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ORIGINAL INVESTIGATION

Benzodiazepine therapy in psychiatric outpatients is associated with deliberate self-poisoning events at emergency departments—a population-based nested case–control study

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Abstract
Rationale Deliberate self-poisoning (DSP), the most common form of deliberate self-harm, is closely associated with suicide. Identifying risk factors of DSP is necessary for implementing prevention strategies.
Objectives This study aimed to evaluate the relationship between benzodiazepine (BZD) treatment in psychiatric outpatients and DSP cases at emergency departments (EDs).
Methods We performed a retrospective nested case–control study of psychiatric patients receiving BZD therapy to evaluate the relationship between BZD use and the diagnosis of DSP at EDs using data from the nationwide Taiwan National Health Insurance Research Database.
Results Regression analysis yielded an odds ratio (OR) and 95 % confidence interval (95 % CI) indicating that the use of BZDs in psychiatric outpatients was significantly associated with DSP cases at EDs (OR=4.46, 95 % CI=3.59–5.53). Having a history of DSP, sleep disorders, anxiety disorders, schizophrenia, depression, or bipolar disorder was associated with a DSP diagnosis at EDs (OR=13.27, 95 % CI=8.28–21.29; OR=5.04, 95 % CI=4.25–5.98; OR=3.95, 95 % CI=3.32–4.70; OR=7.80, 95 % CI=5.28–11.52; OR=15.20, 95 % CI=12.22–18.91; and OR=18.48, 95 % CI=10.13–33.7, respectively). After adjusting for potential confounders, BZD use remained significantly associated with a subsequent DSP diagnosis (adjusted OR=2.47, 95 % CI=1.93–3.17). Patients taking higher average cumulative BZD doses were at greater risk of DSP.

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Conclusion Vigilant evaluation of the psychiatric status of patients prescribed with BZD therapy is critical for the prevention of DSP events at EDs.

Keywords Benzodiazepine · Psychiatric outpatients · Deliberate self-poisoning · Emergency departments · Control study

Introduction

Cases involving deliberate self-harm, including intentional self-poisoning or self-injury, are common psychiatric situations at emergency departments (EDs) (Skegg 2005). Deliberate self-poisoning (DSP) is the deliberate ingestion of an overdose of a medication or substance to effect some change that the person desires through the expected consequences of the act (Hawton et al. 2007; Perry et al. 2012). DSP is the most common form of deliberate self-harm and is closely associated with suicide (Hawton et al. 2007; Perry et al. 2012). The risk of suicide in patients with a history of DSP is higher than that of the general population (Hawton et al. 2003). Therefore, identifying DSP patients and implementing adequate prevention strategies thereafter are critical for reducing the risk of suicide.

Previous studies of DSP have focused primarily on presentations, behaviors, and substance categories (Hawton et al. 2007; Perry et al. 2012; Watve et al. 2012; Prescott et al. 2009; Fliege et al. 2009; Zakiullah et al. 2008; Rhodes et al. 2008; Fathelrahman et al. 2008; Cook et al. 2008). Risk factors for DSP include a history of psychiatric illness, substance abuse, and socioeconomic disadvantage (Skegg 2005; Madsen et al. 2012). However, the relationship between DSP and prescription medication is not clear. Benzodiazepines (BZDs) are frequently prescribed by psychiatrists as anxiolytics (Prescott et al. 2009; Longo and Johnson 2000; Berger et al. 2012). Reports from one National Poison Control Center indicated that drugs with CNS effects were encountered the most frequently, and the majority of these drugs were benzodiazepines (Lin et al. 2003). BZDs are also frequently used for DSP in other countries (Cook et al. 2008; Cox et al. 2011). Therefore, we evaluated the relationship between BZD treatment in psychiatric outpatients and DSP cases at EDs using data from the Taiwan National Health Insurance Research Database (NHIRD).

