: 21-44 years)	**2.04 (2.00, 2.08); <0.001**
Male sex (referent: female)	1.04 (1.03, 1.05); <0.001
Unknown sex (referent: female)	1.46 (0.96, 2.23); 0.078
Ordinal variable denoting residential neighbourhood income quintile (1 = lowest income, 5 = highest income)	0.98 (0.97, 0.98); <0.001
Residential rurality is "popCentreSmall" (referent: "popCentreMed")	1.02 (1.00, 1.03); 0.019
Residential rurality is "ruralArea" (referent: "popCentreMed")	1.05 (1.04, 1.07); <0.001
Residential rurality is "Missing" (referent: "popCentreMed")	1.10 (0.99, 1.23); 0.071
Fraser Health Authority (referent: Vancouver Coastal Health (VCH))	0.97 (0.95, 0.98); <0.001
Interior Health Authority (referent: VCH)	0.96 (0.94, 0.98); <0.001
Vancouver Island Health Authority (referent: VCH)	0.97 (0.95, 0.98); <0.001
Northern Health Authority (referent: VCH)	0.81 (0.80, 0.83); <0.001
Missing Health Authority (referent: VCH)	0.93 (0.84, 1.03); 0.149
Learner license type (referent: Full license)	**2.39 (2.28, 2.50); <0.001**
Novice license type (referent: Full license)	1.44 (1.42, 1.47); <0.001
No license at time of crash (referent: Full license)	2.74 (2.52, 2.99); <0.001
Number of years with Full license	0.99 (0.99, 0.99); <0.001
Number of police-attended crashes in prior 3 years	1.09 (1.08, 1.10); <0.001
Number of non-impairment related contraventions in prior 3 years	1.08 (1.08, 1.09); <0.001
Number of impairment related contraventions in prior 3 years	1.23 (1.22, 1.25); <0.001
Crash resulted in severe injury (referent: Property damage only)	0.94 (0.93, 0.95); <0.001
Crash resulted in fatality (referent: Property damage only)	1.19 (1.12, 1.25); <0.001
Crash occurred at night	0.88 (0.87, 0.89); <0.001
Crash occurred on provincial highway (referent: city streets)	0.87 (0.86, 0.88); <0.001
Crash occurred on rural road (referent: city streets)	1.07 (1.05, 1.10); <0.001
Any documented impairment by alcohol or drugs at time of crash	**5.37 (5.24, 5.51); <0.001**
Hospitalizations for alcohol or other drug use in prior 3 years	1.02 (1.02, 1.02); <0.001
Charlson comorbidity index ≥2	1.02 (1.01, 1.03); <0.001
Years elapsed between first year of study interval and year of the crash	0.99 (0.99, 0.99); <0.001
Crash occurred in the spring (Mar - May; referent: Winter)	1.26 (1.24, 1.27); <0.001
Crash occurred in the summer (Jun - Aug; referent: Winter)	1.37 (1.35, 1.39); <0.001
Crash occurred in the fall (Sep - Dec; referent: Winter)	1.10 (1.08, 1.11); <0.001

Legend. Adjusted odds ratios for all terms included in the final model evaluating the association between schizophrenia and crash responsibility. Driver age ≥65 years, learner license type, and impairment by alcohol or drugs (blue text) are all more strongly associated with crash responsibility than a prior diagnosis of schizophrenia (red text).

Item S13: Subgroup and sensitivity analyses for schizophrenia and crash responsibility

Analysis	Drivers deemed responsible for crash, count (%)	Drivers deemed non-responsible for crash, count (%)	Unadjusted odds ratio (95% CI); p-value	Adjusted odds ratio (95% CI); p-value
Main analysis				
. **Main analysis**	434,119 (46.4%)	374,313 (40.0%)	1.69 (1.56, 1.84); p<0.001	1.67 (1.53, 1.82); p<0.001
Subgroup analyses				
. **Age**				
. ≤20 years	73,042 (60.1%)	35,696 (29.4%)	1.41 (1.01, 1.98); p=0.046	1.29 (0.91, 1.83); p=0.147
. 21 to 44 years	202,189 (44.9%)	185,292 (41.2%)	1.75 (1.57, 1.94); p<0.001	1.61 (1.45, 1.80); p<0.001
. 45 to 64 years	107,132 (40.2%)	120,604 (45.2%)	1.98 (1.69, 2.32); p<0.001	1.81 (1.54, 2.13); p<0.001
. ≥65 years	51,756 (53.4%)	32,721 (33.7%)	2.02 (1.35, 3.03); p<0.001	2.00 (1.33, 3.01); p<0.001
. **Sex**				
. Males	283,487 (47.5%)	233,001 (39.0%)	1.59 (1.44, 1.76); p<0.001	1.51 (1.36, 1.67); p<0.001
. Females	150,566 (44.5%)	141,278 (41.8%)	1.89 (1.63, 2.18); p<0.001	1.99 (1.72, 2.31); p<0.001
. **History of alcohol or other drug use**				
. Yes	14,067 (61.0%)	6351 (27.5%)	1.10 (0.94, 1.29); p=0.22	1.20 (1.02, 1.41); p=0.03
. No	420,052 (46.0%)	367,962 (40.3%)	1.57 (1.43, 1.73); p<0.001	1.66 (1.51, 1.84); p<0.001

Item S13: Subgroup and sensitivity analyses for schizophrenia and crash responsibility (continued)

Analysis	Drivers deemed responsible for crash, count (%)	Drivers deemed non-responsible for crash, count (%)	Unadjusted odds ratio (95% CI); p-value	Adjusted odds ratio (95% CI); p-value
Sensitivity analyses				
. **Alternate exposure**				
. Considered exposed only if prior hospitalization for schizophrenia)	434,119 (46.4%)	374,313 (40.0%)	1.74 (1.51, 2.01); p<0.001	1.75 (1.51, 2.03); p<0.001
. No prior hospitalization for schizophrenia; met exposure criteria based on ≥3 clinic visits for schizophrenia within 36 months	434,119 (46.4%)	374,313 (40.0%)	1.67 (1.51, 1.84); p<0.001	1.63 (1.47, 1.81); p<0.001
. **Alternate outcome (crash type)**				
. Fatality	3676 (51.4%)	2326 (32.5%)	0.81 (0.30, 2.19); p=0.68	0.84 (0.29, 2.43); p=0.74
. Fatality or injury	201,754 (45.4%)	180,496 (40.6%)	1.54 (1.38, 1.73); p<0.001	1.56 (1.39, 1.76); p<0.001
. Property damage only	232,365 (47.3%)	193,817 (39.5%)	1.87 (1.66, 2.10); p<0.001	1.79 (1.58, 2.02); p<0.001
. **Alternate responsibility score contrasts**				
. ≤12 vs ≥17	373,829 (40.0%)	297,285 (31.8%)	1.77 (1.61, 1.94); p<0.001	1.78 (1.62, 1.96) p<0.001
. ≤13 vs ≥16 (main analysis)	434,119 (46.4%)	374,313 (40.0%)	1.69 (1.56, 1.84); p<0.001	1.67 (1.53, 1.82); p<0.001
. ≤14 vs ≥15	480,668 (51.4%)	440,243 (47.1%)	1.66 (1.54, 1.79); p<0.001	1.61 (1.49, 1.74); p<0.001
. **Alternate exclusion criteria**				
Do not exclude individuals with hospitalizations or physician visits for psychosis or prescription fills for antipsychotics in washout (1997-1999)	440,721 (46.5%)	378,627 (39.9%)	1.63 (1.53, 1.73); p<0.001	1.68 (1.58, 1.79); p<0.001

