

The PSY-SIM Model: Using Real-World Data to Inform Health Care Policy for Individuals With Chronic Psychotic Disorders

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Background and Hypothesis: Few microsimulation models have been developed for chronic psychotic disorders, severe and disabling mental disorders associated with poor medical and psychiatric outcomes, and high costs of care. The objective of this work was to develop a microsimulation model for individuals with chronic psychotic disorders and to use the model to examine the impact of a smoking cessation initiative on patient outcomes. **Study Design:** Using health records and survey data from Ontario, Canada, the PSY-SIM model was developed to simulate health and cost outcomes of individuals with chronic psychotic disorders. The model was then used to examine the impact of the Smoking Treatment for Ontario Patients (STOP) program from Ontario on the development of chronic conditions, life expectancy, quality of life, and lifetime health care costs. **Study Results:** Individuals with chronic psychotic disorders had a lifetime risk of 63% for congestive heart failure and roughly 50% for respiratory disease, cancer and diabetes, and a life expectancy of 76 years. The model suggests the STOP program can reduce morbidity and lead to survival and quality of life gains with modest increases in health care costs. At a long-term quit rate of 4.4%, the incremental cost-effectiveness ratio of the STOP program was \$41,936/QALY compared with status quo. **Conclusions:** Smoking cessation initiatives among individuals with chronic psychotic disorders can be cost-effective. These findings will be relevant for decision-makers and clinicians looking to improving health outcomes among this patient population.

Key words: chronic psychotic disorders/microsimulation/psychosis/schizophrenia/smoking cessation

Background

In a time of limited health care resources, it is important to make informed decisions around resource allocation. To do so, decision-makers require real-world evidence to make sound investments. Microsimulation models are computer-based models that can simulate the behavior of micro-entities (eg, individuals) and are commonly employed to estimate long-term outcomes in populations and the potential behavioral and economic effects of interventions and/or health policies.¹ Therefore, these models can be helpful tools for surveillance purposes and to guide decision-making, particularly in cases where evidence is absent. Furthermore, microsimulation models represent an attractive tool to examine potential behavioral and economic effects of interventions/policies before they are rolled out, thus avoiding the potentially high cost of implementing ineffective solutions. Microsimulation models have many advantages compared with other types of models. For example, these models represent hypothetical patients as unique individuals as opposed to average members of a representative cohort (cohort modeling) and can accommodate patient heterogeneity and interdependent health states, allowing analyses within subpopulations of interest and more accurate representation of the natural history of a disease.² Additionally, from a technical perspective, microsimulation models allow for a more seamless integration of information from different data sources and can be more easily scaled up to include additional baseline characteristics or outcomes, once additional information becomes available. Although microsimulation techniques have been used elsewhere to examine schizophrenia/psychosis, unfortunately, there

are few all-purpose, stand-alone microsimulation models focused on individuals with mental disorders, particularly chronic psychotic disorders.²

Chronic psychotic disorders are severe and disabling mental disorders, which, although low in prevalence (0.5%–1%), are associated with poor psychiatric and medical outcomes, including elevated risk of mortality.^{3–8} Furthermore, chronic psychotic disorders are among the costliest mental disorders to treat, with lifetime costs exceeding those of many other chronic conditions.⁹ Despite high costs of care, quality of care and outcomes in this population remain poor, further stressing the need to make timely and cost-effective decisions based on real-world data to improve patient outcomes. Moreover, individuals with psychosis are more likely to engage in heavy smoking and have severe nicotine dependence.¹⁰ The prevalence of smoking among individuals with psychosis ranges from 44% to 85%,¹¹ which is significantly higher than among the general population (19%).¹² Furthermore, one-third of deaths among individuals with severe mental illness, such as psychosis, can be attributed to smoking.¹³ However, compared with the general population, individuals with psychosis are less likely to quit successfully without intervention^{14,15} and require tailored interventions and strategies to optimize smoking cessation.¹⁶ Additionally, strategies to ameliorate the risk of smoking among this patient population are lacking.¹⁷ Microsimulation models can be used to examine the impact of smoking cessation on the development of chronic physical conditions, quality of life, life expectancy, and health care costs.

The objectives of this paper are 2-fold: (1) to describe an all-purpose microsimulation model, the PSY-SIM model, which can be used to simulate lifetime outcomes (eg, life expectancy, long-term risk of comorbidities, and health care costs) of individuals with chronic psychotic disorders and help guide/inform health policy, and (2) to present an application of how the model can be used to understand the impact of smoking cessation initiatives on the development of chronic physical conditions, life expectancy, quality of life, and health care costs over the lifetime and to determine the cost-effectiveness of a smoking cessation program.

Methods

The PSY-SIM model comprises 4 basic components: (1) data infrastructure, (2) behavioral assumptions and parameters, (3) statistical methods, and (4) model output. Other models, such as the Future Americans Model,¹⁸ have been developed using a similar structure.

Data Infrastructure

The core data infrastructure of the PSY-SIM model includes administrative and survey data. Real-world

administrative health records were obtained through ICES, an independent, nonprofit research institute located in Toronto, Ontario. The administrative data were then linked to Statistics Canada's Canadian Community Health Survey, a cross-sectional survey, which collects information on health status, health determinants, and health care utilization for the Canadian population.