Methods

Data source

A retrospective nested case–control study was conducted using data from the Taiwan NHIRD. The NHIRD is a nationwide database that was established in 1996. It contains reimbursement claims data from the Taiwan National Health Insurance system, which has provided coverage for approximately 99 % of the population since 1998. The National Health Research Institutes (NHRI) manages the annual claims data in the NHIRD and established the Longitudinal Health Insurance Database (LHID) for use in medical research. Demographic data, medications, treatments (including operations), and disease diagnoses (coded based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)) for patients attending health-care facilities due to health issues were recorded in the NHIRD. Health facilities that are enrolled in the Taiwan National Health Insurance (NHI) include local clinics, community hospitals, regional hospitals, and medical centers. The Taiwan NHI covers almost all primary, secondary, tertiary, and quaternary health-care facilities in Taiwan, with the exception of some local clinics. The LHID is composed of historical claims data for one million patients who are randomly selected from the NHIRD. The NHRI encrypts patients' personal information for the protection of privacy and provides researchers with anonymous identification numbers that connect to the relevant claim information, including the patient's sex, date of birth, registry of medical services, and medication prescriptions. Patient consent was not needed for the NHID or LHID. Our study was also approved by the Ethics Review Board of China Medical University (CMU-REC-101-012).

Study design

The selection process used in our study is demonstrated in the flow chart in Fig. 1. The psychiatric patient cohort included patients who were diagnosed with a psychiatric illness (ICD-9-CM 291-293, 295-298, 300-301, 303-305, 308, and 311) between 2000 and 2008. Subjects prescribed with BZD for at least 2 months during the study period were identified and defined as the BZD cohort. The initial BZD treatment date was defined as the reference date. Patients younger than 20 years old at the time of the psychiatric diagnosis were excluded from our study. Participants who subsequently presented to an ED and were diagnosed as DSP (ICD-9-CM 960-979 and E930-E949) before December 31, 2009 were included in the DSP study group, and the date of the DSP diagnosis was used as the index date. The control study group contained ten participants from the remaining members of the psychiatric patient cohort for each DSP group participant. Control participants were randomly frequency matched to DSP participants based on age category, sex, and the year of enrollment in the psychiatric patient cohort. The follow-up period for all participants ended on December 31, 2009.

The following BZDs were selected for analysis: clonazepam (ATC code: N03AE01), diazepam (ATC code:

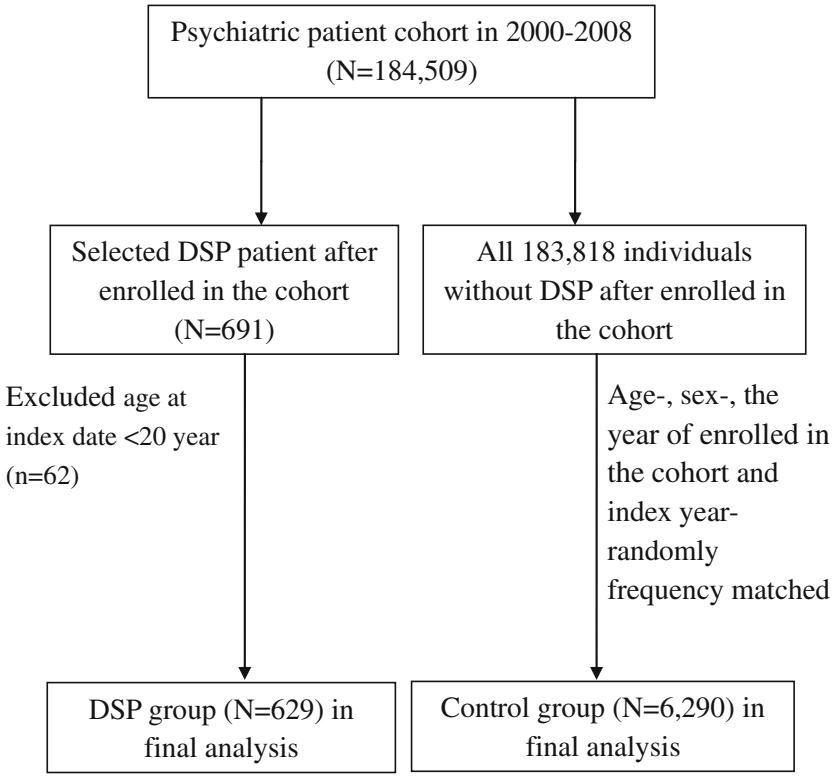

Fig. 1 Flow diagram for patients presenting with deliberate self-poisoning (*DSP*) who were enrolled in this study

