Knowledge and attitude of healthcare professionals toward medication pregnancy category systems in Saudi hospitals

Thamir M. Alshammari, *MS, PhD,* ***Adel A. Alrwisan,*** *MS, BSc,* ***Majed I. Aljeraisy,*** *PharmD, MSc,* ***Khalid W. Taher,*** *BSc,* ***Faisal M. Alissa,*** *BSc,* ***Mansour A. Mahmoud,*** *MS, BSc,* ***Mohamad A. Hassali,*** *MS, PhD,* ***Hisham S. Aljadhey,*** *PharmD, PhD.*

ABSTRACT

الأهداف: تهدف هذه الدراسة إلى تقويم المعارف والسلوكيات للممارسين الصحيين تجاه الأنظمة المستخدمة في وصف سلامة الأدوية خلال فترة الحمل.

الطريقة: أجري مسح ذاتي مقطعي في 4 مستشفيات في مدينة الرياض بالمملكة العربية السعودية خلال فترة ما بين مارس ومايو 2012.م.وكانت فئة الممارسين الصحيين المستهدفة هم الأطباء والصيادلة . تم التحقق من صحة الاستبانة والتي تشمل أربعة أقسام رئيسة. تم استخدام الإحصاءات الوصفية لعرض الردود على أسئلة الاستطلاع.

النتائج: استجاب 393 ممارس صحي للمسح إستجابة بنسبة 97% . كان نصف المستطلعين أطباء.وكانت نسبة المشاركين من الذكور 60%.واتفق غالبية المشاركين (66%) بأنهم قد وصفوا / صرفوا دواء يسبب آثار جانبية على الجنين. علاوة على ذلك، كان 87% من المستطلعين (48% صيادلة و 39% أطباء) على معرفة بنظام تصنيف استخدام الأدوية خلال الحمل من إدارة الغذاء والدواء الأمريكية، والغالبية منهم بنسبة (72%) وجدوا أن هذا النظام مفيد . 11% فقط من المشاركين يوافقون بشدة على استخدامهم نظام الوكالة الأوروبية للدواء لتصنيف استخدام الأدوية خلال الحمل.

الخاتمة: بشكل عام، لدى الممارسين الصحيين في مستشفيات المملكة العربية السعودية معرفة وسلوكيات جيدة تجاه أنظمة تصنيف استخدام الأدوية خلال الحمل، مع أكثر معرفة بنظام إدارة الغذاء والدواء الأمريكية. ويفضلون نظام إدارة الغذاء والدواء الأمريكية على نظام الوكالة الأوروبية للدواء.

Objective: To assess the knowledge and attitudes of healthcare professionals (HCPs) toward systems used in describing the safety of medications use during pregnancy.

Methods: A cross-sectional self-administered survey was conducted in 4 tertiary hospitals in Riyadh, Saudi Arabia between March and May 2012. The targeted HCPs were physicians and pharmacists. The survey was validated and contained 4 main sections. Descriptive statistics were used to report responses to the survey's questions.

Results: A total of 393 HCPs responded to the survey, with a response rate of 97%. Half of the respondents were physicians. Of the participants, 60% were males. Most respondents (66%) stated that they have prescribed/dispensed a drug that may cause teratogenicity. Moreover, 87% of the respondents (48% pharmacists and 39% physicians) were aware of the Food and Drug Administration (FDA) pregnancy category, and most (72%) found it helpful. Only 11% of the participants strongly agree to use the European Medicine Agency (EMA) system for pregnancy category system as their main reference.

Conclusion: In general, HCPs in Saudi Arabian hospitals have good knowledge of and attitudes toward pregnancy category systems, with more familiarity with the FDA system. The FDA system is preferred over the EMA system.