Item S13: Subgroup and sensitivity analyses for schizophrenia and crash responsibility (continued)

Analysis	Drivers deemed responsible for crash, count (%)	Drivers deemed non-responsible for crash, count (%)	Unadjusted odds ratio (95% CI); p-value	Adjusted odds ratio (95% CI); p-value
Additional analyses				
Change in responsibility score per year since schizophrenia onset date (within subset of crash-involved drivers with schizophrenia)	1689 (58.3%)	862 (29.8%)	0.95 (0.93, 0.97); p<0.001	0.96 (0.94, 0.99); p=0.002

Legend. The association between schizophrenia and crash responsibility appears to be stronger among female drivers. A prespecified model adding a male*schizophrenia interaction term confirmed this difference is significant (aOR, 0.77; 95%CI, 0.64-0.92; p=0.004). We found the association between schizophrenia and crash responsibility to be stronger among drivers without recent visits for alcohol or drug use than it was among drivers with recent medical visits for alcohol and drug use. This might indicate that impairment 'overwhelms' schizophrenia as a determinant of crash risk among individuals with recent problematic drug use, and that schizophrenia is a more important determinant of crash responsibility in the absence of the known strong effect that alcohol and drug impairment have on crash risk. Findings are otherwise largely consistent across subgroup and sensitivity analyses.

There is a modest but significant decline in driver crash responsibility with each additional year that elapses between schizophrenia onset date and crash date, suggesting that typical changes in the clinical features of schizophrenia over time (i.e., fewer 'positive' symptoms such as auditory hallucinations, more 'negative' symptoms such as diminished emotional expression) are associated with a modest improvement in driving safety.

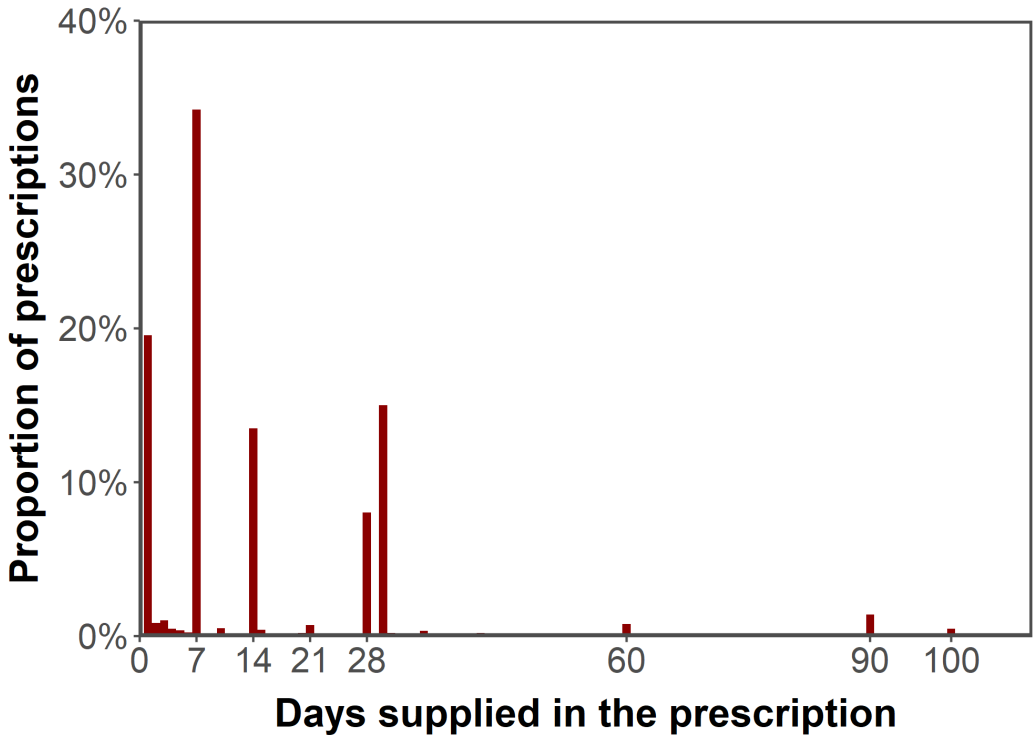
E-value analysis suggested the observed associations were at least moderately robust to potential unmeasured confounding. To make the main analysis odds ratio equivalent to a null effect (i.e., odds ratio = 1.00), an unmeasured confounder would need to be associated with crash responsibility and a prior schizophrenia diagnosis with a risk ratio of 1.91. To shift the lower bound of the 95% confidence interval to include the null value, an unmeasured confounder would need to be associated with crash responsibility and a prior schizophrenia diagnosis with a risk ratio of 1.78; weaker confounding could not account for the observed association.[24,25] We anticipate the main unmeasured confounder to be drug use beyond that captured by our data (i.e., recent medical visits for drug use, impairment suspected by the investigating officer, and documented impairment at the time of crash) and not accounted for through other covariates. We believe unmeasured confounding of this magnitude is unlikely given the effect sizes in **Item S12**.

