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Original article

The prevalence of benzodiazepines utilization and its association with falls among Saudi older adults; results from the Saudi national survey for elderly Health (SNSEH)

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Purpose: First, to determine benzodiazepines prevalence (BDZs) among Saudi older adults (SOA); Second, to quantify the association between BDZs use and falls among SOA. Third, to determine falls effect on all-cause mortality among SOA.
Methods: This is a cross-sectional study that used the Saudi National Survey for Elderly Health; a nationally-representative, population-based survey. Participants were asked about BDZs use and falls history during the 12 months prior to the interview. Demographics, medications, comorbidities and housing conditions were used as covariates. Multiple imputation was used to impute missing data. Modified poisson multivariable regression was used to study the association between BDZs and falls. Cox- proportional hazard regression was used to determine falls effect on mortality over nine years period.
Results: Among 2946 SOA, BDZs prevalence was 4%. Around 13% reported falls. In the multivariable regression, relative risk (RR) of falls was 2 comparing BDZs users to non-users (95CI%: 1.02–3.99). Antidepressants (RR = 1.72; 95%CI: 1.10–2.74), laxatives (RR = 1.38; 95%CI: 1.11–1.7), low body mass index (RR = 1.94; 95%CI: 1.33–2.84), mild cognitive impairment (RR = 1.56; 95%CI: 1.21–2.03), high door steps (RR = 1.54; 95%CI: 1.23–1.93) and insufficient illumination (RR = 1.38; 95%CI: 1.11–1.71) increased falls risk. Lastly, the hazard ratio of falls on death was 1.48 (95%CI: 1.17, 1.89) over nine years.
Conclusion: Despite the recommendation against BDZs use among older adults, still there were subjects who were prescribed these drugs. falls are common among SOA. Preventive strategies such medication therapy management, nutrition improvement, elderly-friendly housing structures can reduce the prevalence of falls and consequent increase in mortality among SOA.

1. Introduction

The association between benzodiazepines use and falls risk, or fall-related complications (i.e., injuries, fracture) has been reported by several researchers in the last two decades (Chang et al., 2011; Rossat et al., 2011; de Vries et al., 2013; Softic et al., 2013; Ballokova et al., 2014). One of the earlier studies in this area demonstrated an increased hospitalization rate from falls within 4 weeks after the first BDZs prescription, especially in older adults (Neutel et al., 1996). Another study showed a 44% increased nocturnal falls risk among current benzodiazepine users who live in nursing homes (Ray et al., 2000). Furthermore, a systematic review of 23 studies showed that benzodiazepines use was associated with a significantly increased fractures risk; Relative Risk (RR): 1.34 (95% Confidence Interval (CI): 1.24, 1.45) (Takkouche et al., 2007). Falls are a common reason for injuries and hospitalizations among older adults. It is associated with significant morbidity and

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mortality worldwide (Huang et al., 2012). Approximately one-third of adults aged 65 years and older fall annually, a proportion that rises with age (World Health Organization, 2007). Benzodiazepines (BDZs) are sometimes prescribed in older adults' patients for anxiety or insomnia management (Bogunovic and Greenfield, 2004). Aside from confusion risk and tolerance development, BDZs use in older adults is considered one of the main risk factors for falls due to their negative impacts on cognitive functions (Leipzig et al., 1999; Arroll, 2009; Woolcott et al., 2009). Sensitivity to benzodiazepine medications increases with age, which contributes to the increased injuries risk from falls among older adults population (Bartlett et al., 2009). Therefore, the American Geriatrics Society Beers Criteria recommend that BDZs use to be avoided in older adults (American Geriatrics Society, 2015).

The association between benzodiazepines use and falls risk, or fall-related complications (i.e., injuries, fracture) has been reported by several researchers in the last two decades (Chang et al., 2011; Rossat et al., 2011; de Vries et al., 2013; Softic et al., 2013; Ballokova et al., 2014). One of the earlier studies in this area demonstrated an increased hospitalization rate from falls within 4 weeks after the first BDZs prescription, especially in older adults (Neutel et al., 1996). Another study showed a 44% increased nocturnal falls risk among current benzodiazepine users who live in nursing homes (Ray et al., 2000). Furthermore, a systematic review of 23 studies showed that benzodiazepines use was associated with a significantly increased fractures risk; Relative Risk (RR): 1.34 (95% Confidence Interval (CI): 1.24, 1.45) (Takkouche et al., 2007).

