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Harmful alcohol use among acutely ill hospitalized medical patients in Oslo and Moscow: A cross-sectional study

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ABSTRACT

Background: The aim was to estimate the prevalence of harmful alcohol use in relation to socio-demographic characteristics among acutely ill medical patients, and examine identification measures of alcohol use, including the alcohol biomarker phosphatidylethanol 16:0/18:1 (PEth).

Methods: A cross-sectional study, lasting one year at one hospital in Oslo, Norway and one in Moscow, Russia recruiting acute medically ill patients (≥ 18 years), able to give informed consent. Self-reported data on socio-demographics, mental distress (Symptom Check List-5), alcohol use (Alcohol Use Disorder Identification Test-4 (AUDIT-4) and alcohol consumption past 24 h were collected. PEth and alcohol concentration were measured in whole blood.

Results: Of 5883 participating patients, 19.2% in Moscow and 21.1% in Oslo were harmful alcohol users, measured by AUDIT-4, while the prevalence of PEth-positive patients was lower: 11.4% in Oslo, 14.3% in Moscow. Men in Moscow were more likely to be harmful users by AUDIT-4 and PEth compared to men in Oslo, except of those being ≥ 71 years. Women in Oslo were more likely to be harmful users compared to those in Moscow by AUDIT-4, but not by PEth for those aged < 61 years.

Conclusions: The prevalence of harmful alcohol use was high at both study sites. The prevalence of harmful alcohol use was lower when assessed by PEth compared to AUDIT-4. Thus, self-reporting was the most sensitive measure in revealing harmful alcohol use among all groups except for women in Moscow. Hence, screening and identification with objective biomarkers and self-reporting might be a method for early intervention.

1. Introduction

Harmful alcohol use is estimated to be more prevalent among hospitalized patients compared to the general population, although data are limited (Moore et al., 1989; Roche et al., 2006; Roson et al., 2010; Smothers et al., 2004). Despite this, screening rates in Emergency Departments (EDs) are still low (Roson et al., 2016; Sanjuan et al., 2014). Hence, the ED might be the first contact point with the health care system, a venue for identification of harmful alcohol users and possible referral to treatment or brief interventions (Broyles et al., 2012).

There has been an increased focus on developing and evaluating methods to identify non-treatment-seeking individuals with harmful alcohol use presented to hospitals (Bogenschutz et al., 2011). Self-reporting might be subject to e.g. recall bias and social desirability, hence

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a blood alcohol biomarker such as phosphatidylethanol might serve as an objective alcohol measure (Hill-Kapturczak et al., 2018; Jain et al., 2014). Phosphatidylethanol is a group of glycerophospholipid molecules, hereinafter called phosphatidylethanol (PEth), with PEth 16:0/18:1 being the most abundant type in human blood (Gnann et., al., 2010). PEth is a direct biomarker formed in the membrane of red blood cells, only after alcohol intake (Gnann et al., 2010). PEth has been shown to correlate with self-reported data such as Alcohol Use Disorder Identification Test (AUDIT) and AUDIT-C (3 first items of AUDIT) (Francis et al., 2015; Piano et al., 2015) and can be measured in blood up to 4 weeks depending on the amount of alcohol consumed (Varga et al., 2000; Viel et al., 2012).

Norway and Russia differ in several aspects, including gross national income per capita (World Health Organization, 2016), health outcomes and health services (World Health Organization, 2016), and drinking patterns (World Health Organization, 2014). The per capita consumption is 7.5 liters in Norway and 11.7 liters in Russia (World Health Organization, 2018). Evidence suggests that various drinking patterns give rise to different health outcomes in population groups with the same level of consumption (Rehm et al., 2003a; World Health Organization, 2014). In this regard, binge drinking is associated with increased risk of cardiovascular disease, even in light to moderate drinkers (Rehm et al., 2017; World Health Organization, 2014). However, data on binge drinking and health consequences are still lacking (Rehm et al., 2017). Growing evidence suggests that screening questionnaires may provide additional information on the severity of drinking habits (Berger et al., 2013; Saitz et al., 2014). Studies from the general population- and drug injected users show that AUDIT-C scores provide more detailed information and are associated with objective biomarkers and in-depth interviews (Bradley et al., 2003; Jain et al., 2014; Rubinsky et al., 2013). The generalizability of these results to acute medically ill patients is unknown. Additionally, detection of harmful alcohol use is a challenge in a busy hospital setting and there is a need for prompt and reliable screening measures to identify alcohol use among acute medically ill patients (Kaarne et al., 2010).

Early identification of harmful alcohol use is essential because it could trigger a consultation for immediate treatment to reduce the chances for onset of alcohol withdrawal, which in some cases might be fatal. A hospital admission offers the possibility for timely and adequate interventions, including probable referral to treatment if the identification and screening of patients is integrated in the clinical practice.

1.1. Study aims

The primary aim of this study was to estimate the prevalence of harmful alcohol use by AUDIT-4 with reference to socio-demographic characteristics among acutely ill medical patients, in one hospital in Oslo and one hospital in Moscow.

The secondary aim of the study was to examine the performance of two screening measures to detect lower to higher patterns of alcohol use by using AUDIT-4 zones as gold standard.