Administrative Health Records The data repository at ICES includes patient-level linkable, longitudinal health records on (most) publicly funded health care services for Ontario residents eligible for public health insurance. Data on institution-based care are captured in the Discharge Abstract Database (all medical inpatient hospitalizations, psychiatric inpatient hospitalizations for children and youth under the age of 16, and psychiatric inpatient hospitalizations for adults in nonpsychiatric-designated beds), the Ontario Mental Health Reporting System (all psychiatric inpatient hospitalizations for individuals over the age of 15 in psychiatric-designated beds), the Continuing Care Reporting System (continuing and long-term care), and the National Rehabilitation Reporting System (rehabilitation); data on ambulatory care (eg, emergency department visits) are recorded in the National Ambulatory Care Reporting System. The Ontario Health Insurance Plan claims database captures data on physician visits and laboratory and diagnostic tests. The Ontario Drug Benefit Program database includes information on all outpatient prescription drugs dispensed to individuals covered under the public provincial drug plan (ie, individuals over the age of 65 years old, individuals living in a long-term care home, a home for special care or a Community Home for Opportunity, receiving professional home and community care services, enrolled in the Trillium Drug Program, or on social assistance). The Home Care Database records all visits provided by home care professionals. A full description of each database can be found elsewhere.¹⁹ The use of these data was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board.

To identify individuals diagnosed with chronic psychotic disorders in the administrative data, a validated algorithm was used, where all patients hospitalized with a diagnosis of schizophrenia, schizoaffective disorder, and psychosis not otherwise specified (ICD-10 codes F20 (excluding F20.4), F25, F29; DSM-IV and DSM-V codes 295.x, 298.x) since 1988, and/or 3 physician visits for schizophrenia-related care within a 3-year window since 1991 were selected.²⁰ Patients with a diagnosis of psychotic disorder not otherwise specified were included as evidence suggests these patients are ultimately diagnosed with schizophrenia or schizoaffective disorder.²¹ Based on data availability, the simulation stock sample (ie, the patient sample used in the model for simulation) included all individuals with chronic psychotic disorders living

in Ontario and eligible for public health insurance from January 1, 1996 to December 31, 2019 (looking back till 1988) and followed until December 31, 2020.

The Registered Persons Database, a population-based registry, was used to obtain population and demographic data, such as date of birth, sex, date of death (where applicable), eligibility for health care insurance and status changes, and postal code of residence, which in turn was used to obtain data on neighborhood-level income quintile and rurality of residence. The presence of the most common chronic physical conditions among individuals with chronic psychotic disorders^{4,5,9}—congestive heart failure, respiratory diseases (asthma, COPD), diabetes, and/or cancer—were determined through either disease registries (eg, Ontario Cancer Registry) or validated algorithms applied to the administrative data^{22–27}; see definitions of algorithms and prevalence of chronic physical conditions in [supplementary tables 1 and 2](#), respectively. Data on quality of life, and respective quality-adjusted life years, for schizophrenia, chronic physical conditions, and smokers and nonsmokers were obtained from the literature.^{28–30} Health care costs incurred by patients and borne by the public third-party payer (ie, the Ministries of Health and Long-term Care) were estimated using a cost algorithm,³¹ which accounts for over 90% of all government-paid costs associated with health care services and includes costs of hospitalizations (both acute and psychiatric), ED visits and other ambulatory care, outpatient clinic visits, physician visits and outpatient care, outpatient prescription drugs (covered under the public provincial drug plan), inpatient rehabilitation, complex continuing care, long-term care, and home care. Details on the costing methodology can be found elsewhere.¹⁹

Statistics Canada's Canadian Community Health Survey. The Canadian Community Health Survey covers the Canadian population 12 years of age and over living in Canada.³² Excluded from the survey's coverage are persons living on reserves and other Aboriginal settlements, full-time members of the Canadian Forces, institutionalized persons, and persons living in the Quebec health regions of Région du Nunavik and Région des Terres-Criées-de-la-Baie-James. Altogether, these exclusions represent less than 3% of the target population. The Canadian Community Health Survey provides data on health, health conditions, health behaviors and lifestyle, social conditions, and prevention and detection of disease.

The simulation stock sample, along with relevant health care utilization and cost data, were linked to the 2001, 2003, 2005, 2007, 2009, 2011, 2012, and 2013 cycles of the Ontario component of the Canadian Community Health Survey to obtain information on health behaviors (there were a few cases where an individual was in the survey data more than once; in these cases, the most recent survey response was used). These cycles, except

2001, asked questions on (self-reported) smoking status and number of years since smoking cessation, which were used to populate the health behaviors component of the model. Based on the survey data, individual smoking status included never smoked, former smoker, current smoker (ie, daily and occasional smokers), and missing smoking status. The Canadian Community Health Survey was also used to determine immigrant status (immigrant vs nonimmigrant).

Linked Dataset All datasets were linked using unique encoded identifiers and analyzed at ICES. Both the unlinked and linked samples looked similar, except for immigrant status, geography, and death, where the linked sample included more immigrants, more individuals with rural residence, and less decedents. [Supplementary table 3](#) provides the full sample obtained from the administrative data and a comparison between the unlinked and linked samples, where a standardized mean difference greater than 0.10 is considered large.³³

Behavioral Assumptions and Parameters

Several assumptions were required to build the model. For example, it was assumed that individuals with chronic psychotic disorders could develop chronic physical conditions at any point between birth and death (and each condition is independent of one another). Furthermore, while the presence of chronic psychotic disorders can lead to the onset of chronic physical conditions via multiple pathways, including modified health behaviors (eg, increased smoking), it was assumed that the reverse could not occur. Information on smoking status was obtained from the Canadian Community Health Survey, which is cross-sectional and thus does not allow examining individual changes in smoking status over time. This required assuming that once an individual was classified as a smoker, the individual remained a smoker, unless exposed to a smoking cessation intervention. Although smoking behavior can increase the risk of developing any of the chronic physical conditions in the model and, in turn, increase the risk of death, background mortality was not differentiated by smoking status as it was assumed that the effect of smoking on other causes of death was small. Given the lack of utility data for individuals with psychosis, some comorbidity-related utilities were obtained from non-psychosis samples^{29,30}; see [Supplementary table 4](#) for the input parameters used in the PSY-SIM, such as the utility values for psychosis states and chronic physical conditions. For individuals with multiple comorbidities, the compounding effect of these physical health conditions on quality of life was accounted for using the multiplicative method, which assigns a relative decrement for each combined condition.³⁴ Other behavioral assumptions and parameters, namely those related to

anticipated patient behavior due to an intervention, such as smoking cessation, were determined from existing evidence¹⁰⁻¹⁷ and expert opinion.