Despite existing concerns with benzodiazepines use in older adult patients, their use among this population remains high. Over a 10-year period, benzodiazepines were prescribed for older adults in 12.4% and 10.5% of all visits made to the United States (US) emergency departments and ambulatory care clinic, respectively (Marra et al., 2015). A recent study that used prescribing data of 60% of all retail pharmacies in the U.S. demonstrated that 9% of older adults are using benzodiazepines (Olfson et al., 2015). Interestingly, older adult patients with pre-existing risk factors for falls were more likely to receive benzodiazepines (Bartlett et al., 2009). In Saudi Arabia, older adults represent approximately 3.2% of the general population (General Authority for Statistics, 2017). With the current aging population trend in Saudi Arabia, the burdens and costs associated with falls or fall-related complications represent substantial challenges to the health care system in Saudi Arabia (Khoja et al., 2018). A study from a military hospital found that benzodiazepines were prescribed in 4.4% of older adults (Al-Omar et al., 2013). However, due the limited generalizability of results and the lack of a national estimate of BDZs utilization, the primary objective of this study is to determine the prevalence of BDZs use among the Saudi older adults (SOA). In addition, we wanted to quantify the association between benzodiazepine use and falls risk among SOA and determine the effect of falls on all-cause mortality among the same population.

2. Methods

2.1. Data source

This study used data from the Saudi National Survey for Elderly Health (SNSEH). SNSEH is a nationally-representative, population-based cross sectional survey of 2946 Saudi older adults aged 60 years or older that was conducted between 2006 and 2007. This dataset is the most recent, and largest source of health-associated information about Saudi older adults. The Saudi ministry of health conducted this survey to guide the development of a national healthcare model for older adults. The study population was sampled based on two inclusion criteria: (1) age $\geq$ 60 i.e. the current retirement age in the country; (2) Saudi citizenship. The survey is described in details in a previous article (Khoja et al., 2018). In brief, in addition to demographic information, the survey contains questions about selected common comorbidities, medications use, physical examination findings, home safety concerns, social network and social services nearby the participants' residence. In 2015, the ministry of interior affairs was contacted to retrieve participants' vital status. Consequently, survival data for participants up until June 2015 was added to the dataset.

2.2. Study design and measures

SNSEH is a cross-sectional study that included subject 60 years or older. In the SNSEH, medication utilization was assessed by asking the subject to bring all medications he/she is actively using during the last 12 months since interview. Thus, the interviewer asked the subject about active BDZ use during the last 12 months. Benzodiazepines included alprazolam, diazepam, oxazepam, chlordiazepoxide, clorazepate, clonazepam, lorazepam, temazepam, triazolam, midazolam, quazepam and estazolam. Similarly, falls was defined as the occurrence of falls in the previous 12 months prior to the interview date. During the interview with study subjects at data collection time, subjects were asked about the history of major falls in the past 12 months prior to the interview. Major falls meant that the subject has fallen to the ground. Consequently, individuals who were about to fall were not considered fallen. To study the association between falls and BDZ, falls was used as the dependent variable in the statistical model while BDZs use was the main independent variable. The model adjustment was made for the following confounders; age, gender, region, education, income, marital status, residence urbanity, body mass index, cognitive impairment, hyptertension, diabetes mellitus, history of car crash, and home safety concerns such as existence of slippery floors, high door steps, insufficient illumination and living in high floor. In addition, medications that may increase falls risk such as laxatives, antidepressant, other sleep drugs and antihypertensive were also explored.

2.3. Statistical analysis

The cohort was described using frequencies and percentages for categorical variables and means and standard deviations for continuous variables. In addition, to assess factors associated with falls risk, characteristics of subjects who reported falls were compared with subjects who did not report falls using chi-square and Fisher's test for categorical variables and *t*-test for continuous variables. Since falls are considered a common outcome among older adults, logistic regression approach might overestimate the association. Therefore, relative risk was calculated through a modified Poisson multivariable regression, and variables with possible confounding effects were adjusted for (Zou, 2004). Multiple imputations were used for missing data (Fox-Wasylyshyn and El-Masri, 2005; Sterne et al., 2009; Schafer, 1999). The Hosmer-Lemeshow test and C-statistic test of the corresponding logistic regression analysis were used to test for goodness of fit (Hosmer et al., 1997). To study falls effect on survival, Cox-proportional hazard model was used. Subjects alive after June 2015 were censored. The Cox model was adjusted for age, gender, diabetes, ischemic heart disease, depression and cognitive impairment, cancer, stroke and kidney failure. Statistical analyses were done using STATA 14 (StataCorp.) (StataCorp, 2015). The study was approved by the institutional review board at the Imam Mohammad Bin Saud Islamic University (HAPO-01-R-011).