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From the Department of Clinical Pharmacy (Alshammari), College of Pharmacy, Hail University, Hail, the Medication Safety Research Chair (Alshammari, Alrwisan, Mahmoud, Aljadhey), the Clinical Pharmacy Department (Tahir, Alissa, Aljadhey), King Saud University, the Vigilence and Crisis Management Directorate (Alrwisan), Saudi Food and Drug Authority, the Research Office (Aljeraisy), King Abdullah International Medical Research Center, the College of Medicine (Aljeraisy), King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Kingdom of Saudi Arabia, and the School of Pharmaceutical Sciences (Hassali), Universiti Sains Malaysia, Penang, Malaysia.

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Address correspondence and reprint request to: Dr. Thamir M. Alshammari, Department of Clinical Pharmacy, College of Pharmacy, Hail University, PO Box 6166, Hail 81442, Kingdom of Saudi Arabia. E-mail: thamer.alshammary@gmail.com/th.alshammari@uoh.edu.sa

The use of medicines by pregnant women has always posed a challenge to health care practitioners, and patients to some extent. A major reason for this is the sparcity of well-designed studies establishing the safety profile of these medicines among this vulnerable group.[1] Furthermore, the quality and type of available information on medications adds to the complexity of judging the benefit-risk balance of such medicines.[2] Healthcare professionals (HCPs) can choose from several category systems available regarding the risk of medication use in pregnancy. However, the system chosen could significantly affect the clinical decision; for example, one study found 74% discrepancy between 3 systems in the assigned pregnancy risk category.[3] Further, there is inconsistencies in the pregnancy information within the same pregnancy category system, and further complicated by discrepancies for the same active ingredient depending on the manufacturer.[4] The variation in use of risk categories could be of greater importance in Saudi Arabia as HCPs come from various countries, and thus their health education varies. Furthermore, there has been a criticism of one of the most widely used risk classifications; that developed by the United States Food and Drug Administration (US FDA), with the suggestion made that it may simplify judgment of the complex benefit/risk balance.[2] Therefore, in 2008 a new form of the pregnancy and lactation labeling rule was proposed by the US FDA.[5] In Saudi Arabia, there are 2 systems used to describe pregnancy safety information in drugs labels: the FDA system, which is classified to A, B, C, D, and X. The second system is based on the European Medicine Agency (EMA), which provides textual description on the safety of the medicine use during pregnancy.[6] There is a lack of studies addressing the knowledge and attitude of HCPs concerning the type of information used in the process of prescribing/dispensing medications to pregnant women. This is important for formulary management to determine what medicine should be considered in the light of their benefits and potential risks. This study aims to assess the knowledge and attitude of HCPs, in Saudi Arabia regarding the pregnancy category systems of medications, and the use of medicines during pregnancy.

Methods. A cross-sectional self-administered survey was conducted in 4 tertiary hospitals in Riyadh, Saudi Arabia, between March and May 2012. The questionnaire was structured to contain 4 main sections. The first section was designed to assess the HCPs' practice toward prescribing or dispensing medications during pregnancy. This section included questions regarding the frequency of prescribing or dispensing medications to pregnant women, if they have had prescribed or dispensed medications known to cause teratogenicity, and whether they check the teratogenicity information for that drug or not (**Appendix A**). The second and third sections assessed the HCPs' knowledge of, and attitude toward the use of the USFDA pregnancy category and the text pregnancy risk information used in Europe (**Appendix A**). For the latter, questions asked included whether the HCPs had used this category system alone when they decide to prescribe or dispense a drug to a pregnant woman, or if they had used it along with the US FDA pregnancy category (**Appendix B**). The last section included participants' demographics. The questionnaire was face and content validated and piloted with 10 HCPs who have research experience. It was then modified accordingly. Questionnaires were distributed by research assistants in the respective hospitals. We included a convenient sample of physicians and pharmacists in this study, since in Saudi Arabia only physicians can prescribe medications, and only pharmacists may dispense medications. We allowed 3 days for questionnaire completion. The HCPs who failed to fill in the survey were reminded once and were given 10 additional days to obtain their responses. Uncompleted surveys within the allotted time were considered as non-respondent.

