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ORIGINAL ARTICLE

Health care disparities among persons with comorbid schizophrenia and cardiovascular disease: a case–control epidemiological study

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Aims. Studies showed health care disparities among persons with comorbid schizophrenia and cardiovascular disease (CVD), including in countries with universal health care. However, the potential positive effect of specific mental health legislation has not been reported. This study aimed to investigate the health care of persons with comorbid schizophrenia and CVD in a country with both a national health insurance and a comprehensive rehabilitation law for persons with mental disabilities.

Method. This study builds on a large case–control epidemiological sample ($N = 52\,189$) of service users. Within the sample we identified a sub-group of persons with CVD diagnoses ($n = 8208$) and compared service users with and without schizophrenia on drug utilisation, laboratory tests, visits to specialists and surgical interventions.

Results. Service users with schizophrenia were less likely to meet similar indexes of care as their counterparts: 91% cholesterol tests ($p < 0.001$), 60% stress tests ($p < 0.001$), 93% visits to specialists ($p = 0.001$), 93% drug utilisation ($p < 0.001$) and 55% CVD surgical interventions (odds ratio 0.55, 95% confidence intervals 0.49–0.61).

Conclusions. In Israel, a country with a national health insurance and a rehabilitation law specific for persons with mental disabilities, service users with schizophrenia still fail to receive equitable levels of health care for CVD. However, the disparities appear to be smaller than in other countries with universal health insurance.

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Introduction

Cardiovascular disease (CVD) constitute a major cause for excess mortality in persons with severe mental disorders) Lawrence *et al*. 2003; Laursen *et al*. 2009; De Hart *et al*. 2011*b*; Haklai *et al*. 2011; Mitchell & Lawrence, 2011; Ajetunmobi *et al*. 2013; Crump *et al*. 2013; Wu *et al*. 2013). Despite this heightened risk, studies also showed that these persons experience inequalities in their medical care (Druss *et al*. 2000, 2001; Young & Foster, 2000; Jones & Carney, 2005) particularly among those with schizophrenia (Young & Foster, 2000; Druss *et al*. 2001; Petersen *et al*. 2003; Jones & Carney, 2005; De Hart *et al*. 2011*b*; Mitchell & Lawrence, 2011). These findings, which were reported by US studies based on population groups protected by special insurance systems (Druss *et al*. 2000, 2001; Petersen *et al*. 2003; Jones & Carney, 2005), were replicated in countries with national health insurances, where care does not depend on out-of-pocket expenditures, e.g., Australia (Lawrence *et al*. 2003), Canada (Kisely *et al*. 2009), Denmark (Laursen *et al*. 2009), Sweden (Björkenstam *et al*. 2012) and Taiwan (Wu *et al*. 2013). Conceivably, health care disparities may contribute to '*the scandal of premature mortality*' among persons with severe mental disorders (Thornicroft, 2011).

Israel, like the above-noted countries, has a national health insurance law (1995) that mandates universal and comprehensive health care. It requires that every *de-jure* resident should be registered with one of the four health care providers. Service users have access to free primary health care, laboratory tests, surgical interventions and almost free specialised care and medications. The health care providers are prohibited to decline applicants for any reason, including national affiliation, age, health and psychiatric status. In addition, people that reach a threshold of mental disability are entitled to a 'basket of services' mandated by a rehabilitation law, including the '*appointment of a treatment*

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coordinator who is responsible for implementation and coordination of the provision of all the services for the mentally disabled person' (Rehabilitation of the Mentally Disabled in the Community Law, 2000). Studies on the implementation of this law have generally reported positive clinical as well as psychosocial outcomes (Roe *et al*. 2010; Aviram *et al*. 2012; Hornik-Lurie *et al*. 2012).

Objective: To study the health care provided to persons with comorbid schizophrenia and CVD in a country wherein structural-based service opportunities are strengthened by a rehabilitation law that specifically addresses the care provided to persons with mental disabilities.

Methods

The study was based on a prospective historical design with data collected between the years 2000–2009. Ethical approval was granted by the head management of the health provider, *Clalit Health Services* (CHS). The identity of the participants was undisclosed to the authors.