N05BA01), oxazepam (ATC code: N05BA04), lorazepam (ATC code: N05BA06), bromazepam (ATC code: N05BA08), alprazolam (ATC code: N05BA12), nordazepam (ATC code: N05BA16), fludiazepam (ATC code: N05BA17), cloxazolam (ATC code: N05BA22), lorazepam combinations (ATC code: N05BA56), flurazepam (ATC code: N05CD01), nitrazepam (ATC code: N05CD02), flunitrazepam (ATC code: N05CD03), estazolam (ATC code: N05CD04), triazolam (ATC code: N05CD05), lormetazepam (ATC code: N05CD06), and midazolam (ATC code: N05CD08).

The average BZD prescribed dose was calculated as the total cumulative BZD dose in grams divided by the duration of BZD use (from prescription to the index date in years). The average benzodiazepine dose was separated into three groups by dose tertiles (33rd and 66th percentiles). Because of the potential confounding effects, the disease history was also collected for sleep disorders (ICD-9-CM 780.5 and 307.4), anxiety disorders (ICD-9-CM 300.0, 300.2, 300.3, 308.3, and 309.81), schizophrenia (ICD-9-CM 295), depression (ICD-9-CM 296.2-296.3, 300.4, and 311), and bipolar disorder (ICD-9-CM 296.4-296.6, 296.80).

Statistical analysis

The distribution of the study population based on the demographic characteristics and the disease history data were analyzed. To evaluate differences among the study groups, the chi-squared test was used for categorical variables, and Student's *t* test was used for continuous variables. The odds ratio (OR) and 95 % confidence interval (95 % CI) were measured for each comparison to estimate the associations between BZD use and DSP using logistic regression. Adjusted odds ratios (AORs) were also determined after adjusting for potential confounders. To evaluate the dose response of the association between average BZD dose and DSP, the average BZD dose was treated as a continuous variable across the range of average doses to evaluate trends in DSP diagnosis using logistic regression. All data management and the statistical analyses were performed using SAS 9.1.3 software (SAS Institute, Cary, NC, USA). All statistical tests were two-sided, and associations with a p value less than 0.05 were considered statistically significant.

Results

A total of 184,509 patient files comprised the psychiatric patient cohort (Fig. 1). The DSP study group contained 629 participants, and the control group contained 6,290 participants.

The demographic characteristics of the study population are presented in Table 1. The DSP and control groups were similar in age (42.4±17.1 vs. 42.3±17.1 years, p=0.9668) and had similar sex ratios (p=1.0000). Approximately 83.5 % of the patients had previously received BZD treatment. Psychiatric patients with a DSP history were more

Table 1 The demographic characteristic and psychiatric disease history for DSP and control group during 2000–2009

Variable	DSP N=629 (%)	Control group N=6,290 (%)	OR (95 % CI)	p value
Age, years (SD)[a]	42.4 (17.1)	42.3 (17.1)		0.9668
<40	331 (52.6)	3,310 (52.6)	Ref	
40–59	199 (31.6)	1,990 (31.6)	1.00 (0.83–1.20)	
≥60	99 (15.7)	990 (15.7)	1.00 (0.79–1.27)	
Sex				1.0000
Female	420 (66.8)	4,200 (66.8)	Ref	
Male	209 (33.2)	2,090 (33.2)	1.00 (0.84–1.19)	
BZD prescription (ref = no)	525 (83.5)	3,341 (53.1)	4.46 (3.59–5.53)	<0.0001
Disease history				
DSP history (ref = no)	40 (6.4)	32 (0.5)	13.27 (8.28–21.29)	<0.0001
Sleep disorder (ref = no)	297 (47.2)	948 (15.1)	5.04 (4.25–5.98)	<0.0001
Anxiety (ref = no)	249 (39.6)	895 (14.2)	3.95 (3.32–4.70)	<0.0001
Schizophrenia (ref = no)	46 (7.3)	63 (1.0)	7.80 (5.28–11.52)	<0.0001
Depression (ref = no)	208 (33.1)	198 (3.1)	15.20 (12.22–18.91)	<0.0001
Bipolar (ref = no)	30 (4.8)	17 (0.3)	18.48 (10.13–33.7)	<0.0001