2. Methods

2.1. Study design

A cross-sectional study conducted during 12 months. The study site in Oslo was Lovisenberg Diaconal Hospital, Medical Emergency Department with about 6000 admissions per year, and with a catchment area comprising four inner city boroughs. In Moscow the study site was V.P. Demikhov Hospital 68, with approximately 60 000 admissions per year and a catchment area consisting of a working class-central city region. Both hospitals are general hospitals, not specialized in treatment of alcohol harms and problems. Self-reported questionnaires were completed and a blood sample was collected. The recruitment was performed by ED-nurses, in Oslo. In Moscow, recruitment staff comprised addiction doctors. The recruitment of patients in both sites was performed seven days and nights per week from November 2016 through December 2017. The blood samples were analyzed at Oslo University Hospital and at Moscow Research and Practical Center on Addiction (MRPCA). Although we refer to Moscow and Oslo study sites/samples and countries, the samples were not designed to be representative for the cities or countries.

The study was approved by Regional Ethics Committee for South Eastern Norway (2015/2404), and by the Moscow Local Ethical Committee of MRPCA.

2.2. Participants

All eligible inpatients admitted to the medical wards (acute medically ill patients aged ≥18) were recruited to the study after written consent was obtained. Patients were excluded from the study if they were injured, did not speak the language and/or for other reasons were unable to provide informed consent.

2.3. Measures

Self-reported questionnaires were completed, blood alcohol concentration (BAC) and PEth 16:0/18:1 were analyzed in whole blood (Berg et al., 2018; Kristoffersen and Smith-Kielland, 2005). Gender and age (recorded into four groups: 18–40, 41–60, 61–70 and ≥71 years) were included. Socioeconomic factors on partnership status (being married/living with a partner (LWP), being single or widowed) and occupational status (economically active, not economically active and retired) were recorded. Mental distress was assessed with the Symptom Check List-5 (SCL-5) questionnaire (Tambs and Moum, 1993). SCL-5 is a validated measure comprising 5 items (three items on depression and two on anxiety) extracted from the full version of SLC-90. SCL-5 is used as a dichotomized variable with a cut-off score of > 2 as a valid predictor of mental distress (Strand et al., 2003; Tambs and Moum, 1993). SCL-25 questions are translated and previously utilized in Russian, allowing us to compare between the study sites (Hoffmann et al., 2006).

In our study we utilized PEth 16:0/18:1, hereinafter denoted as PEth only. PEth was used as a dichotomized variable where concentrations > 0.3 μM were defined as positive and indicative of excessive alcohol use, and as a continuous variable ranging from 0 μM to 7 μM (Wurst et al., 2015). The cut-off level for positive BAC-values was set at 0.02 g/kg. In Oslo, the blood samples for the study were collected immediately upon admission along with the diagnostic samples. In Moscow, due to internal routines at the hospital, the study samples were collected up to 24 h after admission, when diagnostic blood samples are drawn. PEth accumulates in red blood cells and has a relatively long half-life of 4–12 days (Gnann et al., 2012; Viel et al., 2012), allowing us to compare between the countries. Furthermore, for comparison of PEth-results between the study sites, PEth was analyzed by the same LC–MS/MS method on Agilent instruments as previously described by Berg et al. (Berg et al., 2018). Due to the fast metabolism of alcohol, BAC levels are markedly biased due to the time difference in blood sampling. Therefore, the prevalence of BAC-positive cases is included as a description only and not utilized in further analyses.

Self-reported alcohol use included one single question (yes/no) about consumption the past 24 h and AUDIT-4 consisting of the three first and the tenth item of AUDIT (Saunders et al., 1993). AUDIT comprises 10 items and is an internationally validated screening test, allowing us to compare between countries (Cook et al., 2011; Mathew et al., 2010; Saunders et al., 1993). AUDIT-4 presents high levels of correlation with the 10-item AUDIT (Meneses-Gaya et al., 2010) and was chosen for its brevity, which is required in a clinical setting. On AUDIT-4 each item is scored 0–4 points and summed for a total score ranging from 0 - 16. We utilized AUDIT-4 as a dichotomized variable for detection of harmful alcohol use (cut-off scores of ≥7 for men and ≥5 for women) and non-harmful alcohol use (Gual et al., 2002).

AUDIT-4 provides a continuous score reflecting risk and severity. Therefore, in addition to using it as a dichotomized variable it was also divided into four zones. AUDIT-4 was divided according to the proportion of the WHO division of the full AUDIT into four zones reflecting different drinking patterns; Zone 1: low-risk drinking or abstinence (scores 0–3) (Babor et al., 2001). Zone 2: alcohol use in excess of low-risk guidelines (scores 4–6). Zone 3: hazardous drinking (scores 7–8). Zone 4: risky alcohol use and possible alcohol dependence (scores ≥ 9) (Babor et al., 2001). We applied these 'definitions' and modified divisions of zones from the full AUDIT (10 items) to our 4 item AUDIT-4 zones, bearing in mind that the full AUDIT scores from 0 to 40 points, whereas AUDIT-4 scores from 0 to 16 points. AUDIT-4 zones – variable was treated as a nominal variable with four outcomes (four zones) in the conducted analyses.

In order to evaluate the different drinking patterns we assessed separately AUDIT-QF measuring quantity and frequency of alcohol use and the third item of AUDIT-4, item #3, screening for binge drinking (Kaarne et al., 2010) and item #4. This item asks if a relative or friend or a doctor or another health worker has been concerned about your drinking or suggested that you reduce your alcohol use. A cut-off score of ≥4 for women and ≥5 for men indicating unhealthy alcohol use was utilized on AUDIT-QF (Kaarne et al., 2010). Item #3 has been used as a single question previously (Kaarne et al., 2010; Rolland et al., 2017). The question was modified from six drinks per occasion to four for women and five for men at both study sites. Harmful alcohol use is indicated by a positive score on the dichotomized AUDIT-4.