PSY-SIM Model Schematic The PSY-SIM model was built with 5 states described by the following events: (1) *diagnosis via community*, which serves as 1 point of entry into the model for individuals diagnosed in the community; (2) *diagnosis via hospitalization*, which serves as a second point of entry into the model for individuals diagnosed in hospital; (3) *stable psychotic episode*, defined as a stable state, including individuals in recovery post-hospitalization for a severe psychotic episode; (4) *severe psychotic episode* defined as a relapse state for individuals hospitalized post-stable state; and (5) *death*, which serves as the point of exit from the model and thus an absorbing state. **Figure 1** provides a depiction of the model, which was reviewed and validated by a psychiatrist (PK). See **supplementary table 5** for more details on model transitions. In parallel to the above states, the model also considers the *development of chronic physical conditions* (described previously) over an individual's lifetime. It is assumed that individuals have these conditions

for life. Finally, the PSY-SIM incorporates the role of psychosis-related *risk factors/health behaviors* informed by the literature³⁻⁹: sex (female, male), age, immigrant status (nonimmigrant, immigrant), household income at the neighborhood level (expressed as quintiles), rurality of residence, and smoking status.

Statistical Models

Estimation of Transition Models Multistate parametric regression modeling was used to estimate transition probabilities between health outcomes and states.³⁵ Multistate models based on survival analysis were used to accommodate the transition of individuals across multiple discrete states over time, such as from stable psychotic episode to severe psychotic episode and vice-versa, from stable and severe psychotic episodes to death, and to model the probability of developing chronic physical conditions at any point over the patient's lifetime. Risk factors were included as covariates in the transition models and the chronic physical conditions development models. For the death transition model, the total number of chronic

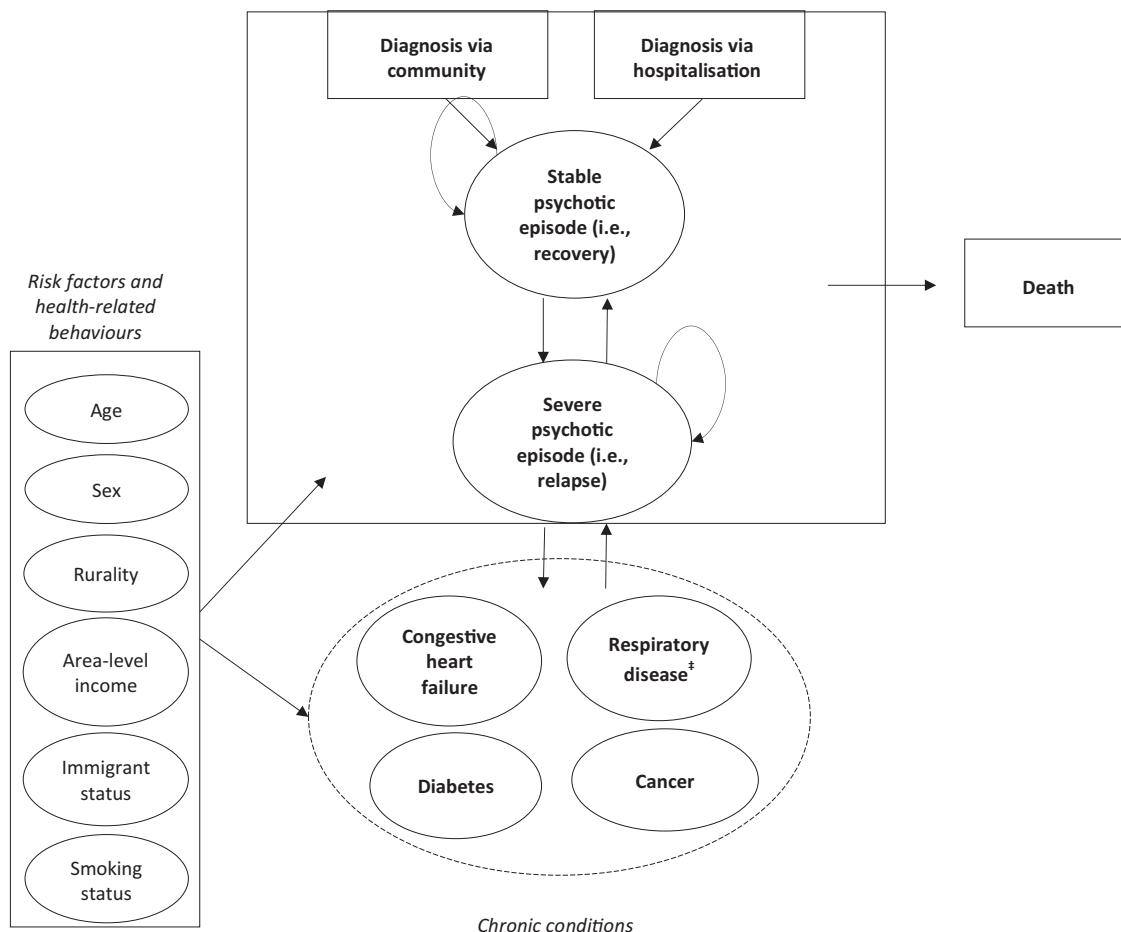


Fig. 1. PSY-SIM model schematic. *Note:* ‡ respiratory disease includes asthma and chronic obstructive pulmonary disease.

physical conditions (defined as a multimorbidity indicator, expressed as dummy variables for 1, 2, 3, and 4 chronic conditions) was included as a time-varying covariate in addition to the risk factors. Each time-based transition was modeled using 6 different distributions (ie, Weibull, exponential, log-normal, log-logistic, gamma, Gompertz) in addition to a more flexible Royston-Parmar spline model with 3 internal knots.³⁶ See [supplementary table 6](#) for the transition equations. Models with the best extrapolation and fit for each transition were selected using fit statistics (eg, Akaike Information Criterion and Bayesian Information Criterion), visual assessment of survival curves, and expert opinion. For cases where the chronic physical condition was present at baseline, the probability of having this condition at the time of diagnosis of a chronic psychotic disorder was modeled using a generalized linear model with a binomial distribution. Monthly health care costs (in 2020 Canadian dollars) in all 5 states were modeled using a generalized linear model using a gamma distribution and included sex and age as covariates.

