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What Research Is Being Done on Prenatal Alcohol Exposure and Fetal Alcohol Spectrum Disorders in the Russian Research Community?

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Abstract — Aims: Although Russia has one of the highest rates of alcohol consumption and alcohol-attributable burden of disease, little is known about the existing research on prenatal alcohol exposure (PAE) and Fetal Alcohol Spectrum Disorders (FASDs) in this country. The objective of this study was to locate and review published and unpublished studies related to any aspect of PAE and FASD conducted in or using study populations from Russia. **Methods:** A systematic literature search was conducted in multiple English and Russian electronic bibliographic databases. In addition, a manual search was conducted in several major libraries in Moscow. **Results:** The search revealed a small pool of existing research studies related to PAE and/or FASD in Russia (126: 22 in English and 104 in Russian). Existing epidemiological data indicate a high prevalence of PAE and FASD, which underlines the strong negative impact that alcohol has on mortality, morbidity and disability in Russia. High levels of alcohol consumption by women of childbearing age, low levels of contraception use, and low levels of knowledge by health and other professionals regarding the harmful effects of PAE put this country at great risk of further alcohol-affected pregnancies. **Conclusions:** Alcohol preventive measures in Russia warrant immediate attention. More research focused on alcohol prevention and policy is needed in order to reduce alcohol-related harm, especially in the field of FASD.

INTRODUCTION

Russia has one of the highest rates of alcohol consumption in the world. According to the *Global Burden of Disease Study (2010)*, alcohol use is the second leading risk factor contributing to the disease burden in Russia (Institute for Health Metrics and Evaluation, 2012). The *World Health Organization (WHO) European and Global Status Report on Alcohol and Health* reported that on average, for 2003–2005, the level of per capita consumption of pure alcohol in liters among adults older than 15 years of age reached 26.7 l (16.3 l for women and 35.4 l for men; WHO, 2010, 2011). In Russia, 5.8% of women and 22.1% of men are heavy episodic drinkers (i.e. consume at least 60 g or more of pure alcohol on at least one occasion weekly; WHO, 2010, 2011). The prevalence of alcohol use disorders is also high in Russia—2.6% for women and 16.3% for men (WHO, 2011). As a result, Russia is characterized as having the most risky pattern of drinking and the greatest alcohol-attributable burden of disease in the world.

A recent study conducted in Saint Petersburg and the Nizhnyi Novgorod region revealed that 89% of non-pregnant women reported consuming alcohol and 65% reported binge drinking in the past 3 months (Balachova *et al.*, 2012a). Forty-seven percent of women in the Nizhny Novgorod region and 28% in Saint Petersburg reported at least one binge-drinking episode at least monthly. Women who might become pregnant consumed alcohol similar to women who were not likely to become pregnant, and 54% of women in the Nizhny Novgorod region and 32% of women in Saint Petersburg were considered to be at risk of having an alcohol-exposed pregnancy (Balachova *et al.*, 2012a).

Popovitch *et al.* (2004) conducted a telephone-based behavioral risk factor surveillance survey in three Russian cities in 2000–2001. A random sample of 3032 residential telephone numbers was selected and 1693 interviews were conducted among adults 25–64 years of age in each selected household: 21% of women from Moscow, 8.2% of the women in Arkhangelsk and 10.8% of women in Murmansk abstain from alcohol. From 3 to 5% of women (and about 30% of men) in the above Russian cities consume >20 g of pure alcohol per day. Among women, about 30% of consumed beverages were spirits and 40% was beer. The highest level of hazardous alcohol consumption (>20 g of pure alcohol per day) among women was reported for those between 25 and 34 years of age, the most reproductive age group (Popovitch *et al.*, 2004).

An article from the mid-1990s reported that 80–94% of high-school girls consumed alcohol and in major Russian cities, girls drank at the same level or higher than boys of the same age (Koshkina and Paronyan, 1995).

According to the official report of the Russian National Research Center on Addiction for 2011, the prevalence of alcoholism in the general population of Russia is estimated to be 1.4% (1402 per 100,000 persons), and ~0.5% of women (505 per 100,000) have been diagnosed with alcoholism (Koshkina *et al.*, 2012). A ratio of 1:5 (women:men) has been reported to exist between the genders (Altshuler, 2010). Given that the official figures are based on reported cases only, the actual number of cases of alcoholism among women in Russia may be higher (if unreported cases are considered; Kirganova,

2009). It has also been suggested that in Russia, from 1999 to 2003, the number of registered cases of alcoholism in women increased from 2.2 to 3.7% (Altshuler *et al.*, 2006).