Identification of persons with severe and persistent mental disorder

Psychiatric care in Israel is freely available by law to all *de-jure* residents (Levav & Grinshpoon, 2004).To identify the sample of persons with schizophrenia we used the Psychiatric Case Register (PCR). The PCR is legally mandated to maintain a cumulative record of all psychiatric hospitalisations in mental and general hospitals (Lichtenberg *et al*. 1999; Mental Health in Israel, 2008). The PCR provided the subjects' sociodemographic information and psychiatric diagnoses upon admission and discharge. These were based on ICD-10 (World Health Organization, 1992), diagnoses made prior to its introduction have been updated. Tests of agreement between research and PCR diagnoses were found satisfactory (Rabinowitz *et al*. 1994; Weiser *et al*. 2005). The following inclusion criteria were applied: (a) persons with last discharge diagnosis of schizophrenia (F20–F29) and (b) born prior to 1960.

We identified 28 579 persons who met the inclusion criteria. The information gathered was: year of first and last psychiatric hospitalisation, total number of hospitalisations, and total length of hospital stay (Table 1). The latter was done annually between the years 2000–2009 to control for possible artefacts during those episodes when the service user would not be under the care of CHS unless referred by the mental hospitals.

General health services

Data from CHS, the largest health care provider with 3.8 million insured persons, were extracted from its electronic data base. The sampling frame was defined according to the second inclusion criterion (i.e., age), and comprised 1 040 000 individuals. Data on the cohort were gathered annually during the years 2000–2009; however, some of the data were available from the year 2002 onwards when the CHS started to develop a central data base.

Table 1. *Sociodemographic characteristics and clinical data of service users diagnosed with schizophrenia and matched controls*

	Schizophrenia ($n = 2277$)	Matched controls ($n = 5931$)
Gender (M) (%)	59.5	61.5
Age (2009)	67.8 (S.D. 9.2)	68.3 (S.D. 9.2)
Birthplace		
Israel (%)	31.9	30.7
Asia (%)	19.0	18.0
Africa (%)	19.7	19.4
Europe–America (%)	29.4	32.0
National-sector		
Jewish–Israelis (%)	92.6	91.5
Socioeconomic status		
Low (%)	37.4	43.4
Middle (%)	47.1	44.2
High (%)	15.5	12.5
CVD diagnose		
IHD (%)	83.7	86.5
CHF (%)	34.7	24.2
Cardiomyopathy (%)	5.7	4.2
IHSS (%)	0.7	0.7
Pulmonary hypertension (%)	6.9	6.5
Carotid artery disease (%)	6.4	12.1
Age at first hospitalisation	34.0 (S.D. 12.7)	–
Number of psychiatric hospitalisations	7.5 (S.D. 10.0)	–
Mean hospitalisation stay, days (2000–2009)	41.4 (S.D. 227)	–

The following data were collected:

1. Sociodemographic data: Sex, year and place of birth, national sector (Jews, Arabs), year of death and socioeconomic status (Table 1). The latter was based on information gathered from the National Central Bureau of Statistics on average income levels according to geographical data. We used the geographical location of the clinic as a proxy for the income and hence the socioeconomic rank of the user: low (income deciles 1–3), middle (deciles 4–7) and high (deciles 8–10).
2. Medical diagnoses: The cardiovascular ICD-10 diagnoses included were: ischaemic heart disease (IHD)

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(I20-I25); congestive heart failure (CHF)(I50); cardiomyopathy (I42); idiopathic hypertrophic subaortic stenosis (IHSS)(I42.1–I42.5); pulmonary hypertension (I27); and carotid artery disease (I65.2) (World Health Organization, 1992) (Table 1). In addition, type 2 diabetes mellitus (E11) was recorded. These were extracted from the service users' files, as well as the respective dates in which they were made.

3. Laboratory tests: The number of the following tests were recorded annually: blood cholesterol fraction tests (LDL) (2002–2009); haemoglobin-A1C tests (2002–2009); visits to specialists (2000–2009); stress tests (2000–2009); and chest X-rays (2000–2009). In addition, the results of estimated LDL cholesterol and haemoglobin-A1C tests were recorded annually (2002–2009). For each measure the highest annual level was used. Haemoglobin-A1C is measured primarily to identify the average plasma glucose concentration over prolonged periods of time, and is required in the use of second-generation anti-psychotic medications because of the associated risk for diabetes.
4. Drug utilisation: The number of months per year in which prescribed medications were dispensed to service users was recorded (2000–2009). The utilisation refers to the following categories of cardiovascular drugs: inotropic drugs, antihypertensive, diuretics, peripheral vasodilators, vasoprotective, beta-blockers, calcium channel blockers, antihypertensives (renin–angiotensin agents) and statins (blood lipid level modifying agents). For each drug category, the mean months of utilisation per year was calculated (2000–2009). Two measures were created based on the user's annual utilisation: mean months of utilisation of the drug most frequently used, and mean annual months of utilisation for all drugs combined. Also, we analysed the utilisation of the two most common medication groups: statins and antihypertensives.
5. Surgical interventions: Cardiac catheterisation, coronary artery bypass graft (CABG) and cardiac pacemaker implantation performed between the years 2000 and 2009 were extracted from the service users' files, as well as the dates the intervention was conducted.