2.4. Data analysis

Statistical analyses were performed using IBM SPSS 25.0 (Armonk, NY) and R statistical software version 3.5.2. In the subsequent analyses, we first evaluated the association between AUDIT-4 as a dichotomized dependent variable and socio-demographic factors- and mental distress as independent variables, using binary age- and gender-adjusted logistic regression.

We quantified the relationship between PEth concentration (ranging from 0 μM to 7 μM) and AUDIT-4 scores (continuous variable ranging from 0 to 16 points) using Spearman rank correlation coefficient.

Furthermore, in order to adjust for age and gender, two separate multinomial logistic regression analyses were performed to test for the association between PEth and AUDIT-4 zones, and the association between the single question about alcohol consumption past 24 h and AUDIT-4 zones, respectively. In each of the analyses AUDIT-4 zones was the dependent variable, while PEth and the single question about alcohol consumption past 24 h were the independent variables. Zone 1 of AUDIT-4 was used as a reference category in each of the analyses.

Lastly, the Oslo- and Moscow data were merged to compare the harmful alcohol use among the age groups, and female- and male patients between the two study sites. Two separate multivariate logistic regressions were performed one for AUDIT-4 and one for PEth on the merged Oslo and Moscow data. AUDIT-4 and PEth were each set as dependent variables and age groups, gender and location were the independent variables.

3. Results

Overall, 81% (n = 2874) and 91% (n = 3009) in Oslo and Moscow, respectively, consented to complete the self-reported screening survey and to provide a blood sample. The patients' characteristics for Oslo and Moscow are presented in Table 1. The gender- and age distribution in both study sites was as follows: 47.6% female patients in Oslo and 52.9% in Moscow. The largest age group in Oslo was patients aged 18–40 years (27.8%) and 41–60 years in Moscow (30.7%).

In total 21.1% and 19.2% of patients in Oslo and Moscow, respectively, reported a harmful alcohol use measured by AUDIT-4 while the total prevalence of PEth-positive patients was lower comprising 11.4% and 14.3%, in Oslo and Moscow, respectively (Table 1). At both study sites the prevalence of harmful alcohol use differed by age, gender and the alcohol measure used. In Oslo, in total, 20.5% of men and 21.7% of women reported to have a harmful alcohol use in AUDIT-4, while the prevalence of PEth-positive samples was lower with 14.9% of men and

Table 1
Descriptive characteristics of the study-sample in each country.

Characteristics	Oslo (n = 2874) %	Moscow (n = 3009) %
Socio-demographics Gender (Oslo n = 2832; Moscow n = 3009)		
Female	47.6	52.9
Age (Oslo n = 2823; Moscow n = 3009)		
18-40	27.8	17.5
41-60	24.7	30.7
61-70	21.2	24.7
≥71	26.3	27.1
Marital status (Oslo n = 2747; Moscow n = 3009)		
Married/Living with a partner	43.1	48.4
Divorced	17.0	13.2
Widowed	8.8	26.9
Single	31.1	11.4
Occupational status (Oslo n = 2734; Moscow n = 3008)		
Active (employed, student)	47.2	29.8
Non-active (unemployed, incapacitated)	14.9	16.3
Retired	37.9	53.9
Mental distress (Oslo n = 2629; Moscow n = 3002)		
SCL-5 (cut-off: > 2)	29.9	7.9
Drinking patterns		
Abstainers categorized by AUDIT-4 (Oslo n = 2796; Moscow n = 3006)	24.2	41.2
Never (0 points)		
Harmful alcohol use categorized by AUDIT-4 cut-off (Oslo n = 2709; Moscow n = 3005)		
Harmful use (cut-off women: ≥5/ men: ≥7)	21.1	19.2
Alcohol patterns categorized by AUDIT-4 zones (Oslo n = 2714; Moscow n = 3006)		
Low-risk drinking/abstention (0-3 points)	57.4	73.7
Exceeding the lower drinking limit (4-6 points)	27.7	7.9
Hazardous drinking (7-8 points)	7.2	4.1
Risky drinking (9-16 points)	7.7	14.3
Frequency and quantity		
- AUDIT-QF (Oslo n = 2742; Moscow n = 3008)		
Unhealthy alcohol use (cut-off women: ≥4/ men: ≥5)	21.0	16.8
Binge drinking/HED frequency (Oslo n = 2756; Moscow n = 3007)		
- AUDIT Item #3		
Never (0 points)	40.4	75.5
Once per month or less (1 point)	35.2	8.8
2–4 times per month (2 points)	17.6	4.6
2–3 times per week (3 points)	4.7	6.9
Almost daily (4 points)	2.1	4.3
Has someone worried about your drinking (Oslo n = 2713; Moscow n = 3006)		
- AUDIT Item #4		
No (0 points)	90.4	82.9
Yes, but not during the past year (2 points)	4.4	4.0
Yes, during the last year (4 points)	5.2	13.1
Was alcohol consumed past 24 hours (Oslo n = 2808; Moscow n = 3009)		
Yes	19.9	7.5
Blood alcohol concentration (Oslo n = 2607; Moscow n = 3009)		
Positive (> 0.02 g/kg)	4.3	1.3
Blood alcohol biomarker - PEth (Oslo n = 2607; Moscow n = 3009)		
Excessive alcohol use (> 0.3 μM)	11.4	14.3

Abbreviations: HED: Heavy episodic drinking.