In addition to the alarming data on alcohol consumption by women in the general population, research indicates that there is a low level of contraception use. Only 49% of all women in Russia who have ever been sexually active use contraception, and that number increases to only 51% when women in the age group of 50–54 were excluded (Barden-O'Fallon *et al.*, 2010). In another sample of 347 non-pregnant women 18–44 years of age recruited at women's clinics, 44% of women in Saint Petersburg and 70% in the Nizhny Novgorod region were sexually active and not using contraception consistently (Balachova *et al.*, 2012a).

Due to high levels of alcohol consumption within the population, paired with low rate of contraceptive use, many Russian women of childbearing age are at risk of having an alcohol-exposed pregnancy, which may result in having a child with Fetal Alcohol Spectrum Disorder (FASD). FASD is a non-diagnostic umbrella term that is used to represent the full spectrum of birth defects that are caused by prenatal alcohol exposure (PAE), which encompasses four categorical diagnostic entities: fetal alcohol syndrome (FAS), partial FAS (pFAS), alcohol-related neurodevelopmental disorder (ARND) and alcohol-related birth defects (ARBD; Chudley *et al.*, 2005). PAE is a leading preventable cause of the birth defects, which can include physical, mental, behavioral and/or learning disabilities with possible lifelong complications. In North America, the lifetime cost for some cases of FASD has been estimated to be more than one million dollars (Popova *et al.*, 2011).

Despite the high risk of, and potentially high cost associated with, FASD in Russia, there are no official surveillance efforts targeting FASD and no social facilities for children and/or adults with FASD in the country. Furthermore, very little is known about the existing pool of research on PAE or FASD in Russia. Therefore, the purpose of this study was to perform a systematic literature review in order to locate published and unpublished studies related to any aspect of PAE and FASD that were conducted in Russia or used study populations from Russia.

METHODS

Systematic literature search

Participating researchers from Canada and from Russia simultaneously conducted a systematic literature search. The procedure varied due to the differences in the availability of sources of information. For detailed search strategy in both countries and results, see Supplementary material, File S1.

The search was not limited by language of publication and was conducted up to and including December 2012.

RESULTS

In total, 22 studies in English and 104 studies in Russian were included in the present review. The results of the search strategy are shown in Fig. 1.

The 126 examined studies were categorized into the following six major groups, those that:

(1) assessed the prevalence of alcohol consumption during pregnancy and the clinical complications of alcohol-exposed pregnancies;
(2) examined the prevalence of FASD in the general population, or other specific populations (e.g. orphanages);
(3) assessed the efficacy of preventive measures, methods of diagnostics and interventions for individuals with FASD;
(4) conducted literature reviews on FASD and developed educational materials for health professionals;
(5) clinically examined children and adults and demonstrated the lifelong polysystemic teratogenic effects of alcohol on the fetus and
(6) experimentally studied the teratogenic effects of alcohol on laboratory animals or human biological material.

A summary of all examined studies in chronological order is available in Supplementary material, Table S1.

Studies on the prevalence of alcohol consumption during pregnancy and the clinical complications of alcohol-exposed pregnancies

Some studies reported both the prevalence of alcohol consumption and clinical complications. Therefore, these studies have been categorized by the primary purpose of the study.

(a) The prevalence of alcohol consumption during pregnancy

The search revealed 11 studies reporting the prevalence of alcohol consumption during pregnancy (see Supplementary material, Table S1). It was found that alcohol consumption during pregnancy in Russia varies from 3.1% (Talykova *et al.*, 2007) to 83% (Kurianova *et al.*, 2006) and heavy drinking during pregnancy varies from 0.2–1% (Radzinsky, 2002) to 9.2% (Shilko *et al.*, 2011a). In a study by Kosyh *et al.* (2010) it was reported that 50% of females consumed seven or more alcoholic drinks during the 3 months prior to pregnancy. Chambers *et al.* (2006) conducted a longitudinal pregnancy outcome study in the Moscow Region of Russia and revealed that 52% used alcohol in their most recent month of pregnancy. Further, these authors reported that, of those 'ever drinkers', 4.8% had at least one episode of five or more standard drinks, and 10.5% had at least one episode of three or four standard drinks in the most recent month of pregnancy. The survey conducted by Kristjanson *et al.* (2007) in Saint Petersburg among 899 pregnant women revealed that 96% of them drank alcohol in the year before they became pregnant; of these women, 60% reported drinking when they knew they were pregnant, and 35% had reported drinking within the past 30 days. Among pregnant women who drank within the past 30 days, 7.4% reported having 5 or more drinks on at least 1 occasion. One recent study reported that 16% of pregnant women with disorders of the pancreas and liver practiced heavy drinking (Egorova *et al.*, 2012). The drink of choice among pregnant Russian women was reported most commonly as wine, sparkling wine and beer (Kurianova