Simulation and Prediction Simulation and prediction of individual health and economic outcomes were undertaken using 2 parallel and interconnected discrete-time microsimulation models, one for chronic psychotic disorders and another for chronic physical conditions. Using the multistate parametric transition models, the microsimulations predict an individual's disease progression based on their risk factors. The 2 microsimulation models were connected by the presence of chronic physical conditions as a covariate for transitions between states within chronic psychotic disorders.

The model was run for a lifetime horizon of 85 years in monthly cycles, with a maximum age of 110. Additional probabilities of death associated with long-term survival not captured by the multistate transition models were added using sex-specific 2019 Canadian life tables.³⁷ In accordance with Canadian guidelines in decision modeling, costs were discounted at an annual rate of 1.5% from diagnosis onwards.³⁸ Probabilistic analysis, an iterative approach used in decision modeling to propagate the uncertainty around model input parameters onto the final model outcomes, was used to incorporate uncertainty around the cost and multistate regressions parameters and to quantify the level of confidence in the output. For each regression model, parameters were generated for each probabilistic analysis run by sampling from the regression model coefficients' multivariate normal distribution, with separate distributions for each regression model. A synthetic cohort of newly diagnosed individuals was then generated and fed into the microsimulation model. The risk factors and point of entry of individuals in the stock sample were modeled using multiple chained regression equations.

Data analyses were done in SAS version 9.4, while modeling was done in R version 4.2.0.

Validation and Generalizability

The synthetic (ie, simulated) cohort was internally validated against the observed (ie, stock) cohort. In particular, the prevalence of chronic physical conditions at maximum follow-up was compared between the simulated and observed data. While the simulated value for cancer was quite similar to the observed one, the simulated values for the other conditions differed by a few units; see [supplementary table 7](#). Given the paucity of studies on long-term outcomes among individuals with schizophrenia/psychosis and the lack of microsimulation models focused on schizophrenia/psychosis, external validation was not possible.

The proportions of simulated chronic physical conditions (at baseline) were generally in line with values found in other work from Ontario^{5,39} and other Canadian provinces, such as Alberta,⁴⁰ thus confirming the generalizability of the PSY-SIM model. The only exception was the value for respiratory disease (ie, asthma and COPD), which differed from the prevalence estimate for serious pulmonary disease (ie, bronchitis, emphysema, bronchiectasis, chronic airways obstruction, empyema, and surgical procedures on the lung) obtained from a study from Saskatchewan⁴¹ (likely due to the lack of a comparable estimate). See [supplementary table 8](#) for a comparison between simulated outcomes at baseline and published data.

Model Output: Application Examining the Impact of a Smoking Cessation Program

The PSY-SIM model was used to examine the impact of the STOP program on patient outcomes and health care costs and to estimate the cost-effectiveness of the smoking cessation program compared with the status quo (ie, the absence of the STOP program). The STOP program is publicly funded and delivers smoking cessation treatment at partnering health care organizations.⁴² Patients can enroll in the program through either practitioner-referral or self-referral. It is a pragmatic, real-world program in which treatment, consisting of nicotine replacement therapy for up to 26 weeks and behavioral counseling, is individually tailored. STOP has been found to be effective in both the general and schizophrenia populations, with 26.4%⁴¹ and 16.2%⁴³ of patients reporting abstinence at 6-month follow-up, respectively. It is also important to understand the long-term abstinence rate among individuals with chronic psychotic disorders. Research suggests nicotine replacement therapies like the STOP program have showed to have a long-lasting cessation effect of 7.2% at 4 years.⁴⁴ Using this information, a 4.4% ([16.2%/26.4%]*7.2%) long-term abstinence rate for the

schizophrenia population was determined (see [supplementary table 4](#) for the model input parameters regarding smoking behavior).

Baseline descriptive statistics were produced for a simulated cohort of individuals with chronic psychotic disorders ($N = 200,000$). Next, simulated patient events (development of chronic physical conditions), outcomes (life expectancy and QALYs), and lifetime health care costs were estimated assuming 4.4%, 7.2%, and 100% continuous quit rates due to the STOP program. Finally, incremental cost-effectiveness ratios (ICERs) of the program compared with the status quo were estimated for each case, assuming an intervention cost of \$230.95 in 2020 Canadian dollars, where the intervention was comprised of nicotine replacement therapy and some elements of behavioral intervention (data obtained from the STOP program manager through personal communication). All simulations were conducted 250 times to construct credible intervals. The choice of the number of simulations was informed using convergence plots.⁴⁵

Results

[Table 1](#) provides the baseline descriptive statistics for the stock and simulated samples. The stock population included slightly more females (53%), with a mean age of 51, and mainly non-immigrants mostly living in low-income, urban neighborhoods. Excluding individuals with missing data, over one-third of the sample was made up of current smokers (37.8%) with the most prevalent chronic physical condition being respiratory conditions (28.1%).