Anxiety: 300.0, 300.2, 300.3, 308.3, and 309.81; sleep disorder: 780.5 and 307.4; schizophrenia: 295; depression: 296.2–296.3, 300.4, and 311; and bipolar: 296.4–296.6 and 296.80

SD standard deviation, *BZD* benzodiazepines

[a]Student's *t* test

likely to present with repeat episodes of DSP (6.4 vs. 0.5 %, p<0.0001). Psychiatric patients who presented with DSP had a higher proportion of BZD use (83.5 vs. 53.1 %, p< 0.0001), sleep disorders (44.8 vs. 14.4 %, p<0.0001), and anxiety disorders (39.6 vs. 14.2 %, p<0.0001).

Psychiatric patients under BZD treatment and those with a history of DSP were significantly more associated with DSP diagnosis in EDs (OR=4.46, 95 % CI=3.59–5.53 and OR=13.27, 95 % CI=8.28–21.29, respectively, both p< 0.0001) compared with psychiatric patients who did not receive BZD treatment, and patients with other psychiatric diseases were more likely to be diagnosed with DSP. Sleep disorder (OR=5.04, 95 % CI=4.24–5.98, p<0.0001), anxiety disorder (OR=3.95, 95 % CI=3.32–4.70, p<0.0001), schizophrenia (OR=7.80, 95 % CI=5.28–11.52, p<0.0001), depression (OR=15.20, 95 % CI=12.22–18.91, p<0.0001), and bipolar disorder (OR=18.48, 95 % CI=10.13–33.7, p<0.0001) diagnoses were significantly associated with the diagnosis of DSP at EDs.

After adjusting for age, sex, anxiety disorder, sleep disorder, depression, schizophrenia, and bipolar disorder as potential confounders, BZD use remained significantly associated with DSP (AOR=2.47, 95 % CI=1.93–3.17, p<0.0001; Table 2). All average cumulative BZD dose ranges analyzed were significantly associated with DSP (<0.005 g/year, AOR=1.75, 95 % CI=1.28–2.39, p=0.0004; 0.005–0.04 g/year, AOR= 2.57, 95 % CI=1.93–3.42, p<0.0001; and >0.04 g/year, AOR=4.30, 95 % CI=3.17–5.83, p<0.0001). Regression analysis also showed a significant dose–response association between average BZD dose and DSP diagnosis (p<0.0001).

The relationship between duration of BZD use before DSP events and DSP was analyzed; regardless of the duration of BZD treatment (i.e., within 1 week, 1 month, or 1 year prior to the index date of the DSP event at EDs), patients receiving BZD treatment were significantly associated with DSP events at EDs (Table 3). Patients with a BZD treatment duration of only 1 week were more likely to present with DSP than those treated for 1 month, 3 months, or 1 year (<1 week, AOR=5.67, 95 % CI=3.90–8.25; <1 month, AOR=5.47, 95 % CI=4.25–7.04; <3 months, AOR=4.66, 95 % CI=3.71–5.85; <6 months, AOR=4.23, 95 % CI=3.40–5.26; <1 year, AOR=3.72, 95 % CI=3.01–4.59, all p<0.0001).

Limitation

The limitations of our study include the limited nature of the clinical data that were collected from the NHIRD, the difficulty associated with controlling for confounding factors because of the retrospective study design, and the incomplete verification of data in the NHIRD. The NHIRD does not provide detailed information regarding smoking habits, disease severity markers, alcohol consumption, body mass index, physical activity, socioeconomic status, or family history, which all represent possible confounding factors for our analysis. The registries in the NHI claims system were primarily designed for administrative billing, and the registry data are not subjected to the stringent levels of verification that are appropriate for many types of scientific studies. We were unable to contact the patients directly to obtain more information on their use of BZDs because the participants remained anonymous. Furthermore, dose equivalence weighting and disease severity analysis were difficult to apply due to the lack of laboratory data and detailed clinical information. The relationship between substance abuse, DSP, and BZD

Table 2 Effects of BZDs and dose response on psychiatric patients receiving BZD prescriptions