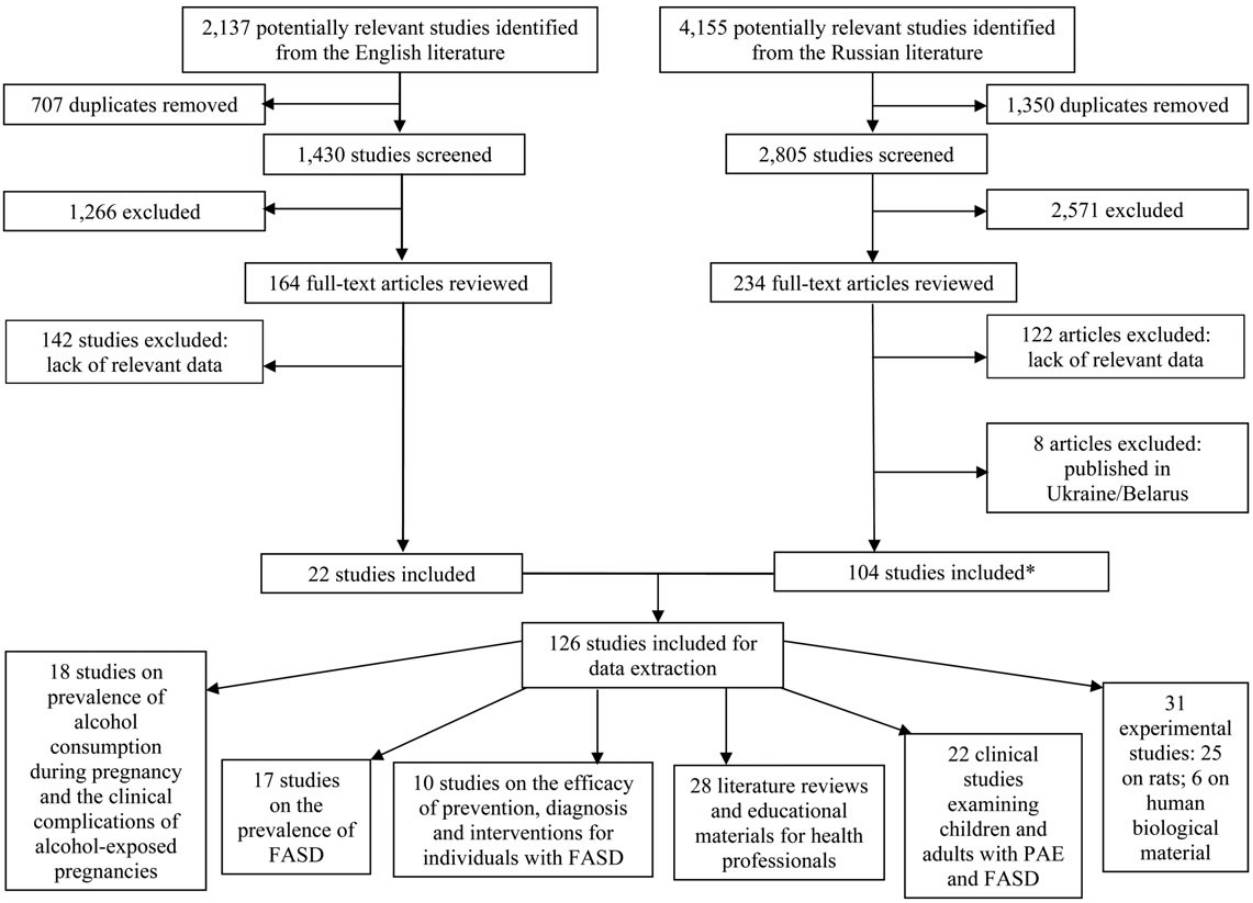

Fig. 1. Schematic diagram of the systematic search strategy. *Articles published in iteration are excluded from the total reported number of included studies.

et al., 2006; Kurianova, 2006; Sashchenko, 2007; Kalinina *et al.*, 2012).