Table 1
Univariable and Bivariable analyses of the effect of Benzodiazepins on Falls among Saudi Older Adults 2006–2007 (N = 2946).

Characteristics	Total (N = 2946)		Falls during the last 12 months				Chi-squared P-value
			No (N = 2558)		Yes (N = 388)		
	n	(Col%)	n	(Row%)	n	(Row%)	
Benzodiazepines use							
No	2827	(96)	2468	(87.3)	360	(12.7)	<0.001
Yes	119	(4)	90	(75.9)	29	(24.1)	
Age (Years)							
60–65	1107	(37.6)	995	(89.8)	112	(10.2)	<0.001
66–70	678	(23)	597	(88.1)	81	(11.9)	
71–75	486	(16.5)	419	(86.3)	66	(13.7)	
76–80	329	(11.2)	279	(84.8)	50	(15.2)	
81–85	178	(6)	138	(77.6)	40	(22.4)	
86–90	99	(3.4)	76	(76.4)	23	(23.6)	
>90	69	(2.3)	54	(78.1)	15	(21.9)	
Gender							
Female	1461	(49.6)	1205	(82.5)	255	(17.5)	<0.001
Male	1485	(50.4)	1353	(91.1)	133	(8.9)	
Five regions of Saudi Arabia							
Central	684	(23.2)	589	(86.2)	94	(13.8)	0.236
Western	917	(31.1)	786	(85.7)	131	(14.3)	
Eastern	403	(13.7)	371	(91.9)	33	(8.1)	
Southern	739	(25.1)	623	(84.3)	116	(15.7)	
Northern	203	(6.9)	189	(93)	14	(7)	
Level of education							
Illiterate	2050	(69.6)	1728	(84.3)	323	(15.7)	<0.001
Less than 8 years	642	(21.8)	591	(92)	51	(8)	
Intermediate to High school	191	(6.5)	179	(94.1)	11	(5.9)	
University or higher	63	(2.1)	60	(95)	3	(5)	
Income (SR)							
>10,000	167	(5.7)	163	(97.4)	4	(2.6)	<0.001
9999–7500	121	(4.1)	118	(98)	2	(2)	
7499–5000	283	(9.6)	252	(89.1)	31	(10.9)	
4999–2500	689	(23.4)	607	(88.1)	82	(11.9)	
<2500	1687	(57.3)	1418	(84.1)	269	(15.9)	
Marital status							
Monogamy	1689	(57.3)	1519	(89.9)	170	(10.1)	<0.001
Polygamy	385	(13.1)	355	(92.2)	30	(7.8)	
Widowed	679	(23.1)	529	(77.8)	151	(22.2)	
Single	107	(3.6)	83	(77.8)	24	(22.2)	
Separated	86	(2.9)	72	(84.5)	13	(15.5)	
Urban vs. Rural							
Urban	2359	(80.1)	2041	(86.5)	318	(13.5)	0.645
Rural	587	(19.9)	517	(88.1)	70	(11.9)	
Antidepressants							
No	2453	(87.4)	353	(12.6)	2805	(95.2)	<0.001
Yes	105	(74.7)	36	(25.3)	141	(4.8)	
Laxatives							
No	2466	(83.7)	2168	(87.9)	298	(12.1)	0.008
Yes	480	(16.3)	389	(81.2)	90	(18.8)	
Other sleep drugs							
No	2528	(87.1)	373	(12.9)	2901	(98.5)	<0.001
Yes	30	(66.3)	15	(13.2)	45	(1.5)	
Antihypertensives							
No	1501	(88.6)	193	(11.4)	1694	(57.5)	0.002
Yes	1057	(84.4)	195	(15.6)	1252	(42.5)	
Joint pain drugs (Steroids or DMARDs)							
No	1471	(49.9)	1282	(87.2)	188	(12.8)	0.652
Yes	1475	(50.1)	1275	(86.4)	200	(13.6)	
Antidiabetics							
No	1562	(53)	1363	(87.2)	199	(12.8)	0.490
Yes	1384	(47)	1195	(86.3)	189	(13.7)	
Cancer							
No	2890	(98.1)	2512	(86.9)	378	(13.1)	0.974
Yes	56	(1.9)	46	(82.4)	10	(17.6)	
BMI WHO categories							
Less than 18.5	54	(1.8)	33	(62.3)	20	(37.7)	<0.001
From 18.5 to 25	836	(28.4)	706	(84.5)	129	(15.5)	
From 25 to 30	1114	(37.8)	977	(87.8)	136	(12.2)	