Linkage procedure and selection of a matched control group

The data extracted from the PCR and CHS databases were merged according to the personal ID. To generate a matched control group (2 : 1 ratio) we defined an algorithm based on age (groups of three consecutive years), sex, birth continent (Israel, Asia, Africa and Europe–America), socioeconomic status (high, middle and low) and national sector (Arabs and Jews). If the service user with schizophrenia had missing information on one of the matching variables, then controls with missing data on that same variable were chosen. Service users were omitted in case of: death that occurred before 2002; and an average annual psychiatric hospitalisation of 270 days or more. The matching procedure yielded 17 396 service users diagnosed with schizophrenia and 34 793 matched controls, and found satisfactory. CVD diagnosis was found in 11 071 service users, 3163 with schizophrenia (18.2%) and 7908 of the matched controls (21.2%).

Further inclusion criteria were applied to this sample: (a) the first CVD diagnosis was made during the follow-up period (2000–2009); and (b) the first psychiatric hospitalisation of service users with schizophrenia preceded the first CVD diagnosis. Applying these criteria, the final sample was comprised of 8208 service users who met both criteria: 2277 with schizophrenia and 5931 matched controls. Sociodemographic characteristics were comparable, except for the socioeconomic status as persons with schizophrenia were in a slightly higher status than their counterparts ($\chi^2 = 27$, df = 2, $p < 0.001$) (Table 1).

Data analysis

The total number of follow-up years since CVD diagnosis (min = 1, max = 10) was calculated for each service user and all service utilisation measures were analysed accounting for the relevant years. The associations between the group (schizophrenia, comparison) and laboratory tests, visits and drug utilisation were analysed using general linear models. Rates of CVD, mortality and surgical interventions in the two groups were analysed using logistic regression models. Statistical outcomes of the logistic regression tests were estimated using odds ratios (ORs) and 95% confidence intervals (95% CI). In addition, surgical interventions in the two groups were analysed using Cox proportional-hazards models. Statistical outcomes of Cox-regression tests were estimated using hazard ratios (HR) and 95% CI. Univariate analysis was conducted for all models to test the association between medical procedures conducted and potential confounders, e.g., sex, age, national sector and socioeconomic status. The association between group and surgical interventions accounted, in addition, for the age at first CVD diagnosis. Adjusted analysis followed the univariate analysis to include confounding variables showing significant univariate associations with the outcome variables. Analysis was performed using the SPSS 21.0 software (IBM Inc.)

Results

Age at first CVD diagnosis did not differ between service users with schizophrenia (67.8 ± 9.2) (mean ± S.D.)

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and matched controls (68.3 ± 0.2). Mortality rate was higher among service users with schizophrenia (41.9%) compared to matched controls (21.7%) (univariate OR 2.6, 95% CI 2.4–2.9; adjusted OR 3.0, 95% CI 2.7–3.3). Total person years of follow-up were 76 131, with shorter average follow-up period for persons with schizophrenia (8.8 ± 2.2) than for their counterparts (9.4 ± 1.6) ($F = 196$, df = 17 974, $p < 0.001$).

The average annual blood tests, stress tests, chest X-rays and visits to specialists were lower among service users diagnosed with schizophrenia compared to matched controls (Table 2). Throughout the study period, 6.5% of the service users with schizophrenia and 3.9% of the comparison group did not have any LDL test (univariate OR 0.58, 95% CI 0.47–0.73; adjusted OR 0.75, 95% CI 0.58–0.96). The mean LDL level was higher among service users with schizophrenia (121.8 ± 31.1) than in the comparison group (119.6 ± 28.3) (unadjusted $F = 8.2$, df = 17 036, $p = 0.004$; adjusted $F = 8.0$, df = 16 902, $p = 0.005$), while no difference of haemoglobin-A1C was observed (schizophrenia: 7.2 ± 1.8; comparison: 7.1 ± 1.6; $p = 0.14$).