Several studies revealed that Russian women substantially reduce their alcohol consumption after pregnancy recognition, when compared with pre-pregnancy levels (Balachova *et al.*, 2012a; Gaidukov *et al.*, 2008); however, about 20% continued to consume alcohol after pregnancy recognition (Balachova *et al.*, 2012a). Binge drinking after pregnancy recognition declined by a factor of 10, but did not disappear completely; ~6% of women had at least one binge episode.

It is important to note that the levels of alcohol consumption during pregnancy within all of the reviewed studies were based on maternal self-reports, which are likely to be imprecise and most likely underreported due to bias (e.g. recall and social desirability biases). Furthermore, the term 'standard drink' is not a term commonly used in Russia; therefore, the respondents may have had difficulty understanding this concept. In addition, there were inconsistencies between studies in the definition of a 'binge drinking'. For example, Balachova *et al.* (2012a) defined binging as 'four or more standard drinks on a single occasion', while Chambers *et al.* (2006) defined binge drinking as an episode of 'five or more drinks'.

It should also be noted that Russia is geographically large and culturally diverse; therefore, regional variations are important. Thus, findings on the prevalence and patterns of alcohol consumption during pregnancy from individual studies may not be representative of all Russian women.

(a) The clinical complications of alcohol-exposed pregnancies

There were seven studies describing the clinical complications of alcohol-exposed pregnancies in Russia (Supplementary material, Table S1). The research studies included in this analysis have reported that alcohol consumption during pregnancy increases the risk of miscarriage (Sashchenko, 2007; Komarova, 2008), fetoplacental insufficiency (Orazmuradov *et al.*, 2007), premature or accelerated delivery (Komarova, 2008; Alekseeva, 2011a,b), pathology of amniotic fluid (Komarova, 2008; Alekseeva, 2011a,b) and disturbances in the mother's immune system (Kurianova *et al.*, 2006; Sashchenko, 2007; Komarova, 2008). Several other research studies reported that alcohol consumption during pregnancy decreases the levels of zinc and copper in the blood stream of pregnant women, as well as the levels of cobalt, iodine, magnesium and phosphorus in pregnant women's hair (Ogotoeva and Borisova, 2008; Ogotoeva *et al.*, 2009a,b; Alekseeva, 2011a,b). Furthermore, these studies reported that newborns of these mothers are deficient in certain essential minerals, such as cobalt, iron, iodine and zinc, and have increased levels of lithium and nickel. Shilko *et al.* (2010c, 2011c) stated that increased levels of transforming growth factor (TGF-β1), found in the blood of alcohol misusing pregnant women, might explain the growth retardation in newborns.

Due to the small sample sizes of the studies presented above (Orazmuradov *et al.*, 2007; Ogotoeva and Borisova, 2008; Ogotoeva *et al.*, 2009a,b; Uliyanovskaia and Solovev, 2010; Shilko *et al.*, 2010c, 2011c; Kalinina *et al.*, 2012), and the fact that the level of alcohol consumption during pregnancy was not defined, was based on self-reported data obtained via unstructured interviews, and the timing of alcohol use was not specified (i.e., first, second or third trimester; Shilko *et al.*, 2010c, 2011c; Alekseeva, 2011a,b; Alekseeva and Ivanova, 2011; Kalinina *et al.*, 2012), these results should be interpreted with caution.

Studies reporting on prevalence of FASD

In total, 17 studies reported the prevalence of FASD in different populations of Russia (see, for example, Warren *et al.*, 2001; Riley *et al.*, 2003; Grigovich *et al.*, 2006; Miller *et al.*, 2007; Malakhova *et al.*, 2008; Konovalova *et al.*, 2009) (Supplementary material, Table S1). The prevalence of FAS in the general population was estimated in one study to be 18–19 per 1000 live births (Malakhova, 2012). However, a study of 326 kindergarten-aged children of the same area did not report any cases of FAS (Bubnov, 2009, 2010). The prevalence of FAS in maternity hospitals in Saint Petersburg was reported from 0.79 to 3.62 per 1000 live births; however, in specialized neonatal clinics it was almost 10 times higher—ranging from 3 to 35 per 1000 during 2000–2009 (Palchik *et al.*, 2006; Palchik and Legonkova, 2011).