Table 1 (*continued*)

Characteristics	Total (N = 2946)		Falls during the last 12 months				Chi-squared P-value
			No (N = 2558)		Yes (N = 388)		
	n	(Col%)	n	(Row%)	n	(Row%)	
More than 30	943	(32)	841	(89.1)	102	(10.9)	
Cognitive impairment[a]							
Normal cognition	2415	(82)	2149	(89)	265	(11)	<0.001
Mild	349	(11.9)	282	(80.8)	67	(19.2)	
Moderate	118	(4)	77	(64.7)	42	(35.3)	
Severe	64	(2.2)	50	(77.7)	14	(22.3)	
Presence of slippery floors							
No	2417	(82)	2127	(88)	290	(12)	0.012
Yes	529	(18)	431	(81.4)	98	(18.6)	
Present of high door steps							
No	2516	(85.4)	2213	(88)	303	(12)	0.008
Yes	430	(14.6)	344	(80.1)	86	(19.9)	
Feeling unsteady							
No	2464	(83.6)	2179	(88.5)	284	(11.5)	0.002
Yes	482	(16.4)	378	(78.5)	104	(21.5)	
Insufficient illumination							
No	2648	(89.9)	2301	(86.9)	347	(13.1)	0.734
Yes	298	(10.1)	257	(86)	42	(14)	
Living in high floors in the house							
No	2326	(78.9)	2129	(91.5)	197	(8.5)	<0.001
Yes	620	(21.1)	429	(69.1)	192	(30.9)	
Feeling of dizziness							
No	2132	(72.4)	2007	(94.2)	125	(5.8)	<0.001
Yes	814	(27.6)	550	(67.6)	264	(32.4)	
History of car accident							
No	2824	(95.9)	2518	(89.2)	306	(10.8)	<0.001
Yes	122	(4.1)	39	(32.4)	82	(67.6)	

BMI: Body mass index; WHO: World Health Organization; Disease-Modifying Antiheumatic Drugs.
[a] Based on Short Portable Mental Status Questionnaire (SPMSQ).

3. Results

In this nationally representative sample that included 2946 SOA, BDZs prevalence was 4%. Approximately, 13.2% of the sample had a history of falls during the last twelve months prior the interview. While 24.1% of subjects on BDZs have history of falls during the previous 12 months prior to the interview date, only 12.7% of subjects who were not using BDZs have a history of falls during the same period (unadjusted Relative Risk (uRR) = 1.93; 95% confidence interval (95%CI):1.38–2.70). Females were more likely to report a history of falls than males (17.5% vs. 8.9%; P < 0.001). Characteristics of Saudi older adults fall status are shown in Table 1. Table 1. There was an inverse relationship between the levels of education, income, obesity and the risk of falls (p = <0.001, Table 1. In contrary, there was a semi-proportional relationship between cognitive impairment and history of falls (p = <0.001, Table 1.

The housing conditions also had an impact on the prevalence of falls among SOA. For instance, falls prevalence was higher among subjects who had high doorsteps compared to those who did not (19.9% vs. 12%, p = 0.008), among subjects who were living on higher floors in the house compared to those living in lower floors (30.9% vs. 8.5%, P = 0.001) and among subjects who had slippery floors compared to those who did not (18.6% vs. 12%, P = 0.012). Subjects with a history of car accidents had a high risk of falls compared to those without (67.6% vs. 10.8%, P < 0.001). With regards to medication use, older adults who reported using any antidepressants, antihypertensive, laxatives, or other sleep medications have a significantly higher risk of falls than older adults who were not on any of these drugs.