Variable	OR (95 % CI)	*p* value	AOR (95 % CI)	*p* value
Benzodiazepine treatment				
No	Ref		Ref	
Yes	4.46 (3.59–5.53)	<0.0001	2.44 (1.90–3.12)	<0.0001
Average benzodiazepine dose, g/year				
No	Ref		Ref	
≤0.005	1.84 (1.36–2.49)	<0.0001	1.74 (1.27–2.37)	0.0005
0.005–0.04	3.20 (2.46–4.17)	<0.0001	2.54 (1.91–3.38)	<0.0001
>0.04	9.42 (7.46–11.91)	<0.0001	4.19 (3.09–5.69)	<0.0001
p value for trend				

Model was adjusted for age, sex, anxiety, sleep disorder, depression, schizophrenia, and DSP history

AOR adjusted OR

prescriptions was also not established because the substance abuse information database was not connected to the NHIRD. However, the data from the NHIRD regarding BZD prescriptions, the diagnosed psychiatric illness, and the coding of DSP patients visiting EDs were highly reliable, and the results of our study indicate that further studies, such as population-based, unbiased, randomized, observational trials, are warranted to confirm the causal relationships between DSP and BZD use.

Discussion

Prescribing BZDs for sleep and anxiety disorders is a common psychiatric practice because of their relative safety and the rare occurrence of death following overdose (Longo and Johnson 2000). There is little doubt of the therapeutic efficacy of BZDs in reducing anxiety, inducing sleep, and quelling panic symptoms (Longo and Johnson 2000; Bandelow et al. 2012). The anxiolytic and hypnotic efficacy of BZDs has been well established by numerous studies. Compared with antidepressants, which have a longer onset of action but are the best agents for the long-term treatment of anxiety disorders, and anticonvulsants and antipsychotics, which are effective but have an intermediate onset of action, patients with these disorders often prefer BZDs because these agents have immediate effects to treat fluctuating conditions if patients use BZDs judiciously (Longo and Johnson 2000; American Psychiatric Association 1990). However, the greatest asset is also their greatest liability: drugs that work immediately tend to be addictive. It is difficult to evaluate and optimally prescribed dosage for anxiety and insomnia patients taking BZDs during their routine follow-up because most patients typically ask for more drugs, not fewer (Prescott et al. 2009; Sansone and Sansone 2012).

The relationships among BZD therapy, DSP, and suicide have been reviewed (Neutel and Patten 1997; Neale and Smith 2007; Centers for Disease Control and Prevention 2012). Previous studies have suggested that BZD use may

Table 3 Effects of BZDs on psychiatric patients receiving BZD prescriptions, by various periods of BZD use

BZDs treatment	OR (95 % CI)	*p* value	AOR (95 % CI)	*p* value
Within 1 week prior to index date				
No	Ref		Ref	
Yes	15.63 (11.46–21.33)	<0.0001	5.61 (3.85–8.17)	<0.0001
Within 1 month prior to index date				
No	Ref		Ref	
Yes	12.55 (10.24–15.38)	<0.0001	5.41 (4.21–6.96)	<0.0001
Within 3 months prior to index date				
No	Ref		Ref	
Yes	9.41 (7.85–11.28)	<0.0001	4.58 (3.65–5.77)	<0.0001
Within 6 months prior to index date				
No	Ref		Ref	
Yes	7.96 (6.69–9.48)	<0.0001	4.17 (3.35–5.18)	<0.0001
Within 1 year prior to index date				
No	Ref		Ref	
Yes	6.58 (5.55–7.81)	<0.0001	3.66 (2.96–4.52)	<0.0001

Model was adjusted for age, sex, anxiety, sleep disorder, depression, schizophrenia, and DSP history