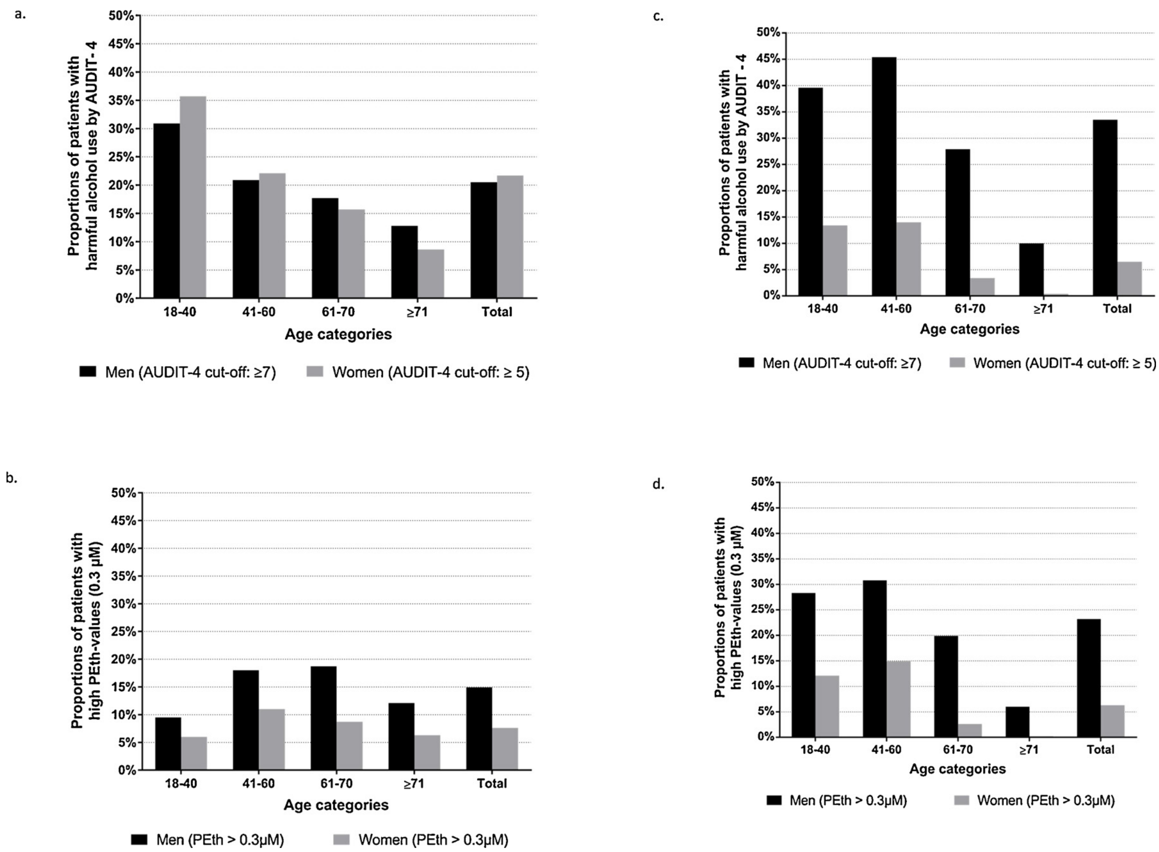

Fig. 1. a,b,c,d: Country-specific prevalence of harmful alcohol use (measured by AUDIT-4, cut-off score of ≥5 for women and ≥7 for men) and excessive alcohol use measured the biomarker PEth (cut-off value in blood > 0.3 μM) by age and gender. (a). Proportion of patients having harmful alcohol use measured by AUDIT-4 in Oslo. (b). Proportion of patients having high values of PEth of > 0.3 μM, indicating an excessive alcohol use in Oslo. (c). Proportion of patients having harmful alcohol use measured by AUDIT-4 in Moscow. (d). Proportion of patients having high values of PEth of > 0.3 μM, indicating an excessive alcohol use in Moscow.

7.6% of women being excessive alcohol users (Fig. 1a, b). In Moscow, 33.5% of men and 6.5% of women reported a harmful alcohol use in AUDIT-4, whereas 23.2% of men and 6.3% of women were excessive users when assessed with PEth (Fig. 1c, d). At both study sites, among all age groups the prevalence of harmful alcohol use varied between AUDIT-4 and PEth, except for women in Moscow, where the prevalence between AUDIT-4 and PEth was comparable (Fig. 1a - d). Furthermore, the prevalence of PEth-positive values among women and men < 61 years was greater in Moscow than Oslo (Fig. 1b – d). The same was observed for men when measured with AUDIT-4 but not for women < 61 years, where the prevalence of women reporting harmful alcohol use was substantially lower in Moscow compared to Oslo; whereas 35.7% of 18–40 years old women in Oslo reported harmful alcohol use, only 13.4% did so in Moscow, among those aged 41–60 22.1% reported harmful use in Oslo compared to 14.0% in Moscow (Fig. 1a and c).