Using a multivariable regression model Table 2, users of benzodiazepines were two times more likely to have a history of falls compared to individuals not using benzodiazepines (adjusted RR = 2.01; 95%CI:1.02–3.99). The adjusted model indicated a good fit by the insignificant Hosmer-Lemeshow test (P = 0.502) and a C-statistic test of 0.80. History of car crash during last 12 months was the most significant predictor of falls risk with a RR of 4.22 (95%CI:3.40–5.24) compared to SOA who did not report car crash history. In this cohort, males were less likely to fall compared to females (RR = 0.72; 95% CI:0.55–0.94). Similarly, monthly income levels greater than 7500 Saudi Riyal (SAR) were associated with lower risk of falls. On the other hand, the risk of falls was 39% higher among widowed compared to married subjects (RR = 1.40; 95%CI: 1.09–1.79). Similarly, subjects who never married were 1.84 times more likely to report falling compared to subjects who were married (RR = 1.84; 95%CI: 1.24–2.75).

With respect to the association between BMI and falls, the risk of falls increased with subjects with low BMI Table 2. On the other hand, there was a positive relationship between the risk of falls and cognitive impairment. For instance, the risk of falls among subjects with mild cognitive impairment was higher compared to subjects with normal cognition (RR = 1.56; 95%CI: 1.21–2.03). Similar trend was seen with both moderate and severe cognitive impairment Table 2.

Housing conditions such as the presence of slippery floors, high doorsteps, insufficient illumination and living on higher floors remain to be important variables that increase the risk of falling in the adjusted model Table 2.

Table 2
Multivariable modified poisson regression of factors associated with falls among Saudi Older adult 2006–2007 (N = 2946).

Characteristics	RR	95% CI
Benzodiazepines use	2.014*	[1.017, 3.989]
Antidepressants	1.722*	[1.084, 2.736]
Benzodiazepines*Antidepressants	0.400*	[0.165, 0.974]
Age (Ref: 60–65)	1	[1,1]
66–70	1.11	[0.844, 1.462]
71–75	1.163	[0.867, 1.559]
76–80	1.01	[0.738, 1.383]
81–85	1.357	[0.960, 1.918]
86–90	1.033	[0.696, 1.532]
>90	1.378	[0.855, 2.220]
Gender (Ref: Female)	1	[1,1]
Male	0.721*	[0.553, 0.940]
Five regions of Saudi Arabia (Ref: Central)	1	[1,1]
Western	0.96	[0.745, 1.237]
Eastern	0.409***	[0.272, 0.614]
Southern	0.777	[0.603, 1.002]
Northern	0.472*	[0.265, 0.839]
Level of education (Ref: Illiterate)	1	[1,1]
Less than v8 years	0.857	[0.636, 1.153]
Intermediate to High school	0.881	[0.515, 1.506]
University or higher	1.083	[0.365, 3.214]
Income (SR) (Ref: < 2,500)	1	[1,1]
>10000	0.287**	[0.121, 0.685]
9999–7500	0.147**	[0.0375, 0.580]
7499–5000	1.039	[0.729, 1.482]
4999–2500	0.996	[0.778, 1.276]
Marital status (Ref: Monogamy)	1	[1,1]
Polygamy	1.031	[0.724, 1.468]
Widowed	1.396**	[1.089, 1.789]
Single	1.843**	[1.238,2.745]
Separated	1.113	[0.662, 1.870]
Residence (Ref: Urban)		
Rural	0.804	[0.614, 1.052]
Other sleep drugs	1.818**	[1.194, 2.769]
Antihypertensives	1.283	[0.981, 1.678]
Laxatives	1.378**	[1.111, 1.710]
Joint pain drugs (Steroids or DMARDs)	0.98	[0.811, 1.185]
Antidiabetics	1.112	[0.761, 1.625]
Cancer	1.183	[0.613, 2.281]
Diabetes mellitus	1.047	[0.715, 1.532]
Hypertension	0.876	[0.668, 1.149]
Cognitive impairment[ℵ] (Ref: Normal)	1	[1,1]
Mild	1.563***	[1.205, 2.026]
Moderate	2.747***	[1.998, 3.777]
Severe	2.056***	[1.370,3.087]
BMI WHO categories (Ref:18.5 to 25)	1	[1,1]
<18.5	1.940***	[1.327, 2.836]
From 25 to 30	1.029	[0.817, 1.297]
More than 30	0.92	[0.708, 1.196]
Presence of slippery floors	1.420**	[1.148,1.757]
Present of high door steps	1.539***	[1.228, 1.929]
Insufficient Illumination	1.376**	[1.110, 1.706]
Living in high floors in the house	0.845	[0.612, 1.167]
History of car accident	4.222***	[3.404, 5.238]
Observations:	2946	