The prevalence of FAS in orphanages ranged from 46 (Legonkova, 2011; Palchik and Legonkova, 2011) to 340 (Sofronova and Palchik, 2012) per 1000 live births by Russian researchers and from 55 (Stromland *et al.*, 2005) to 330 (The St. Petersburg-USA Orphanage Research Team, 2005) per 1000 live births by international researchers. For comparison purposes, it is believed that the prevalence rate of FAS in the North American general population is ~1 per 1000 live births (Roberts and Nanson, 2000; May and Gossage, 2001).

Studies by Marincheva *et al.* (2003) reported the prevalence of FAS to be 129 per 1000 in a boarding orphanage, 58 per 1000 in boarding schools, 49 per 1000 in regular orphanages and 164 per 1000 in a school of the social welfare system. The highest prevalence of FAS was found in 'psycho-correctional' orphanages for children with special needs, ranging from about 427–680 per 1000 (Legonkova, 2011; Palchik and Legonkova, 2011).

The prevalence of FAS among adopted children from Russia (or in some cases, from Eastern Europe, including Russia) currently living in the USA was estimated to range from 15 to 70 per 1000 live births (Aronson, 2003; Robert *et al.*, 2009). Farina *et al.* (2004) reported that 34% of children adopted from Russia were diagnosed with ARND. However, the records of alcohol-exposed pregnancy were significantly higher and constituted 19% (Albers *et al.*, 1997) to 41% (McGuinness *et al.*, 2000) of the cases. Albers *et al.* (1997) stressed that the majority of prospective adopting parents are concerned about the high risk of FASD among children adopted from Russia, due to the widespread availability of alcohol and the limited public awareness of alcohol's detrimental effects on the fetus.

The existing FASD prevalence estimates in Russia vary greatly from population to population and study to study. These variations may reflect not only differences in maternal drinking behavior, but also different diagnostic criteria, methods of case ascertainment (i.e. surveillance method) and populations surveyed in the different studies.

The existing studies have a number of limitations due to (a) inadequate and/or unavailable diagnostic capacity across the country and (b) lack of nation-wide diagnostic guidelines and definitions. Further, the studies presented above have weak methodologies, small sample sizes that are restricted to sub-populations, used convenience sampling and had a low response rate. There are also inconsistencies in the use of the terms 'incidence' and 'prevalence' across the studies.

Studies on FASD prevention, diagnostics and interventions

There were five studies found on selective prevention measurement, two on interventions, and three on diagnostic procedures (Jones *et al.*, 2006; Shilko *et al.*, 2008a, 2009c, 2010b, 2011a; Kuznetsova *et al.*, 2011). (Supplementary material, Table S1).

The studies by Balachova *et al.* (2007) and Isurina *et al.* (2009) demonstrated that, in Russia, with the exception of pediatricians, professionals such as physicians, psychologists, nurses and social workers have insufficient knowledge about FASD and usually do not discuss the negative effects of alcohol consumption during pregnancy with their female patients. These studies also demonstrated that gynecologists and pediatricians often had misinformed or inconsistent attitudes toward alcohol exposure during pregnancy such as 'it is tolerable to consume low doses of alcohol in cases involving a healthy pregnancy' (a misinformed attitude). Pediatricians, who were characterized as having inconsistent attitudes, assumed that it is important to convince a woman to abstain from alcohol consumption during pregnancy; however, good quality alcoholic beverages can be consumed during the late stage of pregnancy. Only medical doctors specializing in addiction treatment stated that complete abstinence from alcohol during pregnancy is necessary. Despite the small number of participants, these results (Balachova *et al.*, 2007; Isurina *et al.*, 2009) indicate a lack of knowledge regarding the detrimental effects of alcohol use during pregnancy, even among highly educated individuals in Russia.

In a brief PAE prevention intervention based on evidence-based interventions using techniques of motivational interviewing (Balachova *et al.*, 2010a,b), women were counseled to choose safe contraception or complete abstinence from alcohol consumption. It was recommended that gynecologists of the maternity welfare centers conduct this intervention because Russian women considered them as a reliable source of information (Moskalenko 2002, 2008a,b; Balachova *et al.*, 2010a,b).