Item S14: Description of antipsychotic prescription fills

Item S14a: Most commonly filled antipsychotics among drivers with schizophrenia

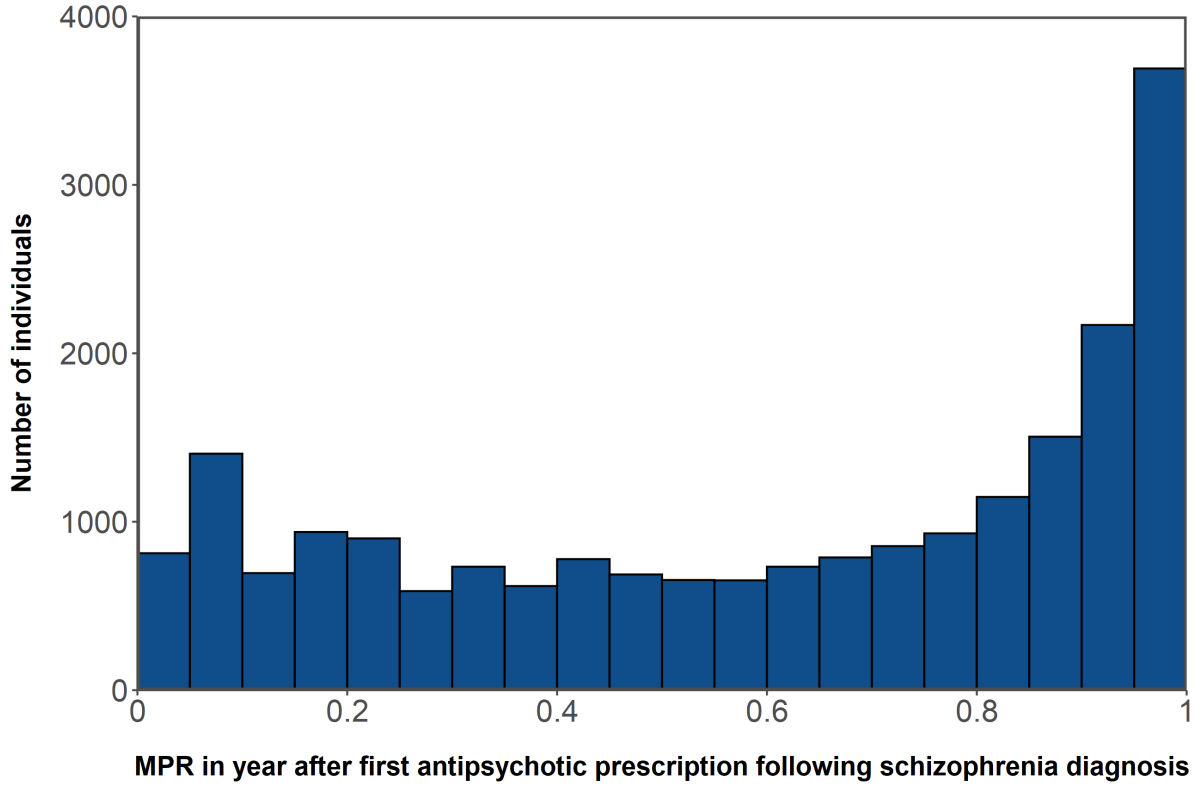
Antipsychotic	Prescriptions filled after schizophrenia diagnosis, count (%)	Days supplied after schizophrenia diagnosis
Quetiapine	908,704 (29.1%)	10,931,354 (26.2%)
Risperidone	677,381 (21.7%)	10,314,549 (24.8%)
Olanzapine	582,203 (18.6%)	8,220,296 (19.8%)
Clozapine	344,595 (11.0%)	6,381,103 (15.3%)
Aripiprazole	204,911 (6.6%)	3,117,308 (7.5%)
Other	406,221 (13.0%)	2,656,378 (6.4%)

Item S14b: Distribution of days supplied for antipsychotic prescription fills



Legend. Histogram of the proportion of prescriptions with specific 'days supplied' after the diagnosis of schizophrenia in the adherence cohort. Almost 96% of prescription fills supplied ≤30 days of antipsychotics. Medication possession ratios calculated using prescription fills with lower 'days supplied' are more likely to generate accurate estimates of medication adherence.

Item S15: Antipsychotic medication possession ratio in the first year after initiation of antipsychotics for schizophrenia



Legend. Histogram of individuals' antipsychotic medication possession ratio in the first year after the first antipsychotic prescription fill following the schizophrenia diagnosis date.

The mean MPR in the first year after antipsychotic prescription following schizophrenia diagnosis was 0.60. This is somewhat higher than other studies examining antipsychotic MPR among individuals with schizophrenia (e.g., 0.41 in Rezansoff Schizophrenia Bulletin 2017, 0.41 in Rezansoff Soc Psych Psych Epi 2016, 0.5 in Patel Curr Ther Res Clin Exp 2020). Our study design selected for individuals who filled at least one antipsychotic prescription in the year after schizophrenia diagnosis and at least one in the year prior to crash; these individuals may be more likely to be adherent than unselected individuals. We also selected crash-involved drivers who typically held a driver license and evidently had access to a vehicle on at least one occasion; these individuals may have less symptomatic forms of schizophrenia and more social support, factors that might result in improved antipsychotic adherence.

Item S16: Responsibility score components among responsible and non-responsible drivers (exposure: antipsychotic adherence)

Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Road Type				
Traffic flow				
One-way	91 (8.2%)	21 (4.1%)	17 (8.1%)	<0.001
Two-way	986 (88.7%)	484 (94.5%)	182 (87.1%)	
Other/unknown	35 (3.1%)	7 (1.4%)	10 (4.8%)	
Road class				<0.001
Single lane	54 (4.9%)	17 (3.3%)	12 (5.7%)	
Single lane, ramp	5 (0.4%)	0 (0.0%)	0 (0.0%)	
Multi-lane	852 (76.6%)	446 (87.1%)	163 (78%)	
Multi-lane, ramp	<5	0 (0.0%)	0 (0.0%)	
Not applicable	129 (11.6%)	20 (3.9%)	12 (5.7%)	
Other/unknown	71 (6.4%)	29 (5.7%)	22 (10.5%)	
Crash location				<0.001
At intersection	442 (39.7%)	281 (54.9%)	106 (50.7%)	
Between intersection	458 (41.2%)	182 (35.5%)	73 (34.9%)	
Parking lot	87 (7.8%)	9 (1.8%)	8 (3.8%)	
Other/unknown	125 (11.2%)	40 (7.8%)	22 (10.5%)	
Roadside hazard/design listed as contributory factor	<5	6 (1.2%)	<5	0.109