RR: Relative Risk; 95%CI: 95% Confidence Interval; BMI: Body mass index; WHO: World Health Organization; DMARDs: Disease-Modifying Antiheumatic Drugs.
† based on Short Portable Mental Status Questionnaire (SPMSQ).
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

Finally, out of 2068 subjects whose mortality information were available for analysis, there were 580 cases of death (28.05%). Percentage of death was significantly higher among subjects who reported falls (39.1%) compared to subjects who did not (26.65%; P < 0.001). The adjusted hazard of death between 2006 and 2015 was 51% greater among subjects who reported falls compared to those who did not (adjusted HR = 1.48; 95%CI: 1.17,1.89; Fig. 1).

4. Discussion

In this nationally representative, population-based study, the risk of falls was two times greater among subjects who were on benzodiazepines compared to subjects who were not (RR = 2.01; 95%CI:1.02–3.99). Several, studies and *meta*-analyses (Ray et al., 2000; World Health Organization, 2007; Woolcott et al., 2009; Olfson et al., 2015; Al-Omar et al., 2013; Diaz-Gutierrez et al., 2017) have concluded similar results in different settings. Benzodiazepines have been on Beer's list for medications not recommended for elderly since the first version in 1991 (Beers et al., 1991). Despite this recommendation, in 2007, 4% of SOA were prescribed benzodiazepines. These drugs are used as sleep aids and/or anxiolytics in older populations (Bogunovic and Greenfield, 2004). Even though experts may still use short-acting benzodiazepines in achieving this goal (Balon et al., 2015), there is still a high risk of falling reported by repeated use of these agents (Ray et al., 2000; Passaro et al., 2000). Furthermore, the evidence suggests that many older adults have been prescribed long-acting benzodiazepines in doses exceeding the ceiling doses expected in their age (Martinez-Cengotitabengoa et al., 2017).

Recently antidepressants have been implicated in increasing the risk of falls. Selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) are known to increase drowsiness and dizziness which increases the risk of falls (Arfken et al., 2001). Among SOA in this cohort, the risk of falls was 72% greater among antidepressant users compared to non-users (RR = 1.72; 95%CI:1.10–2.74). Furthermore, there is mounting evidence that SSRIs are associated with hip fractures and falls more than TCAs (Arfken et al., 2001; Coupland et al., 2011; Ensrud et al., 2002; Hien le et al., 2005; Liu et al., 1998; Thapa et al., 1998).

Paradoxically, one would expect a higher risk of falls among subjects who were on both benzodiazepines and antidepressant. However, the data in this study showed a decreased risk with this combination (RR = 0.40; 95%CI:0.17–0.97). A possible explanation of this finding is that the combined effects of both pills might further increase the risk of dizziness and sleepiness among older adults, henceforth, it may increase walking dependency and/or limit ambulation leading to the observed reduction in falls risk. Also, due to the cross-sectional nature of the study, temporal relationship cannot be assessed. Consequently, reverse causality cannot be precluded where falls may have occurred first which eventually led to the prescribing of antidepressants and benzodiazepines.

In this study, falls risk was lesser in males compared to females (RR = 0.72; 95%CI:0.55–0.94). The observed difference may be explained by the biological differences between them after menopause (Geusens et al., 2003). For instance, females tend to lose bone density earlier and faster than males which may contribute to the eventual increase in the risk of falls (Duckham et al., 2013; Stevens and Sogolow, 2005; Alswat, 2017). In addition, due to the fact that females are less likely to be involved in muscle building activities, women tend to lose muscle mass over time more frequently than men (World Health Organization, 2007). Furthermore, a recent systematic review that summarized osteoporosis research in Saudi population suggested a higher incidence of osteoporosis among females (34%) compared to males (30.7%), which might increase the risk of falls due to bone fragility (Sadat-Ali et al., 2012).