Balachova *et al.* (2012b) also evaluated different types of informational leaflets with positive (positive visual images, list of positive outcomes for baby's health in case of abstinence from alcohol), negative (negative visual images, list of negative consequences of alcohol consumption during the pregnancy) and neutral information (general information about healthy life style during pregnancy). The study found that information about FASD increases the general awareness of woman of childbearing age regarding FASD, stimulates them to consider changing their behavior toward abstinence from alcohol in case of pregnancy planning or pregnancy and decreases the level of alcohol consumption among women, in

general. It was also found that women who read the leaflets with positive information had better memories and were able to reproduce factual information about FASD. However, women who read negative information were more likely to develop a strong decision to abstain from alcohol during pregnancy (Balachova *et al.*, 2012b; Regentova, 2012).

As can be seen from the above, there are few published studies on FASD prevention, diagnosis and interventions in Russia. Studies of prevention efforts targeting high-risk women are completely absent.

Only two studies concerning the treatment of individuals with FAS were found in the Russian literature. Transcranial direct current stimulation was reported to be beneficial in normalizing the altered sleep-wake cycle in 13 children with FAS (Malakhova and Bubnov, 2011; Malakhova *et al.*, 2011). Another study reported that after implementing peptide-antiminotoxic therapy on 56 children with FAS, an improvement in psychomotor development was observed in 56–77% of cases, while a positive effect of standard therapy on psychomotor development was observed in 45% cases (Khasianova, 2010). These studies should be considered with caution due to (a) the absence of an appropriate control group, (b) the lack of a clear definition of the outcomes, (c) small sample sizes and (d) lack of appropriate statistical analyses.

Literature reviews and educational materials for health professionals

The search revealed 28 literature reviews that included information on FASD for health professionals (see, for example, Petrov-Maslakov, 1961; Lezhepekova, 1981; Bakanov, 1986, 1999; Mastiukova, 1986, 1989; Skalny and Skosyreva, 1987; Radzinsky and Kostin, 2009; Popova, 2010). (Supplementary material, Table S1). The reviews provided information on a variety of topics including: the evaluation of medical views on the FASD problem through the years, descriptions of the mechanisms of the damaging effects of alcohol on a fetus, descriptions of the clinical characteristics of children with FAS (e.g. growth retardation, birth defects/abnormalities, changes in phenotype, and neurodevelopmental and intellectual disorders) and strategies for FASD prevention (see, for example, Badalyan, 1986; Tabolin and Uryvchikov, 1986; Alipov and Korkhov, 1988; Lisitcyn and Sidorov, 1990; Akhmadeeva, 1997; Ramazanova and Semiatov, 2002; Palchik and Shabalov, 2009; Balachova *et al.*, 2012c).

An educational trial was conducted to evaluate FASD training developed for obstetricians/gynecologists and pediatricians (Balachova *et al.*, 2010a,b). This study claimed that the inclusion of a 3-h FASD education module in continued medical education led to significant changes in physicians' knowledge, attitudes and skills necessary for diagnosing FASD and conducting brief prevention interventions. Furthermore, this study implemented new technologies to disseminate developed FASD education materials and designed the first internet-based FASD educational resource in the Russian language for physicians and other health professionals (www.NetFAS.net; Balachova *et al.*, 2010a,b).

Several studies discussed the ways in which alcohol influences the development of FASD such as the direct damage of alcohol on sex cells, genitals (Koshkina *et al.*, 1998; Shilko *et al.*, 2008b), indirect autoimmune effects (Shilko *et al.*, 2008b) and metabolic disturbance (Lebedev, 1974; Bakanov, 1986; Anokhina and Moskalenko, 1987; Garmasheva and Konstantinova, 1988). The negative effect of alcohol on newborns through breastfeeding has also been reported (Bisiarina and Lisitcyna, 1987; Koshkina *et al.*, 1998). Additionally, some studies discuss the role of acetaldehyde in fetal central nervous system damage (Bakanov, 1986; Anokhina and Moskalenko, 1987; Garmasheva and Konstantinova, 1988). These studies report that an increase in acetaldehyde, ethanol's metabolite, due to insufficient maternal alcohol dehydrogenase activity, is the leading damaging factor in FAS development.

Several studies underline the dose-dependent effect of alcohol on the fetus. Some studies suggest that consumption of 60–80 g of pure alcohol per day leads to FAS (Frolova and Nikolaeva, 1987), while others report that consumption of 150 g of pure alcohol per day increases the chance of FAS development by 50% (Koshkina *et al.*, 1998).

Interestingly, in the older Russian sources from the 1980s, the detrimental effects of alcohol on the fetus were described and pregnancy termination for women with alcohol dependency was strongly recommended (Skosyreva, 1980; Kirushenkov, 1986).