The results presented above were supported by the binary logistic regressions at each study site depicted in Fig. 2. In Moscow, females were negatively associated with harmful alcohol use (AOR: 0.15; 95% CI: 0.12-0.19), while in Oslo there were no significant gender differences. The likelihood of having harmful alcohol use decreased with increasing age at both study sites compared to the youngest age group of 18–40 years, although no significant association between the age group of 41–60 and harmful alcohol use was observed in Moscow.

Moreover, the association between age groups, gender and AUDIT-4 was tested in a pooled multivariate analysis for Oslo and Moscow (Table 2a). At all age groups men in Moscow were more likely to be harmful users measured by AUDIT-4 and PEth compared to men in Oslo (Table 2a – b). However, this was not the case for the oldest age group of ≥ 71 years, were men in Oslo were more likely to be harmful users when measured by both AUDIT-4 and PEth (Oslo-men displayed AUDIT-4 - AORs of 46.33; 95% CI: 15.04–100.35 and PEth-AORs of 58.67; 95% CI: 16.58–100.87 vs. those in Moscow displaying AUDIT-4 - AORs of 34.69; 95% CI 9.69–80.64 and PEth-AORs of 26.75; 95% CI: 7.90–53.12) (Table 2a and 2b). Meanwhile, when measured with AUDIT-4 women in Oslo were more likely to be harmful users compared to those in Moscow, at all age groups (Table 2a). In contrast to AUDIT-4 - AORs, the AORs for PEth showed that women in Oslo at the age group of 18–40 and 41–60 were less likely to be harmful users compared to those in Moscow, AOR for 18–40 years: 0.49; 95% CI 0.27 – 0.80 and AOR for 41–60 years: 0.72 95% CI 0.43–1.10 (Table 2b).

The prevalence of low-drinkers/abstainers categorized by zone 1 in AUDIT-4 was higher in Moscow than in Oslo, 73.7% vs. 57.4% (Table 1). Moreover, the total abstainer group (those scoring 0 points on AUDIT-4) was almost twice as large in Moscow compared to Oslo, 41.2% vs. 24.2%. (Table 1). Overall, the patterns of drinking in the two countries differed regarding the highest responses on the item #3, item #4 and AUDIT-zones (Table 1). The prevalence of patients bingeing almost daily (Item #3 - 4.3% in Moscow vs. 2.1% in Oslo), those having someone worried for their drinking the past year (Item #4 - 13.1% in Moscow vs. 5.2% in Oslo), as well as patients classifying in the fourth zone of AUDIT-4 (Zone 4–14.3% in Moscow vs. 7.7% in Oslo) was highest among the Moscow-sample (Table 1). Conversely, when measured by AUDIT-QF, 21.0% of patients had an unhealthy alcohol use in Oslo compared to 16.8% in Moscow. Furthermore, 24.4% of patients in Oslo vs. 15.8% in Moscow reported binge drinking (at least monthly) when measured by the dichotomized cut-off ≥2 on item #3, as shown in Table 1.

There were 29.9% of patients having a positive score of 2 points on SCL-5 questionnaire (indicating mental distress) in Oslo compared to