Item S16: Responsibility score components among responsible and non-responsible drivers (exposure: antipsychotic adherence) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Driving Conditions				
Road condition				<0.001
Dry	752 (67.6%)	273 (53.3%)	147 (70.3%)	
Wet	288 (25.9%)	162 (31.6%)	53 (25.4%)	
Snow/slush/ice/mud	58 (5.2%)	72 (14.1%)	7 (3.3%)	
Other/unknown	14 (1.3%)	5 (1.0%)	<5	
Road surface				0.287
Asphalt/concrete	1090 (98.0%)	507 (99.0%)	204 (97.6%)	
Stone/gravel/earth/wood	20 (1.8%)	<5	<5	
Other/unknown	<5	<5	<5	
Weather				<0.001
Clear/cloudy	896 (80.6%)	364 (71.1%)	171 (81.8%)	
Rain/strong wind	163 (14.7%)	106 (20.7%)	32 (15.3%)	
Fog/smoke/smog	9 (0.8%)	8 (1.6%)	0 (0.0%)	
Snow/sleet/hail	28 (2.5%)	30 (5.9%)	<5	
Other/unknown	16 (1.4%)	<5	<5	
Lighting				0.735
Daylight	721 (64.8%)	325 (63.5%)	127 (60.8%)	
Dusk/dawn	74 (6.7%)	28 (5.5%)	15 (7.2%)	
Dark with full illumination	91 (8.2%)	43 (8.4%)	17 (8.1%)	
Dark with no/some illumination	216 (19.4%)	112 (21.9%)	48 (23.0%)	
Other/unknown	10 (0.9%)	<5	<5	
Weather/visibility listed as contributory factor	52 (4.7%)	50 (9.8%)	<5	<0.001
Vehicle Condition				<0.001
Vehicle condition listed as contributory factor	11 (1.0%)	32 (6.2%)	<5	
Vehicle condition not listed as contributory factor	1101 (99%)	480 (93.8%)	206 (98.6%)	

Item S16: Responsibility score components among responsible and non-responsible drivers (exposure: antipsychotic adherence) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Unsafe Driving Actions				<0.001
Index driver driving safely, obeying road laws	221 (19.9%)	506 (98.8%)	206 (98.6%)	
Index driver not driving safely or disobeying road laws	891 (80.1%)	6 (1.2%)	<5	
Contribution Other Parties				<0.001
Yes	0 (0.0%)	318 (62.1%)	5 (2.4%)	
No/index driver driving unsafely	1112 (100%)	194 (37.9%)	204 (97.6%)	
Crash Type				
Number of vehicles involved				<0.001
Single vehicle	337 (30.3%)	87 (17%)	36 (17.2%)	
Two vehicles	677 (60.9%)	341 (66.6%)	138 (66.0%)	
Three or more vehicles	98 (8.8%)	84 (16.4%)	35 (16.7%)	
Diagram description				<0.001
Intersection - right angle	112 (10.1%)	95 (18.6%)	26 (12.4%)	
Head on	34 (3.1%)	16 (3.1%)	9 (4.3%)	
Rear end	252 (22.7%)	173 (33.8%)	40 (19.1%)	
Backing	55 (4.9%)	9 (1.8%)	11 (5.3%)	
Turn	131 (11.8%)	79 (15.4%)	38 (18.2%)	
Overtaking	23 (2.1%)	5 (1.0%)	9 (4.3%)	
Off road	244 (21.9%)	52 (10.2%)	23 (11.0%)	
Other/unknown	261 (23.5%)	83 (16.2%)	53 (25.4%)	
Damage location				<0.001
Front	535 (48.1%)	190 (37.1%)	99 (47.4%)	
Front/rear	18 (1.6%)	19 (3.7%)	6 (2.9%)	
Front/side	78 (7.0%)	27 (5.3%)	16 (7.7%)	
Rear	70 (6.3%)	100 (19.5%)	20 (9.6%)	
Rear/side	13 (1.2%)	<5	<5	
Side	125 (11.2%)	73 (14.3%)	18 (8.6%)	
Tires/undercarriage/ windshield/roof	12 (1.1%)	<5	0 (0.0%)	
Whole vehicle	141 (12.7%)	41 (8.0%)	25 (12.0%)	
None	53 (4.8%)	21 (4.1%)	7 (3.3%)	
Other/unknown	67 (6.0%)	37 (7.2%)	16 (7.7%)	

Item S16: Responsibility score components among responsible and non-responsible drivers (exposure: antipsychotic adherence) (continued)

Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Task Involved				
Avoidance manoeuvre listed as contributory factor	11 (1.0%)	12 (2.3%)	0 (0.0%)	0.055
Pre-collision action				<0.001
Straight	607 (54.6%)	348 (68.0%)	120 (57.4%)	
Backing	71 (6.4%)	<5	12 (5.7%)	
Turning	239 (21.5%)	59 (11.5%)	47 (22.5%)	
Changing lanes/merging	29 (2.6%)	<5	<5	
Loss of control	32 (2.9%)	10 (2.0%)	<5	
Stopped/parked	25 (2.2%)	54 (10.5%)	<5	
Other/unknown	109 (9.8%)	34 (6.6%)	26 (12.4%)	

Legend. Responsibility score components for the 1833 crash-involved drivers in the adherence cohort (schizophrenia diagnosis date ≥30 days prior to the crash; ≥1 antipsychotic prescription fill after the diagnosis date; ≥1 antipsychotic prescription fill in the year prior to crash). P-values compare responsible drivers to non-responsible drivers; drivers with indeterminate responsibility are only included here for descriptive purposes.

Item S17: Other crash characteristics among responsible and non-responsible drivers (exposure: antipsychotic adherence)