As can be seen from the literature reviews listed above, the majority of them are outdated—70% were published before 2000. In addition, most of the existing reviews only provide general information on FAS. Information pertaining to the practical aspects of diagnostics, treatment, care and prevention are only touched on very briefly. Thus, they are extremely limited in their clinical applicability.

Clinical studies examining children and adults

There were 22 clinical studies conducted on children affected by FASD (Supplementary material, Table S1). These studies provide a description of neurodevelopmental, mental, cardiovascular, gastrointestinal, metabolic and other disorders presented in children with PAE and/or FASD. (Semenov *et al.*, 1987; Donetc, 1992; Erokhova and Bozhenov, 1997; Grjibovski *et al.*, 2002, 2004; Khatckel and Popov, 2005, 2009a,b, 2011; Miller *et al.*, 2006; Ruchkin *et al.*, 2008; Palchik *et al.*, 2009, 2011; Kashirskaya, 2010; Khoroshkina and Krivtcova, 2010; Sheffer, 2012).

The majority of these studies have serious limitations, including: (a) small sample sizes (Shurygin, 1974; Usova *et al.*, 1981; Grechany, 2002; Legonkova and Palchik, 2009), (b) lack of a control group (Usova *et al.*, 1981; Gummel *et al.*, 2007a,b; Khatckel and Popov, 2011) and (c) a failure to properly confirm PAE and thus, a failure to properly establish an FASD diagnosis (Shurygin, 1974; Kunikovskaia, 1980; Kornilov *et al.*, 2005; Sokolovskaya *et al.*, 2009). Most importantly, in all of the existing clinical studies examining children and adults a standardized diagnostic procedure was not used/indicated.

Experimental studies with laboratory animals or human embryos

The search revealed 25 experimental research studies conducted on rats (see, for example, Skosyreva, 1973; Skosyreva *et al.*, 1973; Anokhina *et al.*, 1989; Kolomeitceva *et al.*, 1989; Maizelis *et al.*, 1989; Nozdracheva *et al.*, 1989; Zabludovsky *et al.*, 1989; Zhulin and Bazyan, 1989; Chebotar and Konopistceva, 1993; Omelianchik *et al.*, 1993; Kataeva *et al.*, 2004; Kurch, 2004, 2011; Sverdlova, 2008; Vyatchanina and

Skalny, 2009; Arzamasova, 2011; Pugach, 2012; Shabanov *et al.*, 2012) and 6 studies using human biological material (Kovetcky *et al.*, 1991a,b; Kuteneva *et al.*, 2005; Solonsky, 2006, 2008; Shushpanova and Solonsky, 2012) (Supplementary material, Table S1). The majority of these studies reported polysystemic pathology due to PAE that affects growth, organ development, metabolism, micro- and macro-element balance and neurocognitive functioning. Experimental studies of rats further reinforce the knowledge on the negative effects of alcohol consumption during pregnancy, such as the possibility of depression-like symptoms or memory disorders in the newborns (Kolomeitceva and Levina, 1989). Furthermore, studies using human biological material demonstrated that when a mother consumes alcohol the embryo may develop many different deviations in brain development (Kovetcky *et al.*, 1991a; Solonsky, 2006, Solonsky and Logvinov, 2008). The details of these studies can be found in the Supplementary material, Table S1.

Many experimental research studies have serious limitations; they used small sample sizes (Skalny *et al.*, 2001; Shilko *et al.,* 2009a,b, 2010a,c, 2011b,c), did not describe their sample(s) (Skalny *et al.*, 2009; Morozova and Popova, 2010; Kurch, 2011) and did not present statistical significance (for example, Babenko and Skalny, 1986; Artiukhina *et al.*, 1989).

DISCUSSION

Overall, in the last five decades (the first identified article is dated as 1961), 126 studies related to alcohol consumption during pregnancy and FASD were found that were published in Russia (or on Russian samples). This seems low considering Russia's large area and population [17.1 million km^2; 143 million people as of 2012 according to the Federal State Statistics Service of Russian Federation (FSSS; FSSS, 2012)]. This is also surprising given that Russia has one of the highest rates of alcohol consumption in the world. This leaves us with the question 'why is there such a low interest in this issue in the Russian research community?'