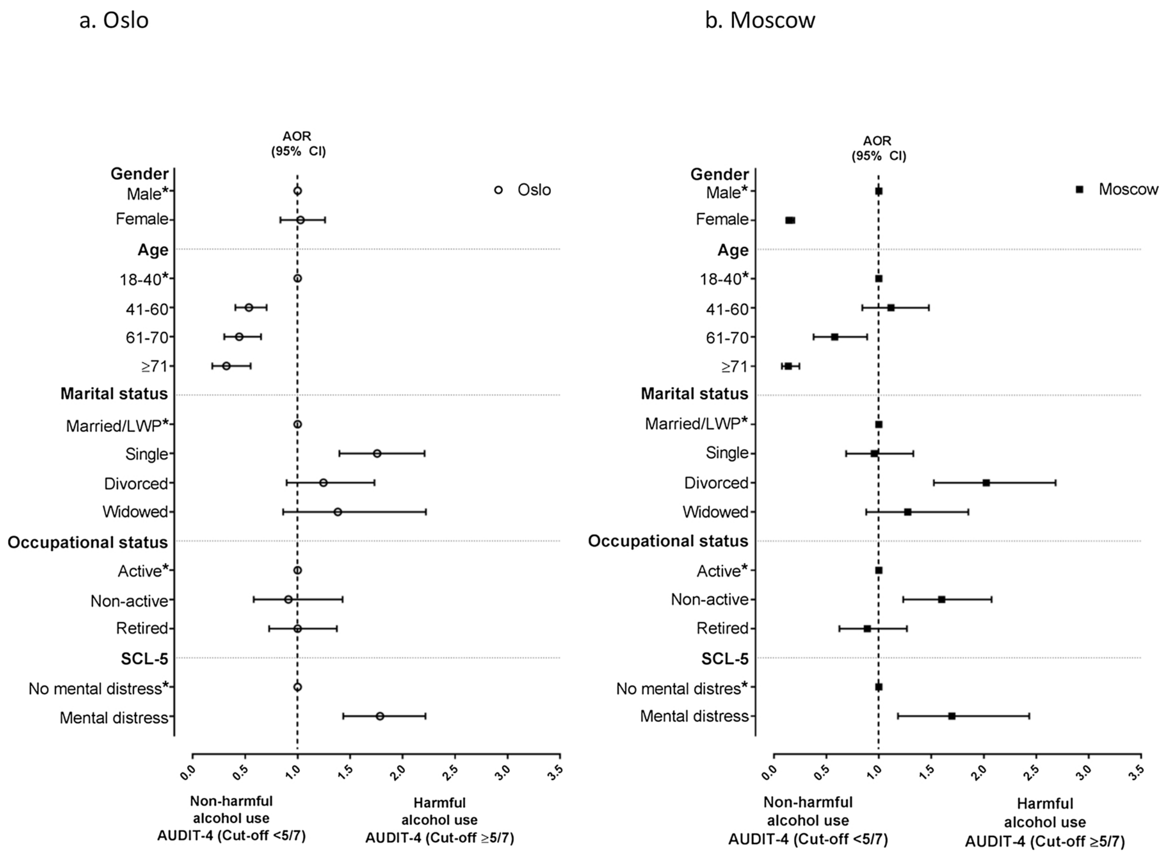

Fig. 2. a, b: Country-specific forest plots comparing subjects meeting the harmful vs. non-harmful alcohol use criterion (AUDIT-4 cut-off for women ≥5 and men ≥7) **2 a.** Adjusted Odds Ratios (AOR) for being a harmful alcohol user in Oslo. **2 b.** AOR for being a harmful alcohol user in Moscow.
*In binary logistic regression analysis male was used as a reference for the gender-variable; The age group of 18–40 was used as a reference to which all the other age groups were compared with; Married/LWP was used as a reference in marital status-variable. Active was used as reference in occupational status-variable; and No mental distress was used as a reference to mental distress.
Abbreviations: LWP: Living With a Partner.

7.9% in Moscow. (Table 1). Additionally, 41.0% of the patients having a harmful alcohol use did have a significant indication of mental distress ($p < 0.001$) in Oslo as opposed to 10.8% in Moscow ($p = 0.040$). This was supported by the binary logistic regression showing an association between mental distress and harmful alcohol use at both study sites ((Oslo - AOR: 1.78; 95% CI: 1.43–2.22 and Moscow – AOR: 1.69; 95% CI: 1.18–2.43) (Fig. 2a and b).

In Oslo, 33.1% that reported harmful alcohol use by AUDIT-4 had a positive PEth-value, compared to 51.2% in Moscow. Nevertheless, Spearman's correlation analysis in the whole population revealed that there was a similar and significant correlation between AUDIT-4 and PEth in both study sites, with a Spearman's rho of 0.70 in Moscow and 0.74 in Oslo. At both study sites, the association between AUDIT-4 and PEth was further tested in the multinomial regression model, in order to adjust for age and gender. Zone 1 of AUDIT-4 was used as a reference category (Table 3). In both study-samples, individuals with PEth-positive values were more likely to end up in zone 2 compared to zone 1, and the likelihood for ending up in zone 3 and 4 was higher than in zone 1. Indicating that PEth as a screening measure performs as good as AUDIT-4 to detect increasing levels of alcohol use (from lowest use to highest). The same was tested for the single question of drinking the past 24 h. The odds ratios for patients responding yes to have drunk the last 24 h did not increase in the same magnitude as PEth, indicating a weaker association with AUDIT-4 zones. Minor differences in the AORs between the countries were observed.

4. Discussion

At both study sites there was a high prevalence of harmful alcohol use. In general, the prevalence of harmful alcohol use was lower when measured with PEth compared to AUDIT-4. Thus, self-reporting was the most sensitive method in revealing harmful alcohol use among all patients except of women in Moscow, where the prevalence between the two alcohol measures was comparable.

In both study sites, despite the significant correlation of AUDIT-4 and PEth, the prevalence of harmful alcohol use measured by AUDIT-4 was higher than when detected with PEth. This might be due to the time perspective in alcohol detection (AUDIT-4 detecting alcohol use the past year and PEth during the last month) or due to the PEth cut-off (> 0.3μM) being too high and hence less sensitive and/or PEths' lack of ability to reflect different drinking patterns (Afshar et al., 2017; McDonald et al., 2013; Schröck et al., 2017). However, there was a small percentage of patients having PEth-positive values where low drinking/abstention (zone 1) was self-reported, indicating that combining these two measures might improve detection of alcohol use. This applied particularly to women in Moscow, which showed a plausible tendency of underreporting, due to the similar prevalence of harmful alcohol use measured with both AUDIT-4 and PEth, 6.5% vs. 6.3%, respectively, in contrast to men in Moscow and men and women in Oslo. Furthermore, this was shown by AORs particularly for the age groups < 61; women in Moscow were less likely to be harmful users when measured by AUDIT-4 than women in Oslo, but the reverse was observed when PEth was used to assess harmful use.