AOR adjusted OR

be associated with DSP events and suicide attempts (Neutel and Patten 1997; Neale and Smith 2007), particularly in elderly people (Carlsten et al. 2003; Ticehurst et al. 2002). In our study, the cumulative BZD doses were significantly associated with increased DSP events at EDs, and the effects of BZD usage were significant if the prescription duration was greater than 1 month. Patients with underlying psychiatric illnesses, such as schizophrenia, depression, and bipolar disorder, and patients who just started to receive BZD treatment had an even higher risk of DSP. After we adjusted for age, sex, anxiety, sleep disorder, depression and schizophrenia, and DSP history, the adjusted OR for psychiatric patients visiting the ED due to DSP in patients who took BZDs remained 2.5-fold higher than that in patients who did not take BZDs. This finding suggests that psychiatrists typically prescribe or that patients typically take higher doses of BZDs to relieve psychiatric symptoms such as anxiety and poor sleep quality, which are the most common symptoms for patients with unstable psychiatric illness (Li et al. 2010; Baylé et al. 2011). Patients taking BZDs have been observed to develop tolerance, dependence, and dose escalation, and studies have shown that both patients and psychiatrists are likely to choose higher dosages to relieve persistent symptoms (Prescott et al. 2009; Sansone and Sansone 2012); therefore, patients who do not respond favorably despite a high therapeutic BZD dosage may choose to take a much higher dose of BZDs, resulting in DSP events. Thus, psychiatrists should be aware of this phenomenon and focus more on patients' unstable emotions and underlying psychiatric illnesses to provide other psychological or social assistances, prescribe antidepressants or antipsychotics that have stable and prolonged effects, and treat potential addiction behaviors, rather than prescribing BZDs, which often only have immediate and short-term effects (Baylé et al. 2011).

As in other countries, DSP events at EDs in Taiwan are regarded as an important warning sign for suicide behaviors that require action. Previous studies have established a relationship between DSP and suicide behaviors and have suggested that aggressive actions should be taken to follow up after DSP events to prevent suicide (Skegg 2005; Hawton et al. 2003). In Taiwan, psychiatric patients with a high-risk status and those that have previously attempted DSP have been required to report to a suicide prevention center since 2006 to undergo aggressive suicide prevention strategies (National Taiwan Suicide Prevention Center 2006; Department of Health 2011).

In conclusion, BZDs prescribed to psychiatric outpatients were associated with the incidence of DSP at EDs. Furthermore, DSP events at EDs were significantly associated with BZD doses, and the effects of BZD usage were significant if the prescription duration was greater than 1 month. Our results indicate that vigilant evaluation of the psychiatric status of patients receiving BZD therapy is critical for the prevention of DSP events.

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Conflict of interest All authors state that they have no conflicts of interest.

References

American Psychiatric Association (1990) Benzodiazepine dependence, toxicity, and abuse: a task force report of the American Psychiatric Association. American Psychiatric Publishing, Washington

Bandelow B, Sher L, Bunevicius R, Hollander E, Kasper S, Zohar J, Möller HJ, WFSBP Task Force on Mental Disorders in Primary Care; WFSBP Task Force on Anxiety Disorders, OCD and PTSD (2012) Guidelines for the pharmacological treatment of anxiety disorders, obsessive–compulsive disorder and posttraumatic stress disorder in primary care. Int J Psychiatry Clin Pract 16:77–84

Baylé FJ, Blanc O, De Chazeron I, Lesturgeon J, Lançon C, Caci H, Garay RP, Llorca PM (2011) Pharmacological management of anxiety in patients suffering from schizophrenia. Encephale 37(Suppl 1):S83–S89

Berger A, Edelsberg J, Sanders KN, Alvir JM, Mychaskiw MA, Oster G (2012) Medication adherence and utilization in patients with schizophrenia or bipolar disorder receiving aripiprazole, quetiapine, or ziprasidone at hospital discharge: a retrospective cohort study. BMC Psychiatry 12:99

Carlsten A, Waern M, Holmgren P, Allebeck P (2003) The role of benzodiazepines in elderly suicides. Scand J Public Health 31:224–228

Centers for Disease Control and Prevention (2012) Suicides due to alcohol and/or drug overdose: a data brief from the National Violent Death Reporting System. http://www.cdc.gov/violenceprevention/nvdrs/nvdrs_data_brief.html. Accessed 27 Aug 2012

Cook R, Allcock R, Johnston M (2008) Self-poisoning: current trends and practice in a U.K. teaching hospital. Clin Med 8:37–40