We identified 3094 service users with CVD who underwent surgical interventions (37.7%). Lower rates of cardiac catheterisation, CABG and pacemaker implantation were recorded among service users with schizophrenia compared with matched controls (Table 3). The total rate of surgical interventions among service users with schizophrenia was 45% lower than the matched controls (adjusted OR 0.55, 95% CI 0.49–0.61). Cox-regression model, adjusted for sex, national sector, socioeconomic status and age at first CVD diagnosis indicated that service users with schizophrenia had 30% decreased likelihood of surgical interventions than matched controls (adjusted HR 0.70, 95% CI 0.64–0.76).

Importantly, two additional survival models were performed to test service users with CVD at higher risk, which may serve as an indication for surgical interventions. First, service users with schizophrenia having two or more CVD diagnoses, had 23% decreased likelihood to receive surgical interventions than matched controls (adjusted HR 0.77, 95% CI 0.64–0.93). Second, service users with schizophrenia and an additional diagnosis of diabetes had 30% decreased likelihood to have surgical interventions than matched controls (adjusted HR 0.70, 95% CI 0.62–0.79).

During the follow-up period death records were noted in 2294 service users. Following the CVD diagnosis service users with schizophrenia showed 2.3-fold risk for death compared to their counterparts (adjusted HR 2.29, 95% CI 2.10–2.50). The heightened death rate was slightly reduced among service users with schizophrenia who had a surgical intervention (adjusted HR 1.88, 95% CI 1.57–2.25).

The analysis of cardiovascular drug utilisation showed that throughout the follow-up period 5.3% of the service users with schizophrenia and 2.9% of the matched controls did not utilise any medication. The annual utilisation was consistently lower among service users with schizophrenia compared with matched controls (Table 4). This was found among users' most utilised drug, the total number of medications utilised, statins and antihypertensive drugs.

Discussion

Results of the current study revealed consistent health services disparities among persons with schizophrenia. Lower rates of laboratory tests, utilisation of cardiovascular medications and surgical interventions were found among service users with comorbid schizophrenia and CVD compared with matched controls.

The disparities found in the current study among service users with schizophrenia with regard to surgical interventions were somewhat reduced compared with reports from other countries with a national

Table 2. *Annual rate of performance of health measures and visits among service users with schizophrenia and matched controls diagnosed with a CVD*

	Schizophrenia Mean (S.D.)	Matched controls Mean (S.D.)	*F*, *p*	
			Unadjusted	Adjusted*
LDL	1.12 (0.82)	1.23 (0.86)	26.7, $p < 0.001$	35.5, $p < 0.001$
Haemoglobin-A1C	0.50 (0.74)	0.54 (0.77)	3.5, $p = 0.06$	4.3, $p = 0.04$
Stress test	0.06 (0.16)	0.1 (0.16)	44.7, $p < 0.001$	106.8, $p < 0.001$
Chest X-ray	0.18 (0.25)	0.21 (0.28)	24.7, $p < 0.001$	24.5, $p < 0.001$
Visits	2.96 (3.65)	3.19 (3.34)	7.1, $p = 0.008$	11.3, $p = 0.001$

*Adjusted model included sex, age, national sector and socioeconomic status.

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Table 3. *Performance of surgical interventions among service users with schizophrenia and matched controls diagnosed with a CVD*

			OR (95% CI)	
	Schizophrenia (%)	Matched controls (%)	Unadjusted	Adjusted*
Cardiac catheterisation	21.7	32.7	0.57 (0.51–0.64)	0.57 (0.50–0.64)
Coronary artery bypass graft	7.4	10.6	0.68 (0.57–0.61)	0.68 (0.57–0.82)
Cardiac pacemaker implantation	1.4	2.3	0.48 (0.28–0.82)	0.50 (0.29–0.86)
Any intervention	28.2	41.4	0.56 (0.50–0.62)	0.55 (0.49–0.61)

*Adjusted model included sex, age, national sector and socioeconomic status.

health insurance. The performance of cardiac catheterisation was 11% lower in Israel in contrast to 11.4 and 15.7%, in Canada (Kisely *et al*. 2009) and Taiwan (Wu *et al*. 2013), respectively. Performance of CABG in service users with schizophrenia was 3.2% lower in Israel compared with 11.3% in Canada (Kisely *et al*. 2009), while in Taiwan the combined rates of CABG with percutaneous transluminal coronary angioplasty had a reduced rate of 14.9% (Wu *et al*. 2013). Further measures were not comparable due to differences in the research design. Plausibly, these reduced disparities resulted from the specific services mandated by the rehabilitation law adopted over a decade ago for service users with mental disabilities (Roe *et al*. 2010; Aviram *et al*. 2012; Hornik-Lurie *et al*. 2012). Another factor that may explain those reductions is the easier geographical access to health centres on account of the small size of the country. However, this explanation may apply to Canada but not to Taiwan.