Given that the dose-response relationship of alcohol use and health

Table 2
a, b. Pooled analyses, including Oslo and Moscow data. Age-, gender-, and location adjusted odds ratios (AOR) for patients having a harmful alcohol use by AUDIT-4 and PEth.

a. AORs for patients having a harmful alcohol use measured by AUDIT-4 in Oslo and Moscow

AOR (95% CI)

Age	Location	Female	Male
18-40	**Moscow**	REF	4.43 (2.70 - 6.97)
	Oslo	3.69 (2.33 - 5.79)	3.03 (1.81 - 4.99)
41-60	**Moscow**	REF	5.21 (3.72 - 7.08)
	Oslo	1.79 (1.16 - 2.58)	1.68 (1.15 - 2.28)
61-71	**Moscow**	REF	12.52 (6.43 - 24.18)
	Oslo	6.08 (2.91 - 12.63)	6.91 (3.45 - 12.98)
≥71	**Moscow**	REF	34.69 (9.69 - 80.64)
	Oslo	29.97 (9.65 - 68.62)	46.33 (15.04 - 100.35)

b. AORs for patients having an excessive alcohol use measured by PEth (> 0.3 μM) in Oslo and Moscow

AOR (95% CI)

Age	Location	Female	Male
18-40	**Moscow**	REF	3.04 (1.92 - 4.91)
	Oslo	0.49 (0.27 - 0.80)	0.83 (0.45 - 1.30)
41-60	**Moscow**	REF	2.57 (1.84 - 3.49)
	Oslo	0.72 (0.43 - 1.10)	1.27 (0.86 - 1.84)
61-71	**Moscow**	REF	10.51 (5.30 - 23.87)
	Oslo	3.84 (1.72 - 9.36)	9.50 (4.90 - 20.70)
≥71	**Moscow**	REF	26.75 (7.90 - 53.12)
	Oslo	27.56 (7.75 - 51.94)	58.67 (16.58 - 100.87)

consequences seem to be accelerated for higher alcohol doses in women (Rehm et al., 2017), there is reason for concern regarding the high prevalence of harmful alcohol use among female patients. Alcohol has been found to be the most significant factor causing low life-expectancy in Russian men (Rehm et al., 2007; Zaridze et al., 2014, 2009). This is also reflected in our results with men being overrepresented particularly in the youngest age groups. Moreover, in Moscow the prevalence of harmful alcohol use was highest in the age group of 41–60 years, corroborated by a similar prevalence of PEth-positive cases. Conversely, in Oslo the highest prevalence of harmful alcohol users was found in the age group of 18–40 years, while a high frequency of PEth-positive cases was found in the age group 41–60 years. Furthermore, the AORs from the multivariate analyses showed that particularly men in Oslo ≥ 71 years were more likely to be harmful users compared to those in Moscow. This is of concern since health consequences of harmful alcohol use more often are manifested in the middle-aged population, due to cumulative exposure to alcohol (Hauge and Irgens-Jensen, 1987; World Health Organization, 2000).

Despite the similar total prevalence of harmful alcohol use measured by AUDIT-4 score of ≥5 for women and ≥7 for men among the patients, the drinking patterns were quite different in the two study sites. The proportion of low-risk drinkers/abstainers was higher in Moscow than Oslo. Nevertheless, in Moscow, there were more patients having someone worried for their drinking the past year, bingeing almost daily, and characterizing in the highest AUDIT-4 zone. These results reveal different drinking patterns in the two countries pertaining to other data from Russia showing that a common pattern of consumption includes long bouts of continuous heavy drinking over several days, also known as zapoi, alternating with days of abstinence (Shield and Rehm, 2015; Tomkins et al., 2007). In Norway, heavy drinking is rather characterized by very heavy drinking in one single occasion (SIRUS, 2016), as reflected in our results. A similar prevalence of binge drinking among medically ill patients has previously been reported in Norway (Oppedal et al., 2011). Regarding the widespread binge drinking in both study sites there is reason for concern, as such drinking has been shown to lead to negative cardiovascular outcomes even after adjustment for average alcohol volume (Rehm et al., 2003b; Roerecke and Rehm, 2010). Overall, the drinking patterns detected in Moscow might reflect the higher prevalence of liver cirrhosis in Russia compared to Norway (World Health Organization, 2014).

The high prevalence of harmful alcohol use in Oslo (20%) was also detected in another Norwegian study (Oppedal et al., 2011), while Vederhus et al. from another county showed a prevalence of 9.3% only (Vederhus et al., 2015). These discrepancies could be described by the differences in life expectancy among different regions in Norway. Our study site included some of the boroughs with the lowest life-expectancy in Norway. The above mentioned studies were performed during a period of 24 -hs and 3 months only; while our study conducted throughout a year presents more robust data by identifying seasonal variations, including summertime and Christmas-holidays when alcohol use is potentially elevated (Egerton-Warburton et al., 2018).

Anxiety and depression prevalence measured by SCL-5 was almost four times higher in Oslo compared to Moscow. Additionally, in Oslo, about 40% of the patients having a harmful alcohol use did have a significant indication of anxiety and depression as well. A recent study suggests that treatment of patients with Alcohol Use Disorder (AUD) was putatively initiated only when severe stages of AUDs were present (Rehm et al., 2015). Simultaneously, although there are several pathways existing on the association of harmful alcohol use and/or AUDs and depressive disorders, studies demonstrate that harmful drinking might cause depressive disorders (Boden and Fergusson, 2011; Fergusson et al., 2009).

Studies on injured patients show that alcohol is a significant factor for hospital admissions (Bogstrand et al., 2011; Borges et al., 2006). In our study with acute medically ill patients, this might be indicated by the high and similar prevalence of harmful alcohol use at the two study sites. Hence, feasible and reliable identification of alcohol use among medically ill patients not being intoxicated upon admission is of high significance for two reasons. Firstly, a hospital admission might be a possibility for a lifestyle change as the patient may be more motivated to reduce the alcohol consumption (Lau et al., 2010). A recently published study on patients with high health care utilization rates in USA showed that 50% of the patients met the criteria for substance use disorder, with alcohol being the most widespread substance. However, only 10% of these received treatment (Rentas et al., 2019). Better identification and intervention for patients with harmful alcohol use

Table 3
Country-specific age- and gender adjusted odds ratios (AOR) for PEth- and alcohol past 24 h - screening measures in relation to AUDIT-4 zones.