[Table 2](#) shows the simulated patient events, outcomes, and health care costs (and respective 95% confidence intervals) over the lifetime, across 3 scenarios of long-term quit rates compared with the “status quo” scenario based on the stock population: 4.4%, 7.8%, and 100%. Individuals with chronic psychotic disorders under the “status quo” scenario had a lifetime prevalence of 63% for congestive heart failure and roughly 50% for respiratory disease, cancer, and diabetes; life expectancy was 76 years (mean age of 51 + 25 years gained). The proportions of chronic physical health conditions were lower with the implementation of the STOP program in all scenarios. These reductions can be attributable to reductions of the comorbidity profile of the population who benefited from the intervention. In particular, the STOP program was associated with an additional 0.03–0.5 life years and 0.014–0.291 QALYs and increased lifetime health care costs (\$356.16–\$7,050.01) compared with the status quo, across the different quit rate scenarios. Based on the simulated results, even at the lowest quit rate (ie, 4.4%), the ICER for the STOP program compared with the status quo was \$41,936/QALY, indicating the intervention is cost-effective against commonly used cost-effectiveness thresholds used in Canada (ie, \$50,000).⁴⁶

Table 1. Baseline Descriptive Statistics for the Stock ($N = 3849$) and Simulated Populations ($N = 200,000$) in the PSY-SIM Model

	N	%	N	%
	Stock Population		Simulated Population	
Socio-demographic characteristics				
Sex				
Female	2027	52.7	105,627	52.8
Male	1822	47.3	94,373	47.2
Age (mean, SD)	50.9	21.9	51.0	21.9
Immigrant status ^a				
Nonimmigrant	3110	80.8	161,590	80.8
Immigrant	739	19.2	38,410	19.2
Neighborhood income (in quintiles)				
Missing	12	0.3	—	0
1—Low	1156	30.0	59,274	29.6
2—Medium low	865	22.5	45,661	22.8
3—Medium	692	18.0	35,678	17.8
4—Medium high	599	15.6	31,240	15.6
5—High	525	13.6	28,147	14.1
Rural residence				
Missing	7	0.2	—	0
No	3170	82.4	165,360	82.7
Yes	672	17.5	34,640	17.3
Health characteristics				
Respiratory disease (asthma and/or COPD)				
Cancer	367	9.5	19,168	9.6
Congestive heart failure	294	7.6	15,687	7.8
Diabetes	566	14.7	29,473	14.7
Smoking status				
Missing	641	16.7	—	—
Non-missing	3208	83.3	—	—
Current smoker	1213	37.8	74,223	37.1
Former smoker	1005	31.3	63,800	31.9
Never smoked	990	30.9	61,977	31.0

^aBased on data in the Canadian Community Health Survey (immigrant = yes, no).

Legend: SD—standard deviation; COPD—chronic obstructive pulmonary disease.

Source: ICES administrative health care data 1996–2020 + Canadian Community Health Survey cycles 2001, 2003, 2005, 2007, 2009, 2011, 2012, and 2013.

Discussion

The main goal of this paper was to describe the development of a unique microsimulation model, the PSY-SIM model, which can be used for surveillance purposes (ie, to monitor health outcomes and health care costs), to examine what-if scenarios, and to undertake economic evaluations. In an application, the model was used to understand the impact of implementing a smoking cessation intervention on lifetime patient outcomes and health care costs. The model found that smoking cessation initiatives, such as the STOP program, targeted at individuals with chronic psychotic disorders can be cost-effective from a health system perspective.

Table 2. Simulated Patient Events/Outcomes and Health Care Costs Over the Lifetime, Respective 95% Confidence Intervals, and Incremental Cost-Effectiveness Ratios Between Current and Former Smokers With the STOP Program for Different Quit Rates

Event (%; 95% CI)	Status Quo	STOP Program 4.4% Quit Rate	STOP Program 7.2% Quit Rate Scenario	STOP Program 100% Quit Rate Scenario
Respiratory disease	49.58 (46.99–51.90)	49.31 (46.52–51.78)	49.12 (46.32–51.56)	43.27 (39.33–46.89)
Cancer	51.50 (46.38–56.62)	51.47 (46.31–56.57)	51.42 (46.26–56.48)	50.47 (44.34–56.37)
Congestive heart failure	63.26 (47.61–77.96)	63.13 (47.48–77.86)	63.05 (47.41–77.78)	60.43 (44.86–74.78)
Diabetes	51.57 (48.32–55.48)	51.49 (48.21–55.35)	51.45 (48.11–55.23)	49.92 (46.02–54.81)
Outcome (N, 95% CI)				
Life expectancy	25.31 (23.75–26.75)	25.34 (23.78–26.74)	25.35 (23.79–26.77)	25.81 (24.26–27.21)
QALYs gained	10.809 (10.398–11.161)	10.823 (10.421–11.170)	10.830 (10.413–11.172)	11.100 (10.668–11.466)
Health care costs (\$) (2020 CAD)	\$359,698.07 (\$328,687.45–\$394,669.66)	\$360,054.23 (\$329,143.07–\$394,907.24)	\$360,236.97 (329,154.71–\$395,168.56)	\$366,748.08 (335,271.70–399,768.11)
QALYs gained vs status quo	—	0.014	0.021	0.291
Incremental costs vs status quo	—	\$356.16	\$538.90	\$7,050.01
ICER (\$/QALY)	—	\$41,936/QALY	\$36,660/QALY	\$25,020/QALY

^aWhere the intervention cost per person is \$230.95 in 2020 Canadian dollars.

Note: ICER = (intervention costs + Δ health care costs)/Δ QALYs.

Legend: STOP—Smoking Treatment for Ontario Patients; CI—confidence interval; QALYs—quality-adjusted life years; Δ—change; ICER—incremental cost-effectiveness ratio.

Source: simulated output based on ICES administrative health care data 1996–2020 + Canadian Community Health Survey cycles 2001, 2003, 2005, 2007, 2009, 2011, 2012, and 2013.