Accumulative evidence has pointed out that risk factors for CVD are more common in persons with schizophrenia (De Hart *et al*. 2009; Gardner-Sood *et al*. 2015). Along with excess in mortality, this may suggest that persons with schizophrenia should have higher rates of somatic care and surgical interventions, yet we found lower rates of medical care, including surgical interventions following CVD diagnosis. A possible explanation may argue that symptoms of heart disease were fewer among persons with schizophrenia. However, the same pattern emerged when we examined specific sub-groups of patients in which more severe symptoms could be assumed, with multiple CVD diagnoses or with comorbid diabetes. A similar observation was reported on persons with severe mental disorders following myocardial infraction (Laursen *et al*. 2009).

These disparities constitute a limited observance of the United Nations Convention on the Rights of Persons with Disabilities (CRPD) (United Nations, 2006). Importantly, CRPD establishes to '*Provide persons with disabilities with the same range, quality and standard of free or affordable health care and programs as provided to other persons…' (Art. 25)*. Clearly, and despite the binding nature of CRPD for the signatory countries, in Israel, as in other countries with universal health insurance, persons with schizophrenia do not benefit equal specialised medical care compared to persons free of these disorders (De Hert *et al*. 2011*b*). This disparity requires special attention by providers since the use of atypical antipsychotic drugs may cause overweight and diabetes, both of which are risk factors for CVD (Mitchell *et al*. 2013; Gardner-Sood *et al*. 2015).

Insel & Landis (2013) noted that '*The public health challenge* [in mental health care] *is mortality as well as*

Table 4. *Utilisation of cardiovascular drugs among service users with schizophrenia and matched controls*

			F, *p*	
	Schizophrenia Mean (S.D.)[a]	Matched controls Mean (S.D.)[a]	Unadjusted	Adjusted[b]
Most frequently utilised drug	7.8 (3.9)	8.4 (3.4)	38.5, $p < 0.001$	32.5, $p < 0.001$
Total number of drugs utilised	6.8 (2.8)	7.0 (2.6)	6.6, $p = 0.01$	7.3, $p < 0.01$
Statins	5.0 (4.4)	6.0 (4.2)	72.5, $p < 0.001$	74.5, $p < 0.001$
Antihypertensives	4.7 (4.5)	5.2 (4.4)	13.4, $p < 0.001$	11.7, $p = 0.001$

[a]Mean annual months of utilisation (2000–2009).
[b]Adjusted model included sex, age, national sector, socioeconomic status and follow-up years.

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morbidity'. Innovative strategies are needed to correct deficiencies in the medical practice as well as in the engagement of persons with schizophrenia, their families and the service users associations, in the development of programmes of health promotion, primary prevention and curative care (De Hert *et al*. 2011*a*; van Hasselt *et al*. 2015). A recent study estimated that the reduction of mortality due to comorbid physical disorders among persons with severe mental disorders reaches a ceiling of 50% (Hoang *et al*. 2013). Nevertheless, even within these limits optimal health care can make a substantial reduction of the excess mortality in this population.

This study has several limitations. First, our data are based on the performance of the medical procedures rather than on the examination of doctors' prescriptions. Therefore, we could not differentiate between the actions of the treating physicians, possibly based on stigma (Sartorius, 2002) and the users' adherence to care. This distinction is important with regard to service users with schizophrenia since their clinical condition may compromise their health behaviour, compared with the general population. Second, we did not have access to information on risk factors (e.g., smoking and obesity). Third, the rate of CVD was slightly lower among persons with schizophrenia than in the comparison population. This apparently surprising finding could be explained by either under diagnosis or by age factors in our sample (all subjects were 40+ at the start of the follow-up period). Thus, premature mortality of persons with schizophrenia could cause that patients previously affected with CVD were not included in our sample. A reduced risk in morbidity as age increases has been reported in the literature (Tabbane *et al*. 1993; Osborn *et al*. 2007). We think, however, that the limitations are in part balanced by the large size of the populations investigated, the different nature of the measures used, the careful recording of the information collected on the users and the consistency of the results.

Conclusion

The consistency of our findings with regard to medical examinations, surgical interventions, drug utilisation and death rates strongly suggest that persons with schizophrenia receive suboptimal medical treatment despite the existence of specific protective legislation.

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Conflict of Interest

Dr Munitz is employed by Clalit Health Services.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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