Interestingly, there was no difference between the western region and the central region with regards to the risk of falls (RR = 0.96; 95%CI:0.75–1.24). On the other hand, all other regions in the kingdom were associated with lower risk of falls compared to the central region. Geographic variations always act as proxy for other factors that may contribute to the association between BDZs and Falls. Geographic variations in falls are related to sub-

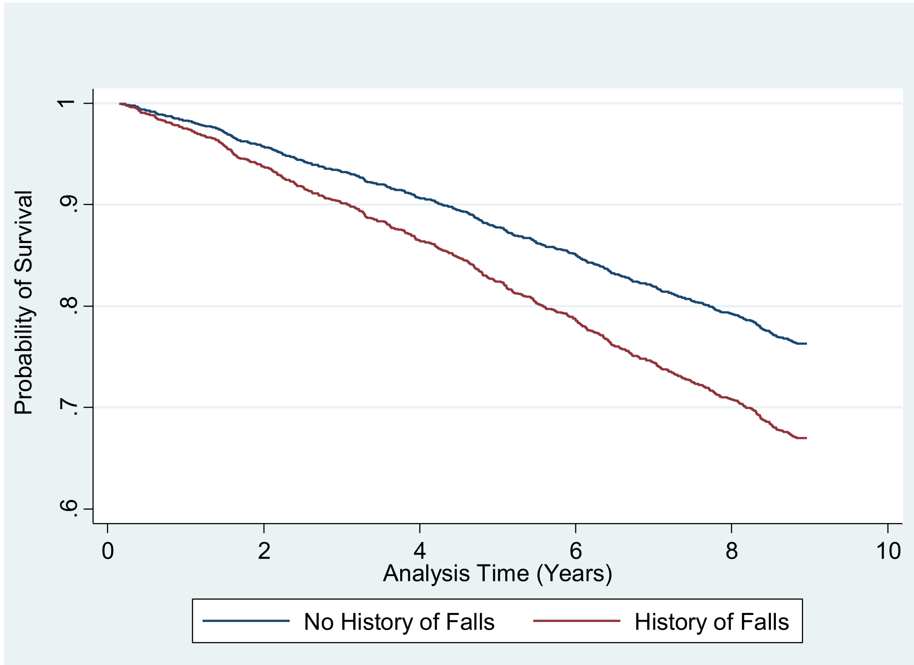

Fig. 1. Survival Curves based on Cox-Proportional Hazard Regression for the Effect of Falls on Survival among Saudi Older Adults Between 2006 and 2015.

jects' characteristics, neighborhood physical status as well housing status. (World Health Organization, 2007) While certain factors regarding the subjects and housing status were included in the analysis, neighborhood physical status was not included which may explain current results. Therefore, in the absence of strong evidence about factors associated with geographic variations in falls among SOA, such area is considered an important gap that requires future research.

Among socioeconomic factors that were included in the model such as monthly income, level of education and urbanity of residence, there was a clear disparity in falls risk with different levels of monthly income. Noteworthy, once monthly income level reached 7500 SAR or higher, the risk of falls decreased by 85%. Income is a measure of socioeconomic status that may serve as a proxy for many other variables such healthy eating and drinking habits, accessibility to devices and non-medical and medical services that may reduce falling risk as well as more social and family support (Luukinen et al., 1996; Trujillo et al., 2011). These factors may explain the large magnitude of reduction in the risk of falls observed with higher monthly income levels in the study cohort. In other studies where these factors were available for analysis, income effect on falls was minimal or non-significant (Trujillo et al., 2011; Dunn et al., 1992; Galizia et al., 2008; Pressley et al., 2007; Tinetti et al., 1988). Therefore, policies that are based solely on increasing individual's income as a mean of reducing falls and subsequent morbidity and mortality might be insufficient to achieve such outcome (Ambrose et al., 2013).