Few microsimulation models have been developed for schizophrenia/psychosis thus far. Although not specifically focused on schizophrenia, the Future Americans Model has been used to examine how changes in education attainment can affect the lifetime economic burden among individuals with severe mental illness, including those with schizophrenia. The authors found that that an intervention aimed at increasing education attainment of individuals with severe mental illness reduces the average per person lifetime economic burden of severe mental illness by 4%.⁴⁷ Using data from the United Kingdom, another study developed a whole-disease model for schizophrenia to inform resource allocation decisions across the schizophrenia care pathway.⁴⁸ The authors used this model to determine whether psychosis-targeted interventions, such as cognitive behavioral therapy and antipsychotic medication, were cost-effective. They found these interventions were likely cost-effective at a willingness-to-pay threshold of £20,000 (\$25,552 USD) per quality-adjusted life-year. However, their model data inputs were not obtained from a simulation stock population and, while it is a whole-disease model, it was mainly designed to undertake cost-effectiveness analyses.

Our model found that smoking cessation initiatives targeted at individuals with chronic psychotic disorders can be cost-effective and lead to improvements in clinical

outcomes and life expectancy. Other interventions, such as those targeted at alcohol consumption and physical activity, may also be helpful to improve health outcomes among these individuals. For example, physical activity represents a promising new treatment option that may supplement current psychosocial and pharmacological interventions.^{49,50} Future updates to the PSY-SIM will include these health behaviors. Moreover, non-health-specific interventions, such as those aimed at increasing educational attainment and/or labor market participation, have also been shown to improve health outcomes and improved quality of life^{47,51} and thus should also be considered in future model iterations.

Strengths and Limitations

The PSY-SIM model uses real-world data to model population-based cohorts, rather than synthetic or estimated cohorts, and can be used for surveillance purposes. It uses a validated algorithm to ascertain diagnoses of chronic psychotic disorders as opposed to using self-reported data, which could be subject to misreporting due to social desirability bias.⁵² Moreover, the PSY-SIM model can produce estimates based on trajectories of health and economic outcomes over a patient's lifetime (ie, from diagnosis to death), rather than on average cohort-level characteristics. Prior work suggests health care costs vary

considerably over the life span,⁹ making average cohort-level characteristics uninformative. Finally, the model has been subjected to validity checks, where many simulated outputs produced by the model are consistent with data from both the original data source and findings published elsewhere.

Like all microsimulation models, the main limitation of the PSY-SIM is that it relies on estimation techniques that are subject to potential error; moreover, there were some computational challenges in estimating these models. The survey data used to populate the model's behavioral outcomes were cross-sectional and therefore it was not possible to examine person-level changes in behavioral outcomes (eg, smoking) over time; this required assuming that once smoking status (smoker, nonsmoker) was assigned, the individual retained that status, unless exposed to a smoking cessation intervention and thus did not account for the fact that some patients might have abstinence periods. Furthermore, given that the survey data employed are self-reported, there is potential for recall bias and/or measurement error (though administrative data were used whenever possible). While internal validation was undertaken, split sample and external validation were not, which would have improved the reliability of the model results. Finally, data regarding the STOP effectiveness were obtained from non-randomized studies^{42,43} that employed causal assumptions, which may have biased the model inputs. Nonetheless, the PSY-SIM model is the first of its kind in Canada. Although based on data from one province, it may help inform decision-making in other Canadian jurisdictions given similarities in provincial health care systems and may serve as a blueprint for other countries with similar health care systems. Furthermore, this model provides a framework for building large-scale policy disease models using administrative data and can be used for other mental disorders using validated algorithms, such as eating disorders. Future work includes adding other risk factors, such as alcohol consumption and physical activity, and more cycles of survey data, as they become available, to increase the sample of the simulation stock population. Moreover, there are future plans to incorporate other data sources, such as electronic medical records, social assistance data, and incarceration data.

Conclusion

Microsimulation models, such as the PSY-SIM model, are helpful tools for health policy planners, decision-makers, and health economists looking to undertake surveillance-related activities, to examine what-if scenarios, and to carry out economic evaluations. The current version of the PSY-SIM model represents a first step toward building a more comprehensive microsimulation model aimed at chronic psychotic disorders. Using this model, we found that smoking cessation initiatives targeted at

individuals with chronic psychotic disorders can reduce chronic morbidity and lead to survival and quality of life gains with a modest increase in health care costs. Based on the simulated results, the STOP program with the lowest quit rate (ie, 4.4%) resulted in an ICER of \$41,936/QALY compared with the status quo. These findings will be helpful for decision-makers and clinicians looking for cost-effective solutions to address smoking cessation among individuals with chronic psychotic disorders.

Supplementary Material

Supplementary material is available at [https://academic.oup.com/schizophreniabulletin/](https://academic.oup.com/schizophreniabulletin/advance-article/doi/10.1093/schbul/sbad175/7476677)

Acknowledgments

The authors would like to thank the team of the Centre for Addiction and Mental Health INTREPID Lab—Peter Selby, Sarwar Hussain, Scott Veldhuizen, and Sabrina Voci—for their assistance regarding data on the STOP program. The authors have declared that there are no conflicts of interest in relation to the subject of this study.

Funding

This study was supported by ICES, which is funded by an annual grant from the Ontario Ministries of Health and Long-term Care. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. The opinions, results, and conclusions reported in this article are also independent from the other sources that provided data and funding. No endorsement by ICES, the Ontario Ministries of Health and Long-term Care is intended or should be inferred. Furthermore, parts of the material are based on data and/or information compiled and provided by the Canadian Institute for Health Information, Immigration, Refugees Citizenship Canada, Ontario Health (Cancer Care Ontario), and the Canadian Community Health Survey (cycles 2001, 2003, 2005, 2007, 2009, 2011, 2012, and 2013) from Statistics Canada. However, the analyses, opinions, results, and conclusions expressed in this material are those of the authors and not necessarily those of the Canadian Institute for Health Information, Immigration, Refugees Citizenship Canada, Ontario Health (Cancer Care Ontario), or Statistics Canada. No endorsement by the Canadian Institute for Health Information, Immigration, Refugees Citizenship Canada, Ontario Health (Cancer Care Ontario), or Statistics Canada is intended or should be inferred.