Cox S, Kuo C, Jamieson DJ, et al. (2011) Poisoning hospitalisations among reproductive-aged women in the USA, 1998-2006. Inj Prev 17:332–337

Department of Health (2011) Major causes of death analysis in Taiwan 2012. http://www.doh.gov.tw/CHT2006/DisplayStatisticFile.aspx?d=84766&s=1. Accessed April 2013

Fathelrahman AI, Ab Rahman AF, Mohd Zain Z (2008) Self-poisoning by drugs and chemicals: variations in demographics, associated factors and final outcomes. Gen Hosp Psychiatry 30:467–470

Fliege H, Lee JR, Grimm A, Klapp BF (2009) Risk factors and correlates of deliberate self-harm behavior: a systematic review. J Psychosom Res 66:477–493

Hawton K, Zahl D, Weatherall R (2003) Suicide following deliberate self-harm: long-term follow-up of patients who presented to a general hospital. Br J Psychiatry 182:537–542

Hawton K, Bergen H, Casey D, Simkin S, Palmer B, Cooper J, Kapur N, Horrocks J, House A, Lilley R, Noble R, Owens D (2007) Self-harm in England: a tale of three cities. Multicentre study of self-harm. Soc Psychiatry Psychiatr Epidemiol 42:513–521

Li SX, Lam SP, Yu MW, Zhang J, Wing YK (2010) Nocturnal sleep disturbances as a predictor of suicide attempts among psychiatric outpatients: a clinical, epidemiologic, prospective study. J Clin Psychiatry 71:1440–1446

Lin TJ, Hsueh CC, Shih YL, Tsai JL, Tsai MS (2003) Drug overdoses in an epidemiologic report of Kaohsiung Poison Control Center. Taiwan Crit Care Med 5:143–150

Longo LP, Johnson B (2000) Addiction: part I. Benzodiazepines—side effects, abuse risk and alternatives. Am Fam Physician 61:2121–2128

Madsen T, Agerbo E, Mortensen PB, Nordentoft M (2012) Predictors of psychiatric inpatient suicide: a national prospective register-based study. J Clin Psychiatry 73:144–151

National Taiwan Suicide Prevention Center (2006) Annual report for National Taiwan Suicide Prevention Center. http://www.tspc.doh.gov.tw/tspc/portal/center/index.jsp?sno=85. Accessed 28 Aug 2012

Neale G, Smith AJ (2007) Self-harm and suicide associated with benzodiazepine usage. Br J Gen Pract 57:407–408

Neutel CI, Patten SB (1997) Risk of suicide attempts after benzodiazepine and/or antidepressant use. Ann Epidemiol 7:568–574

Perry IJ, Corcoran P, Fitzgerald AP, Keeley HS, Reulbach U, Arensman E (2012) The incidence and repetition of hospital-treated deliberate self harm: findings from the world's first national registry. PLoS One 7:e31663

Prescott K, Stratton R, Freyer A, Hall I, Le Jeune I (2009) Detailed analyses of self-poisoning episodes presenting to a large regional teaching hospital in the UK. Br J Clin Pharmacol 68:260–268

Rhodes A, Bethell J, Jaakkimainen RL, Thurlow J, Spence J, Links PS, Streiner DL (2008) The impact of rural residence on medically serious medicinal self-poisonings. Gen Hosp Psychiatry 30:552–560

Sansone RA, Sansone LA (2012) Antidepressant adherence: are patients taking their medications? Innov Clin Neurosci 9:41–46

Skegg K (2005) Self-harm. Lancet 366:1471–1483

Ticehurst S, Carter GL, Clover KA, Whyte IM, Raymond J, Fryer J (2002) Elderly patients with deliberate self-poisoning treated in an Australian general hospital. Int Psychogeriatr 14:97–105

Watve SV, Sivan M, Raza WA, Jamil FF (2012) Management of acute overdose or withdrawal state in intrathecal baclofen therapy. Spinal Cord 50:107–111

Zakiullah N, Saleem S, Sadiq S, Sani N, Shahpurwala M, Shamim A, Yousuf A, Khan MM, Nayani P (2008) Deliberate self-harm: characteristics of patients presenting to a tertiary care hospital in Karachi, Pakistan. Crisis 29:32–37