Certain medication categories are associated with falls in elderly through different mechanisms. For instance, in this study, the use of laxatives was associated with falls risk by 38%. Laxatives increase the sense of urgency among older adults which, if accompanied with movement discoordination, may increase falls risk (Ambrose et al., 2013; Abreu et al., 2015; Bloch et al., 2010; Haring et al., 2013). On the other hand, older adults who had fallen may end up with fractures and disability. Such devastating consequences will increase the risk of constipation and the need for laxatives (De Giorgio et al., 2015; Spinzi et al., 2009). Like laxatives, antihypertensives can also increase falls risk either by increasing orthostatic hypotension and/or increasing urination urgency in case of diuretics (Ambrose et al., 2013). Therefore, medications taken by older adults should frequently be examined through collaborative efforts between physicians, pharmacists, and patients. To this end, comprehensive medication management clinics will become essential to prevent the undesired consequence of these drugs; namely, falls (Butler et al., 2015).

Underweight older adults had a higher risk of falls compared to those with normal weight (RR = 1.94, 95%CI = (1.33–2.84)). While many studies have focused on the effect of obesity on falls, fewer studies looked at low BMI on fall. Mazur K et al. reported that low BMI was associated with increased risk of falls. Consequently, in their study, there was an inverse relationship between BMI and falls risk (OR = 0.91; 95% CI = 0.83–0.99) (Mazur et al., 2016). Similarly, both Coutinho et al. and O'Neil et al. found that BMI $\leq$ 20 and BMI $\leq$ 18.5, respectively, were associated increased falls risk (Coutinho et al., 2008; O'Neil et al., 2015). Lower BMI has been associated with frailty syndrome that is linked not only falls but also to lower survival (Barreto Pde et al., 2012; Byard and Bellis, 2016).

Walking is a complex process that requires both sufficient cognition and functional locomotor ability. Cognitive impairment leads to poor balance which is manifested by gait asymmetry, postural sway, and slower walking; such factors have been shown to increase the risk of falls among older adults (Deandrea et al., 2010; Makizako et al., 2013; Woollacott, 1993). In our study, even mild cognitive impairment was associated with increased risk of fall among older adults (RR = 1.56; 95%CI: 1.21–2.03) indicating the importance of cognitive impairment screening as an approach to assess the risk of falls among elderly.

Unsuitable housing conditions such as high steps, slippery floors, and insufficient illumination have contributed to the increased risk of falls among Saudi older adults. On the patient-physician level, such modifiable conditions should be taken into considerations while assessing older adults' risk of falls during their annual checkup. In addition, such factors should also be considered in designing nursing homes, social welfare homes and community centers to reduce the risk of falls and subsequent increase in morbidity and mortality.

Road traffic crashes (RTC) in Saudi Arabia are among the highest worldwide (DeNicola et al., 2016; Fa et al., 2015). Annually, around half a million RTCs are being reported in Saudi Arabia with approximately 7% develop permanent injuries (Fa et al., 2015; Report: Saudi Arabia records 526,000 road accidents annually, 2016). Such complications are usually associated functional and cognitive disabilities that explain the strong relationship seen between RTCs and risk of falls (RR = 4.22; 95%CI: 3.40;5.24). In this study, the hazard of death over nine years period was 48% higher among subjects who reported a history of falls compared to those who did not. Several studies have reported a similar increase in mortality in different settings such nursing homes, hospitals and even among community-dwelling elderlies (Ayoung-Chee et al., 2014; Galizia et al., 2012; Kato et al., 2012; O'Neal et al., 2015; Sylliaas et al., 2009; Yohannes et al., 2016).

Our study has its own limitations; first, due to the cross-sectional design, it is hard to assess the temporal relationship between BDZs and falls. Second, despite our control for multiple confounding factors in assessing the relationship between BDZ and falls, the lack of certain factors in the database such as the use of antipsychotics, anticonvulsants or opioid analgesics does not preclude the existence of residual confounding. Lastly, lumping variables such steroids and disease modifying antirheumatic drugs on one group prevented assessing the effect of steroids on falls.

In conclusion, falls are common among Saudi older adults. Not only BDZs use was associated with increased risk of falls, many other factors such as laxatives, antihypertensives, antidepressants, low BMI, cognitive impairments, unsuitable housing conditions and car accidents history were also associated with increased falls risk. This study creates a national baseline for elderly research with respect to the association between BZDs and falls. It is worthwhile to study the same patient population to determine the change over time since this study. Preventive strategies such medication therapy management, nutrition improvement, elderly-friendly housing structures as well as enforced traffic rules should be warranted to reduce falls prevalence and consequent increase in mortality among SOA.

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