Data Accessibility

The principal investigator (Claire de Oliveira) had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Data Availability

The dataset from this study is held securely in coded form at ICES. While legal data sharing agreements between ICES and data providers (eg, healthcare organizations and government) prohibit ICES from making the dataset publicly available, access may be granted to those who meet prespecified criteria for confidential access, available at www.ices.on.ca/DAS (email: das@ices.on.ca). The full dataset creation plan and underlying analytic code are available from the authors upon request, understanding that the computer programs may rely upon coding templates or macros that are unique to ICES and are therefore either inaccessible or may require modification.

References

- Abraham JM. Using microsimulation models to inform US health policy making. *Health Serv Res.* 2013;48(2 Pt 2):686–695.
- de Oliveira C, Matias MA, Jacobs R. Microsimulation models on mental health: a critical review of the literature. *Value Health* 2023; Online ahead of print. doi: <https://doi.org/10.1016/j.jval.2023.10.015>
- Zaheer J, Jacob B, de Oliveira C, Rudoler D, Juda A, Kurdyak P. Service utilization and suicide among people with schizophrenia spectrum disorders. *Schizophr Res.* 2018;202:347–353.
- Kurdyak P, Vigod S, Duchon R, Jacob B, Stukel T, Kiran T. Diabetes quality of care and outcomes: comparison of individuals with and without schizophrenia. *Gen Hosp Psychiatry.* 2017;46:7–13.
- Chiu M, Rahman F, Vigod S, Wilton AS, Kurdyak P. Temporal trends in cardiovascular disease risk factor profiles in a population-based schizophrenia sample: a repeat cross-sectional study. *J Epidemiol Community Health.* 2018;72(1):71–77.
- Mahentharan M, Kouyoumdjian FG, de Oliveira C, et al. Prevalence and predictors of reincarceration after correctional center release: a population-based comparison of individuals with and without schizophrenia in Ontario, Canada. *Can J Psychiatry.* 2021;66(4):376–384.
- Kurdyak P, Vigod S, Calzavara A, Wodchis WP. High mortality and low access to care following incident acute myocardial infarction in individuals with schizophrenia. *Schizophr Res.* 2012;142(1–3):52–57.
- Gatov E, Rosella L, Chiu M, Kurdyak PA. Trends in standardized mortality among individuals with schizophrenia, 1993–2012: a population-based, repeated cross-sectional study. *CMAJ.* 2017;189(37):E1177–E1187.
- de Oliveira C, Cheng J, Rehm J, Kurdyak P. The economic burden of chronic psychotic disorders in Ontario. *J Ment Health Policy Econ.* 2016;19(4):181–192.
- de Leon J, Diaz FJ. A meta-analysis of worldwide studies demonstrates an association between schizophrenia and tobacco smoking behaviors. *Schizophr Res.* 2005;76(2–3):135–157.
- Evins AE, Cather C, Rigotti NA, et al. Two-year follow-up of a smoking cessation trial in patients with schizophrenia: increased rates of smoking cessation and reduction. *J Clin Psychiatry.* 2004;65(3):307–311.
- Tran K, Asakawa K, Cimon K, et al. *Pharmacologic-based Strategies for Smoking Cessation: Clinical and Cost-Effectiveness Analyses.* CADTH Technology Report no. 130. 2011;(September 2010). <http://www.cadth.ca/index.php/en/hta/reports-publications/search?&type=16>
- Tam J, Warner KE, Meza R. Smoking and the reduced life expectancy of individuals with serious mental illness. *Am J Prev Med.* 2016;51(6):958–966.
- Quigley H, MacCabe JH. The relationship between nicotine and psychosis. *Ther Adv Psychopharmacol.* 2019;9:2045125319859969.
- Cather C, Pachas GN, Cieslak KM, Evins AE. Achieving smoking cessation in individuals with schizophrenia: special considerations. *CNS Drugs.* 2017;31(6):471–481.
- Lê Cook B, Wayne GF, Kafali EN, Liu Z, Shu C, Flores M. Trends in smoking among adults with mental illness and association between mental health treatment and smoking cessation. *JAMA.* 2014;311(2):172–182.
- Baker AL, Robson D, Lawn S, et al. Reducing smoking among people with schizophrenia: perspectives on priorities for advancing research. *Front Psychiatry.* 2018;9:711.
- Goldman DP, Leaf DE, Tysinger B. *The Future Americans Model: Technical Documentation.* USC Schaeffer Center, Roybal Center for Health Policy Simulation. <https://healthpolicy.app.box.com/v/FAMTechdoc>
- Wodchis W, Bushmeneva K, Nikitovic M, et al. *Guidelines on Person-Level Costing Using Administrative Databases in Ontario.* Working Paper Series Vol. 1. Toronto: Health System Performance Research Network; 2013.
- Kurdyak P, Lin E, Green D, Vigod S. Validation of a population-based algorithm to detect chronic psychotic illness. *Can J Psychiatry.* 2015;60(8):362–368.
- Pope MA, Joobar R, Malla AK. Diagnostic stability of first-episode psychotic disorders and persistence of comorbid psychiatric disorders over 1 year. *Can J Psychiatry.* 2013;58(10):588–594.
- Schultz SE, Rothwell DM, Chen Z, Tu K. Identifying cases of congestive heart failure from administrative data: a validation study using primary care patient records. *Chronic Dis Inj Can.* 2013;33:160–166.
- Gershon AS, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying patients with physician diagnosed asthma in health administrative databases. *Can Respir J.* 2009;16:183–188.
- Gershon AS, Wang C, Guan J, Vasilevska-Ristovska J, Cicutto L, To T. Identifying individuals with physician diagnosed COPD in health administrative databases. *COPD* 2009;6:388–394.
- Hux JE, Ivis F, Flintoft V, Bica A. Diabetes in Ontario: determination of prevalence and incidence using a validated administrative data algorithm. *Diabetes Care.* 2002;25:512–516.
- Proadhan S, King MJ, De P, et al. Health services data: the Ontario Cancer Registry (a unique, linked, and automated population-based registry). In: Levy A, Goring S, eds. *Data and Measures in Health Services Research.* Boston, MA: Health Services Research; 2016.