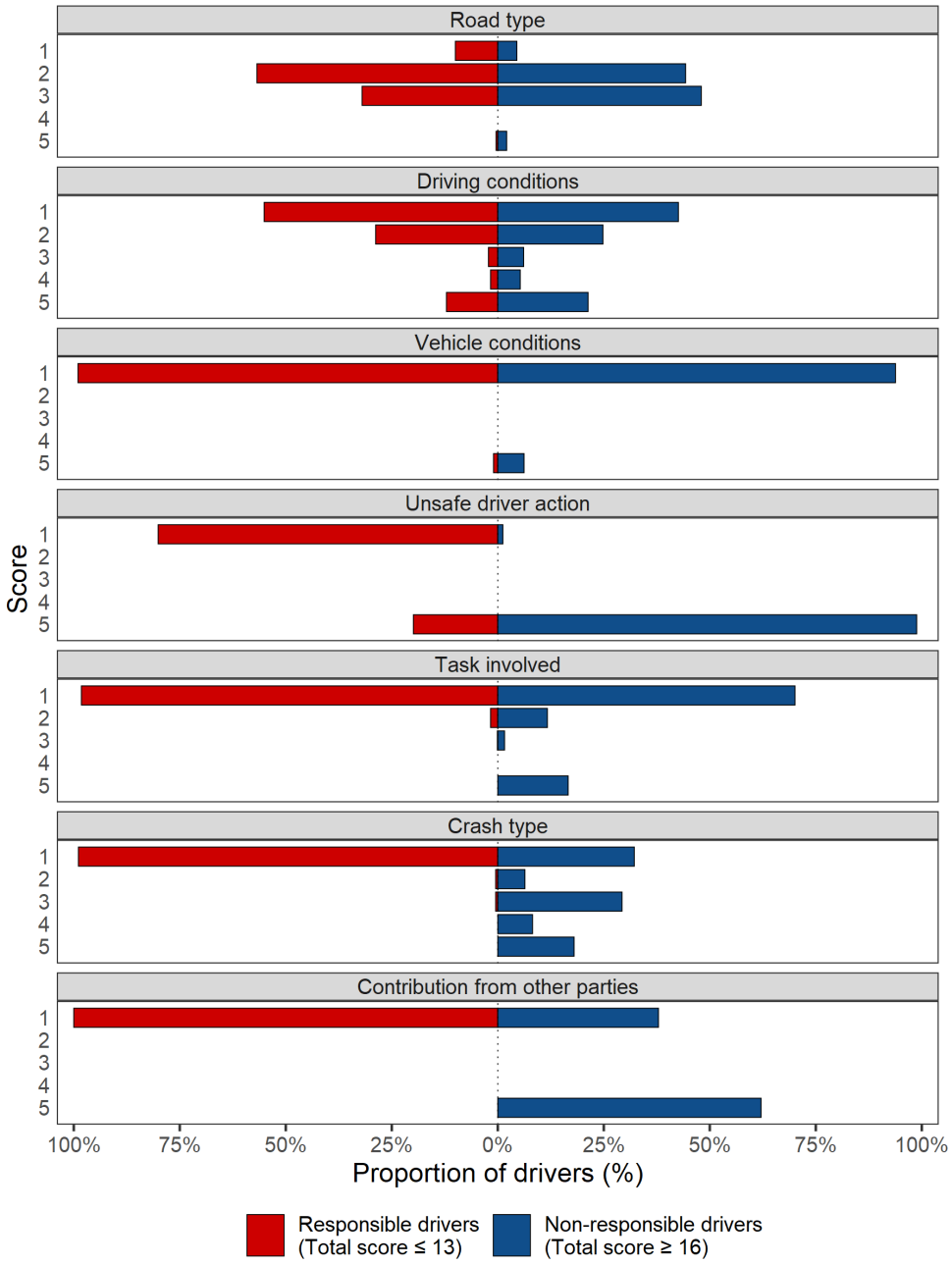
Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Human conditions				
. Alcohol	124 (11.2%)	30 (5.9%)	15 (7.2%)	<0.001
. Medications	32 (2.9%)	<5	5 (2.4%)	<0.001
. Drugs	55 (4.9%)	8 (1.6%)	12 (5.7%)	0.002
. Illness/fatigue	42 (3.8%)	8 (1.6%)	9 (4.3%)	0.025
. Distracted/inattentive	435 (39.1%)	91 (17.8%)	44 (21.1%)	<0.001
. Pre-existing physical disability	7 (0.6%)	<5	<5	0.983
Breath alcohol positive				0.996
. Yes	19 (1.7%)	8 (1.6%)	0 (0.0%)	
. No evidence	1093 (98.3%)	504 (98.4%)	209 (100%)	
Impaired by alcohol or drugs				<0.001
. Yes	176 (15.8%)	39 (7.6%)	29 (13.9%)	
. No evidence	936 (84.2%)	473 (92.4%)	180 (86.1%)	
Crash severity				0.008
. Casualty (fatal or injury)	525 (47.2%)	279 (54.5%)	101 (48.3%)	
. Property damage	587 (52.8%)	233 (45.5%)	108 (51.7%)	
Road location				0.017
. Rural road	55 (4.9%)	10 (2.0%)	6 (2.9%)	
. Provincial highway	299 (26.9%)	140 (27.3%)	40 (19.1%)	
. City street	758 (68.2%)	362 (70.7%)	163 (78.0%)	
Speed zone				<0.001
. <50 km/h	87 (7.8%)	23 (4.5%)	11 (5.3%)	
. 50 km/h	584 (52.5%)	314 (61.3%)	119 (56.9%)	
. 60-70 km/h	144 (12.9%)	55 (10.7%)	23 (11.0%)	
. ≥80 km/h	166 (14.9%)	85 (16.6%)	27 (12.9%)	
. Other/unknown	131 (11.8%)	35 (6.8%)	29 (13.9%)	

Item S17: Other crash characteristics among responsible and non-responsible drivers (exposure: antipsychotic adherence) (continued)