	AOR (95% CI)		
Zone 1 (REF)	Zone 2	Zone 3	Zone 4
Oslo			
PEth – positive	8.80 (5.67 - 3.68)	29.06 (17.23 - 49.01)	71.45 (43.85-117.11)
Alcohol past 24 h - Yes	5.95 (4.57 - 7.74)	9.47 (6.54 - 13.70)	18.65 (13.14 - 26.48)
Moscow			
PEth – positive	4.75 (3.21 - 7.06)	6.57 (4.14 - 10.44)	22.68 (16.45-31.28)
Alcohol past 24 h - Yes	4.59 (2.70 - 7.80)	5.10 (2.72 - 9.56)	16.08 (10.64 - 24.32)

might therefore be beneficial for both the patient and the health care service, as it can reduce admission rates and improve the health of patients having a high utilization of health care services. Secondly, patients with harmful alcohol use are more prone to alcohol related medical complications such as post-operative complications, development of alcohol withdrawal symptoms, e.g. delirium tremens which might result in death if not treated adequately (Goodson et al., 2014; Tonnesen et al., 2010). Therefore, interventions to reduce alcohol consumption in this patient group are essential. In this regard, we have shown that AUDIT-4 and PEth are reliable and feasible identification measures that can identify patients with harmful alcohol use even in a hectic emergency setting. However, lack of time and resources in the face of competing priorities are known as barriers to implementation of screening and interventions in a clinical setting, particularly in a hectic ED-setting. To overcome such barriers, implementation strategies exist and should be investigated in an ED-emergency setting. More specifically, embedded brief screeners such as AUDIT-4 in the electronic medical record systems might provide a fast screening method. Additionally, along with brief screens also embedded in the medical record system, decision support tools such as structured algorithms for specific recommended responses based on the level of risk might facilitate the work of clinicians in identification of patients with harmful use and offer patients the possibility for referral to treatment. Moreover, an objective biomarker such as PEth might corroborate the identification of harmful alcohol use, particularly in groups of patients where self-reported screening is less sensitive due to possible underreporting, such as for women in Moscow, shown in our study. A study demonstrated that a follow-up in primary care appears to be more favorable than interventions at the hospital, particularly at the ED where it is also estimated that brief interventions have a short-term effect on alcohol reduction among patients (Schmidt et al., 2016; Barata et al., 2017). Taking into account the high prevalence rates of harmful alcohol use and the low number of patients receiving adequate treatment at the hospital, an early identification at the hospital followed by a follow-up in the primary healthcare appears to be as an ideal approach.

4.1. Limitations

The ED-nurses recruited the patients in Oslo, in contrast to addiction doctors in Moscow. This might have led to some differences in the recruitment process. However, we have shown that it is possible to detect alcohol use even in a busy ED-setting without having a research staff solely dedicated to the study. Due to the internal practices in Moscow it was not possible to take blood samples upon admission, making it impossible to compare BAC-values between Oslo and Moscow. However, BAC results from Oslo showed that this measure is not suitable to detect harmful alcohol use (only 4% were BAC-positive compared to 19.9% that self-reported drinking the past 24 h), as indicated by previous studies (Kechagias et al., 2015; Wurst et al., 2005). PEth is more suitable as an objective biomarker of alcohol use, particularly in critically ill patients unable to answer questionnaires (Moss and Burnham, 2006). Nevertheless, the blood sampling time being up to 24 h upon admission in Moscow might have led to a slight underestimation of PEth-concentration levels in Moscow compared to Oslo. However, with PEth having a half-life of 4–12 days this is not considered to affect our results substantially.

5. Conclusions

This study has demonstrated that harmful alcohol use was highly prevalent among acutely medical ill patients both in Norway and Russia. Nonetheless, the study samples differed in the prevalence of harmful alcohol use by gender- and age distribution and drinking patterns. A combination of AUDIT-4 and an objective biomarker such as PEth showed to be valuable, particularly for the women in Moscow, who tended to underreport their alcohol consumption. The high prevalence of harmful alcohol use at both study sites suggests that early identification of patients is essential for possible interventions. Subsequently, reduction of alcohol might lead to better compliance and improved health outcomes. Implications of the results in the clinical practice are to be considered in both countries, depending on the health care unit in each country. In Russia, AUDIT-4 might be applied in the hospital to identify patients with problematic alcohol consumption and to predict the associated complications. A comprehensive understanding of the patterns of alcohol use, and of reliable screening measures feasible to utilize in a clinical setting is of significance for future research, and intervention. Nonetheless, additional research is warranted to assess which patterns of drinking that cause the most health related harm in both countries.

Contributors

SK drafted the manuscript and conducted the data analyses. SK, VV, DG, AL, GN and STB organized or contributed to the Oslo data collection. EB, EK, AN, ET, AK, AP, SP and ED organized or contributed to the Moscow data collection. CZ contributed to the statistical analysis of the data. All authors were responsible for study design, interpretation of findings, critical revision of the article and final approval of the manuscript.

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Declaration of Competing Interest

No conflict declared.

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