27. Tu K, Chen Z, Lipscombe LL; Canadian Hypertension Education Program Outcomes Research Taskforce. Prevalence and incidence of hypertension from 1995 to 2005: a population-based study. *CMAJ*. 2008;178:1429–1435.
28. Zhou J, Millier A, François C, Aballéa S, Toumi M. Systematic review of utility values used in the pharmacoeconomic evaluations for schizophrenia: implications on cost-effectiveness results. *J Mark Access Health Policy*. 2019;7(1):1648973.
29. Tsiplova K, Pullenayegum E, Cooke T, Xie F. EQ-5D-derived health utilities and minimally important differences for chronic health conditions: 2011 Commonwealth Fund Survey of Sicker Adults in Canada. *Qual Life Res*. 2016;25(12):3009–3016.
30. Fu SN, Dao MC, Wong CK, Yu WC. SF-6D utility scores of smokers and ex-smokers with or without respiratory symptoms attending primary care clinics. *Health Qual Life Outcomes*. 2019;17(1):1–8.
31. Wodchis WP, Austin PC, Henry DA. A 3-year study of high-cost users of health care. *CMAJ*. 2016;188(3):182–188.
32. Statistics Canada. *Canadian Community Health Survey – Annual Component (CCHS)*. 2013. <https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&Id=144170>. Accessed August 8, 2021.
33. Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Commun Stat - Simul Comput*. 2009;38(6):1228–1234.
34. Ara R, Wailoo AJ. *NICE DSU Technical Support Document 12: The Use of Health State Utility Values in Decision Models*. 2011. <http://www.nicedsu.org.uk>
35. Meira-Machado L, de Uña-Álvarez J, Cadarso-Suárez C, Andersen PK. Multi-state models for the analysis of time-to-event data. *Stat Methods Med Res*. 2009;18(2):195–222.
36. Ng R, Kornas K, Sutradhar R, Wodchis WP, Rosella LC. The current application of the Royston-Parmer model for prognostic modeling in health research: a scoping review. *Diagn Progn Res*. 2018;2:4.
37. Statistics Canada. *Life Expectancy and Other Elements of the Complete Life Table, Single-Year Estimates, Canada, All Provinces Except Prince Edward Island*. 2022. <https://www150.statcan.gc.ca/t1/tbl/en/tv.action?pid=1310083701>. Accessed January 24, 2022.
38. *Guidelines for the Economic Evaluation of Health Technologies: Canada*. 4th ed. Ottawa: CADTH; 2017.
39. Wootten JC, Richard L, Blanchette PS, Wiener JC, Anderson KK. Cancer incidence and stage at diagnosis among people with recent-onset psychotic disorders: a retrospective cohort study using health administrative data from Ontario, Canada. *Psychooncology*. 2022;31(9):1510–1518.
40. Bresee LC, Majumdar SR, Patten SB, Johnson JA. Prevalence of cardiovascular risk factors and disease in people with schizophrenia: a population-based study. *Schizophr Res*. 2010;117(1):75–82.
41. Curkendall SM, Mo J, Glasser DB, Rose Stang M, Jones JK. Cardiovascular disease in patients with schizophrenia in Saskatchewan, Canada. *J Clin Psychiatry*. 2004;65(5):715–720.
42. Baliunas D, Selby P, de Oliveira C, et al. Primary care-based smoking cessation treatment and subsequent healthcare service utilisation: a matched cohort study of smokers using linked administrative healthcare data. *Tob Control*. 2023;32(1):72–79.
43. Veldhuizen S, Behal A, Zawertailo L, Melamed O, Agarwal M, Selby P. Outcomes among people with schizophrenia participating in general-population smoking cessation treatment: an observational study. *Can J Psychiatry*. 2023;68(5):359–369.
44. Etter JF, Stapleton JA. Nicotine replacement therapy for long-term smoking cessation: a meta-analysis. *Tob Control*. 2006;15(4):280–285.
45. Hatswell AJ, Bullement A, Briggs A, Paulden M, Stevenson MD. Probabilistic sensitivity analysis in cost-effectiveness models: determining model convergence in cohort models. *Pharmacoecon*. 2018;36:1421–1426.
46. Binder L, Ghadban M, Sit C, Barnard K. Health technology assessment process for oncology drugs: impact of CADTH changes on public payer reimbursement recommendations. *Curr Oncol*. 2022;29(3):1514–1526.
47. Seabury SA, Axeen S, Pauley G, et al. Measuring the lifetime costs of serious mental illness and the mitigating effects of educational attainment. *Health Aff (Millwood)*. 2019;38(4):652–659.
48. Jin H, Tappenden P, MacCabe JH, Robinson S, Byford S. Evaluation of the cost-effectiveness of services for schizophrenia in the UK across the entire care pathway in a single whole-disease model. *JAMA Netw Open*. 2020;3(5):e205888.
49. Mittal VA, Vargas T, Osborne KJ, et al. Exercise treatments for psychosis: a review. *Curr Treat Options Psychiatry*. 2017;4(2):152–166.
50. Lebiecka Z, Łopuszko A, Rudkowski K, Dańczura E. Effects of physical activity on treatment of schizophrenia. *Arch Psychiatry Psychother*. 2019;21(1):28–35.
51. Bouwmans C, de Sonnevile C, Mulder CL, Hakkaart-van Roijen L. Employment and the associated impact on quality of life in people diagnosed with schizophrenia. *Neuropsychiatr Dis Treat*. 2015;11:2125–2142.
52. Mason J, Laporte A, McDonald T, Kurdyak P, de Oliveira C. Health reporting from different data sources: does it matter for mental health? *J Ment Health Policy Econ*. 2023;26(1):33–57.