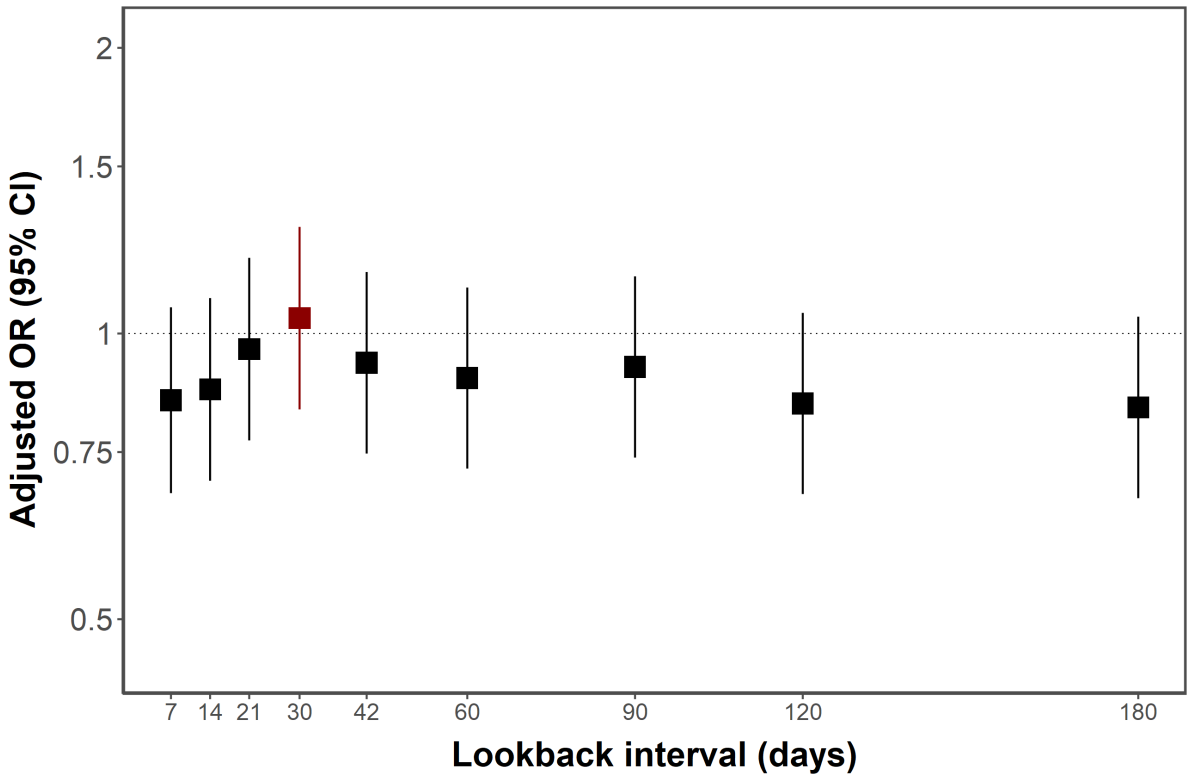
Characteristic	Drivers deemed responsible for crash, count (%) n = 1112	Drivers deemed non-responsible for crash, count (%) n = 512	Drivers with indeterminate responsibility, count (%) n = 209	p-values, responsible vs non-responsible
Vehicle damage severity				<0.001
. Light	233 (21%)	145 (28.3%)	54 (25.8%)	
. Moderate	273 (24.6%)	142 (27.7%)	56 (26.8%)	
. Severe	314 (28.2%)	130 (25.4%)	50 (23.9%)	
. Demolished	148 (13.3%)	35 (6.8%)	26 (12.4%)	
. None	53 (4.8%)	21 (4.1%)	7 (3.3%)	
. Other/unknown	91 (8.2%)	39 (7.6%)	16 (7.7%)	
Crash year				0.121
. 2000-2004	151 (13.6%)	51 (10.0%)	17 (8.1%)	
. 2005-2010	404 (36.3%)	195 (38.1%)	68 (32.5%)	
. 2011-2016	557 (50.1%)	266 (52.0%)	124 (59.3%)	
Crash season				<0.001
. Winter (Dec-Feb)	274 (24.6%)	154 (30.1%)	50 (23.9%)	
. Spring (Mar-May)	263 (23.7%)	108 (21.1%)	50 (23.9%)	
. Summer (Jun-Aug)	305 (27.4%)	105 (20.5%)	63 (30.1%)	
. Fall (Sep-Nov)	270 (24.3%)	145 (28.3%)	46 (22.0%)	
Day of week				0.210
. Weekday (Mon-Thurs)	635 (57.1%)	310 (60.5%)	124 (59.3%)	
. Weekend (Fri-Sun)	477 (42.9%)	202 (39.5%)	85 (40.7%)	
Time of day				0.252
. Morning (6:01-12:00)	273 (24.6%)	112 (21.9%)	45 (21.5%)	
. Afternoon (12:01-18:00)	438 (39.4%)	232 (45.3%)	90 (43.1%)	
. Evening (18:01-24:00)	281 (25.3%)	114 (22.3%)	59 (28.2%)	
. Night (0:01-6:00)	93 (8.4%)	42 (8.2%)	15 (7.2%)	
. Other/unknown	27 (2.4%)	12 (2.3%)	0 (0.0%)	

Legend. P-values compare responsible drivers to non-responsible drivers. Drivers with indeterminate responsibility were not included in analyses and are presented here for descriptive purposes only.

Item S18: Mirrored histogram of responsibility score components among responsible and non-responsible drivers (exposure: antipsychotic adherence)



Item S19: Sensitivity analysis of alternate MPR calculation lookback intervals



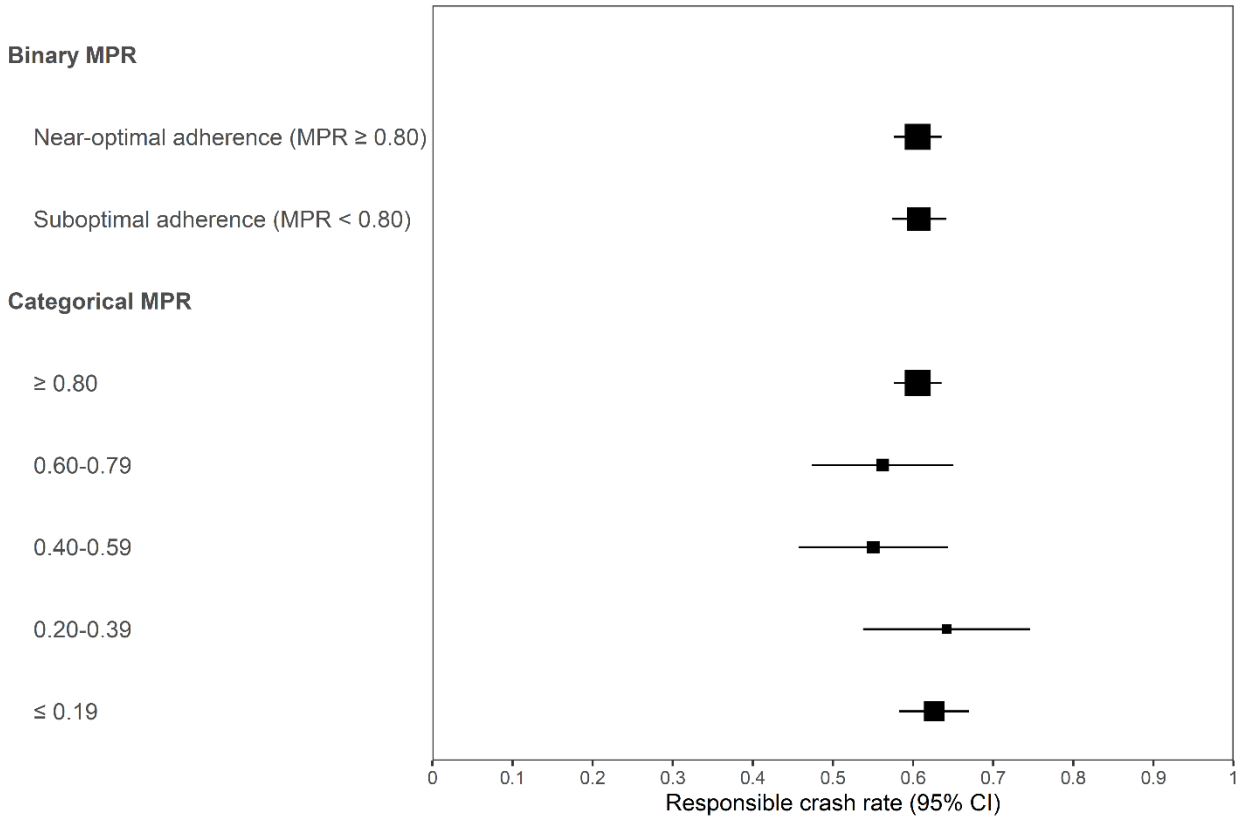
Legend. Forest plot of results using alternate medication possession ratio (MPR) lookback intervals. X-axis depicts the exposure lookback interval used in each analysis, measured in days; Y-axis, the adjusted odds ratio; squares, the adjusted odds ratio, with square size reflecting the inverse of the standard error; vertical lines, the 95% confidence interval. The main analysis is depicted in red. Overall, study results were robust to the duration of the exposure lookback interval.