The reviewed studies suffer multiple methodological limitations and weaknesses outlined in the results section and thus, should be viewed with appropriate caution. Despite the limitations, these studies demonstrate a high level of alcohol consumption among Russian women of childbearing age, a low level of contraception usage and an especially high proportion of pregnant women with a pattern of heavy drinking. Based on these findings, it is conceivable that the prevalence of FASD is likely to be high in the general population of Russia.

The present systematic literature review revealed that only a few epidemiological studies reporting the prevalence of FASD exist. However, the reported figures are not generalizable to the general Russian population due to the methodological limitations of the studies (e.g. conducted in small communities with small sample sizes, or conducted among special populations). Valid population-based epidemiological studies are needed to examine the prevalence of FASD in both the general population and populations likely to be at high risk of PAE in Russia. Such information is crucial for understanding the magnitude of the problem and for initiating preventative measures at the country level.

The present review also revealed that the existing research on the negative effects of PAE and FASD available to health and other professionals is not only limited, but also outdated, as the majority of these studies have been published prior to 2000. Moreover, medical education rarely ever includes a course describing the negative consequences of alcohol consumption during pregnancy; most medical doctors are not trained to recognize the clinical features of FASD in Russia (Isurina *et al.*, 2009).

Aside from medical doctors, other health and human services professionals (for example, social workers) are well positioned to help prevent FASD and to intervene with individuals and families affected by FASD. A major setback is that these professionals are also lacking appropriate knowledge and skills regarding the consequences of PAE in Russia (Balachova *et al.*, 2007, 2010a,b). Given the exceptionally high prevalence of children with FASD in foster care, orphanages and other child welfare systems in Russia, there is a need for proper training for professionals in these systems in order to be able to recognize a child with behavioral and/or mental health problems that may be the result of PAE. It is important to make educational materials available to a variety of professionals—such as guidelines for diagnosing and working with individuals already affected, as well as their parents and caregivers.

As a result of the limited research and medical and other educational information, the awareness and knowledge of Russian medical professionals, psychologists, social workers and other professionals about harmful effects of alcohol consumption during pregnancy and FASD is extremely limited (Balachova *et al.*, 2007, 2010a,b; Isurina *et al.*, 2009). There is a large discrepancy between the number of individuals who need to be diagnosed with FASD and receive proper care and the number of available professionals able to provide a proper diagnosis, treatment and other support services.

There is an urgent need to reduce the harmful use of alcohol among women of childbearing age in Russia and initiate prevention strategies targeting pregnant women. Prevention efforts need to be widely spread and should target women of childbearing age and clearly state that there is no safe time to consume alcohol during pregnancy, nor is there a safe amount or type of alcohol. The present literature review presents some effective strategies that could be implemented in these types of FASD prevention programs. For instance, Moskalenko (2002, 2008a,b) advises that the main method of preventing alcohol intake during pregnancy should involve informing women through primary care physicians, and to use positive reinforcement rather than threats. Also, several studies point out that there are misconceptions about FASD, as well as lack of awareness of FASD symptomatology (Balachova *et al.*, 2007). Improving awareness could be an effective way to minimize drinking in women of childbearing age. A randomized educational trial indicated that including FASD information in standard continuing medical education courses significantly improves physicians' knowledge, attitudes and skills (Balachova *et al.*, 2010a). Another study suggests that simple interventions such as distributing leaflets containing both positive and negative information about the consequences of drinking during pregnancy increase the general awareness of women of childbearing age and their attitudes about FASD (Balachova *et al.*, 2012b; Regentova, 2012). Thus, such research studies are a valuable tool for structuring FASD prevention programs that target women who may become pregnant.

As the literature indicates, the population of alcohol-dependent women in Russia is large; however, the principles

of prevention measures and interventions for alcohol-dependent women are underrepresented in the Russian professional literature. This means that the at-risk women are unlikely to receive an intervention for FASD prophylaxis. System-wide screening strategies and targeted interventions for women of childbearing age with alcohol dependence need to be developed. These recommendations should be primary prevention priorities for substance abuse prevention programs.

To conclude, the existing PAE and FASD research underlines the strong negative impact that alcohol has on mortality, morbidity and disability in Russia (Institute for Health Metrics and Evaluation, 2012; Lim *et al.*, 2012; Neufeld and Rehm, 2013). The regulations introduced within the last decade in Russia seem to show some positive effects on both drinking behavior and health outcomes (Neufeld and Rehm, 2013). However, there is an urgent need for further alcohol-control strategies to reduce alcohol-related harm, especially in the field of PAE and FASD.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Alcohol and Alcoholism* online.

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