Item S20: Comparison of crash rates

Value	Drivers with schizophrenia	Controls
Number of unique drivers	23,691	4,694,300
Number of unique drivers involved in a crash	2365	745,940
Number of unique driver-crash combinations	2896	932,631
Number of unique driver-crash combinations deemed responsible	1689	432,430
Absolute crash rate per driver	**0.122**	**0.199**
Absolute crash rate per driver-year	**0.009**	**0.015**
Responsible crash rate	**0.583**	**0.464**

Legend. Crash rate per driver is calculated by dividing the number of driver-crash combinations by the number of drivers. Crash rate per driver-year is calculated by dividing the number of driver-crash combinations by the number of driver-years of exposure (driver years are calculated by summing the total number of years each driver held an active license in BC during our study interval). Responsible crash rate is calculated by dividing the *number of responsible driver-crash combinations* by the *total number of driver-crash combinations* (note that results presented here include driver-crash combinations with indeterminate crash responsibility in the denominator and consequently and intentionally differ slightly from the responsible crash rates reported in the manuscript text). As expected, absolute crash rates are higher for controls but responsible crash rates are higher for individuals with schizophrenia, reflecting reduced road exposure but higher crash risk while driving among individuals with schizophrenia. This finding highlights a major advantage of using responsibility analysis to evaluate whether schizophrenia is a risk factor for crash.

Item S21: Responsible crash rates by strata of antipsychotic adherence



Legend. Forest plot with x-axis depicting the responsible crash rate; Y-axis, medication possession ratio (MPR) categories; black squares, point estimates, with size reflecting the inverse of the standard error; and horizontal lines, 95% confidence intervals. The proportion of crash-involved drivers deemed responsible for their crash was relatively constant across different levels of adherence, supporting the study conclusion that there is no association between antipsychotic adherence and driver responsibility for crash.

Item S22: Assessment of correlation

Variable	Adjusted OR (95%CI)	Adjusted OR (robust 95%CI)	Ratio of CI width to robust CI width
Intercept	0.98 (0.95, 1.00)	0.98 (0.95, 1.00)	1.001
Schizophrenia diagnosis prior to crash (exposure of interest)	**1.67 (1.53, 1.82)**	**1.67 (1.53, 1.82)**	**1.019**
Crash-involved driver aged ≤20 years (referent: 21-45 years)	1.43 (1.40, 1.46)	1.43 (1.40, 1.46)	1.001
Crash-involved driver aged 45-64 years (referent: 21-45 years)	1.02 (1.00, 1.03)	1.02 (1.00, 1.03)	0.999
Crash driver aged ≥65 years (referent: 21-45 years)	2.04 (2.00, 2.08)	2.04 (2.00, 2.08)	1.007
Male sex (referent: female)	1.04 (1.03, 1.05)	1.04 (1.03, 1.05)	1.000
Unknown sex (referent: female)	1.46 (0.96, 2.23)	1.46 (0.96, 2.22)	0.997
Ordinal variable denoting residential neighbourhood income quintile (1 = lowest income, 5 = highest income)	0.98 (0.97, 0.98)	0.98 (0.97, 0.98)	0.999
Residential rurality is "popCentreSmall" (referent: "popCentreMed")	1.02 (1.00, 1.03)	1.02 (1.00, 1.03)	1.001
Residential rurality is "ruralArea" (referent: "popCentreMed")	1.05 (1.04, 1.07)	1.05 (1.04, 1.07)	1.000
Residential rurality is "Missing" (referent: "popCentreMed")	1.10 (0.99, 1.23)	1.10 (0.99, 1.23)	1.005
Fraser Health Authority (referent: Vancouver Coastal Health (VCH))	0.97 (0.95, 0.98)	0.97 (0.95, 0.98)	1.002
Interior Health Authority (referent: VCH)	0.96 (0.94, 0.98)	0.96 (0.94, 0.98)	1.000
Vancouver Island Health Authority (referent: VCH)	0.97 (0.95, 0.98)	0.97 (0.95, 0.98)	1.001
Northern Health Authority (referent: VCH)	0.81 (0.80, 0.83)	0.81 (0.80, 0.83)	0.997
Missing Health Authority (referent: VCH)	0.93 (0.84, 1.03)	0.93 (0.83, 1.03)	1.006
Learner license type (referent: Full license)	2.39 (2.28, 2.50)	2.39 (2.28, 2.50)	1.007
Novice license type (referent: Full license)	1.44 (1.42, 1.47)	1.44 (1.42, 1.47)	1.001
No license at time of crash (referent: Full license)	2.74 (2.52, 2.99)	2.74 (2.52, 2.99)	0.996
Number of years with Full license	0.99 (0.99, 0.99)	0.99 (0.99, 0.99)	1.003
Number of police-attended crashes in prior 3 years	1.09 (1.08, 1.10)	1.09 (1.08, 1.10)	1.006
Number of non-impairment related contraventions in prior 3 years	1.08 (1.08, 1.09)	1.08 (1.08, 1.09)	1.006
Number of impairment related contraventions in prior 3 years	1.23 (1.22, 1.25)	1.23 (1.21, 1.25)	1.032
Crash resulted in severe injury (referent: Property damage only)	0.94 (0.93, 0.95)	0.94 (0.93, 0.95)	1.000
Crash resulted in fatality (referent: Property damage only)	1.19 (1.12, 1.25)	1.19 (1.12, 1.25)	0.984
Crash occurred at night	0.88 (0.87, 0.89)	0.88 (0.87, 0.89)	0.999
Crash occurred on provincial highway (referent: city streets)	0.87 (0.86, 0.88)	0.87 (0.86, 0.88)	1.000
Crash occurred on rural road (referent: city streets)	1.07 (1.05, 1.10)	1.07 (1.05, 1.10)	0.992
Any documented impairment by alcohol or drugs at time of crash	5.37 (5.24, 5.51)	5.37 (5.24, 5.51)	1.010
Hospitalizations for alcohol or other drug use in prior 3 years	1.02 (1.02, 1.02)	1.02 (1.02, 1.02)	1.080
Charlson comorbidity index ≥2	1.02 (1.01, 1.03)	1.02 (1.01, 1.03)	1.000
Years elapsed between first year of study interval and year of the crash	0.99 (0.99, 0.99)	0.99 (0.99, 0.99)	0.999
Crash occurred in the spring (Mar - May; referent: Winter)	1.26 (1.24, 1.27)	1.26 (1.24, 1.27)	1.000
Crash occurred in the summer (Jun - Aug; referent: Winter)	1.37 (1.35, 1.39)	1.37 (1.35, 1.39)	1.000
Crash occurred in the fall (Sep - Dec; referent: Winter)	1.10 (1.08, 1.11)	1.10 (1.08, 1.11)	1.001

Legend. When crashes involved multiple drivers, all crash-involved drivers could contribute crash data to the analysis. Similarly, individuals involved in more than one police-attended crash could contribute all eligible crashes to the analysis. We decided *a priori* to treat each driver-crash combination as an independent observation, reasoning that:

> 1) Within any given crash, the 'outcome' for each driver ('responsible' vs 'non-responsible') is largely independent of the outcomes for other drivers involved in the same crash because a) each driver is scored independently; b) the crash responsibility scoring tool does not constrain one driver to be responsible and the others to be non-responsible; and c) the actions of the index driver, if unsafe, take precedence over most mitigating factors in the tool (including contributions from other parties).
>
> 2) Exposures (e.g., schizophrenia) for each driver are entirely independent.

We evaluated for evidence of correlation within crashes and individuals to evaluate whether this approach was reasonable. We compared the width of the 95% confidence interval for our model covariates to the width of a 95% confidence interval calculated using robust standard errors. We found that these two values were very similar, suggesting that significant correlation was not present, conditional on model covariates.

Item S23: Sample sizes from prior epidemiological studies on schizophrenia and crash

Study	Exposed group	Control group	Key findings
Waller (1965)[26,*]	231 drivers with mental illness ("mostly schizophrenia & manic-depressive psychoses") currently	926 drivers randomly selected from license renewal applicants in California in June 1963	This retrospective cohort study enrolled 292 individuals with mental illness who were currently under review by the California Department of Motor Vehicles (the "vast majority" because of a periodic medical report). Three-year crash and violation history was obtained. Individuals were asked to estimate their annual mileage. After exclusion of individuals with license revocation or no license in the prior 2 years, 231 drivers with mental illness remained. Drivers with mental illness had 2.1-fold more crashes (15.3 vs 7.2 per million miles; $p<0.001$) and 1.8-fold more violations (5.3 vs 3.0 per million miles; $p<0.001$) than expected based on age and prior license renewal duration (which was based on driving record).
Crancer (1969)[27]	97 individuals hospitalized for "schizophrenic disorders" at King County Hospital in 1964	687,228 drivers "of the same age and sex distribution" as the exposed group	This retrospective cohort study examined crashes and violations occurring between 1961 and 1967 among King County residents with a valid Washington state driver license. Individuals with schizophrenic disorders had a crash rate almost identical to controls (0.33 vs 0.33 crashes per person; 8.2 vs 7.7 injury crashes per 100 persons) but a violation rate about 1.6-fold higher than among controls (0.71 vs 0.44 violations per person in first half of study interval; 0.88 vs 0.53 violations per person in the second half of study interval).
Eelkema (1970)[28,*]	71 individuals with psychosis discharged from the North Dakota State Hospital in 1960 (from among 238 individuals with mental illness)	290 individuals from the general population of drivers, matched by age, sex, and county of residence to exposed	This retrospective cohort study compared driving records of exposed and control groups after stratifying by diagnosis and sex. In the years prior to hospitalization (1949-1960), individuals with psychosis had more crashes (males, 10.4 vs 7.73 crashes per hundred driver-years, IRR 1.35; females, 9.26 vs 4.79 crashes per hundred driver-years, IRR 1.94) and more violations (males, 12.8 vs 10.2 crashes per hundred driver-years, IRR 1.25; females, 3.71 vs 2.93 crashes per hundred driver-years, IRR 1.27) than controls. In the years after hospitalization (1961-1965), individuals with psychosis had fewer crashes (males, 9.15 vs 10.3 crashes per hundred driver-years, IRR 0.89; females, 3.20 vs 9.18 crashes per hundred driver-years, IRR 0.35); males had more and females had fewer violations (males, 28.0 vs 10.9 crashes per hundred driver-years, IRR 2.57; females, 4.26 vs 5.24 crashes per hundred driver-years, IRR 0.81) than controls.

Item S23: Sample sizes from prior epidemiological studies on schizophrenia and crash (continued)

Study	Exposed group	Control group	Key findings
Sacher (1978)[29]	78 individuals with a clinically confirmed diagnosis of schizophrenia who also reported driving during the study interval	100 age- and sex-matched controls drawn from the driver's register in the Canton of Zurich.	This retrospective cohort study examined medical records from the Forensic Medical Institute in Zurich, police reports, and selected criminal records for exposed and control individuals between 1970 and 1975. Among individuals who reported driving during the study interval, those with schizophrenia had a crash rate 2.7-fold higher (0.030 vs 0.082 crashes per person-year; p<0.001) and a violation rate 1.8-fold higher (0.25 vs 0.13 violations per person-year; p<0.001) compared to controls. Among the 34 individuals with schizophrenia and reported mileage (and their age- and sex-matched controls), the crash rate was 3.1-fold higher (4.8 vs 1.5 crashes per million person-kilometers; p=0.039) and the violation rate was 2.3-fold higher (14.4 vs 6.1 per million person-kilometers; 0=0.003) than controls.
Armstrong (1980)[30]	12 individuals with schizophrenia who were admitted to a private psychiatric hospital (drawn from a larger group of 100 with mental illness)	100 individuals receiving treatment "for a variety of physical complaints" in a private general hospital; "matched for age, sex and social background"	This retrospective cohort study interviewed individuals in Australia who were "regular vehicle drivers" about driving distances and crashes in the prior 6 months. Individuals with schizophrenia had a crash risk without adjustment for road exposure was about 3-fold higher than among controls, but this difference was not statistically significant (0.33 vs 0.11 crashes per person; relative risk, 2.8; 95%CI, 1.1-7.4; p=0.06).
Edlund (1989)[31]	70 outpatients diagnosed with schizophrenia who also reported driving a motor vehicle	122 age-matched controls who reported driving a motor vehicle, recruited from among medical centre staff	This retrospective cohort study administered a questionnaire to exposed individuals and controls about possession of a driver license, approximate miles driven (0-100, 100-5000, 5000-10,000, >10,000 miles), and crashes requiring professional medical attention by a physician in the prior year. Individuals with schizophrenia had a crash risk similar to controls (10.0% vs 9%; p>0.05), but they reported driving few miles (40% vs 98% drive >100 miles; p<0.00001). Investigators concluded that per-mile crash risk might be substantially higher among individuals with schizophrenia.
Total	**257***	978,476	

* Studies by Waller and Eelkema were excluded from the tally of individuals with schizophrenia in studies of schizophrenia and driving because their exposures included but were not specific to schizophrenia.

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