Descriptive statistics were used to report responses using Statistical Analyses Software (SAS 9.3) (SAS Institute Inc., Cary, NC, USA). A chi-square test or Fisher exact tests were used to analyze the categorical data. All statistical tests were conducted with a 2-tailed alpha of 0.05. This study was approved by the Research Committee at the Medication Safety Research Chair at King Saud University and the King Abdullah International Medical Research Center at National Guard Hospital.

Results. A total of 393 HCPs responded to the survey with a response rate of 97%. Half of the respondents were physicians, while the other half were pharmacists; 60% of the HCPs were males. In addition, most physicians were consultants and general practitioners. Approximately 36% of the participants have work experience in their field of over 10 years. Nearly 41% of the respondents reported prescribing or dispensing medications to pregnant women on a

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daily basis (**Table 1**). Further, most respondents (61%) have prescribed or dispensed a drug that may cause teratogenicity to pregnant women. When stratified by HCP type, there was no difference among the HCPs, 29% for each type. Approximately 30% of HCPs always check the pregnancy safety information of medications prior to prescribing or dispensing. Pharmacists (19%) checked safety information more often than physicians (11%) did; however, this difference was not statistically significant (p=0.08). Additionally, 16% and 21% of the participants reported they rarely or never checked the pregnancy safety information. As a source of information on drug use in pregnancy, approximately one fifth of HCPs used the drug leaflet information, while 55% preferred to use Micromedex®.

Table 2 shows types of references used by HCPs. The proportion of pharmacists (15%) that used Drug and Poison Information Centers was greater than physicians (11%). Over 32% of physicians always used Micromedex® while only 7% of pharmacists used it. Furthermore, 20% of physicians always used Lexicomp®, compared to 12% of pharmacists. The vast majority of respondents (87%) (pharmacists 48% and physicians 39%) were aware of the FDA pregnancy category, and 72% found it helpful (**Figure 1**). Approximately 23% of the participating physicians reported the FDA system was not useful and practical during their daily practice. When the participants were asked on each pregnancy category (category A-X), they stated all these categories play a role in their decision. However, the vast majority of them agreed that categories A and B are the most useful, while category D and X have lower rates of usefulness with 22% and 34% (**Table 3**). Thirty-eight percent of the respondents strongly agreed that they use the FDA as their sole source (**Figure 2**). On the other hand, only 11% of the participants strongly agreed they use the EMA system for pregnancy category system as their main reference (**Figure 3**). Twenty-seven percent of the respondents strongly agree that they use both the FDA pregnancy category and EMA system (**Figure 4**).

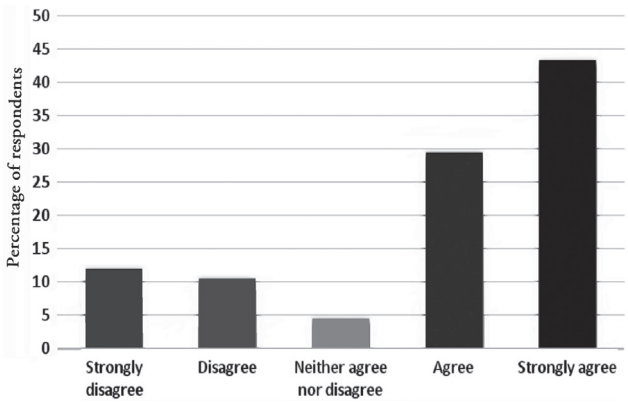

Figure 1 - The Food and Drug Administration category system (A, B, C, D, or X) is very helpful and practical for decision making when there is a need to prescribe/dispense a medication to a pregnant woman (n=284)

Table 1 - Frequency of prescribing/dispensing medication to pregnant women on a daily, weekly, monthly, and non-basis.

Frequency	n (%)
On a daily basis	157 (41)
On a weekly basis	71 (19)
On a monthly basis	100 (26)
Never	53 (14)
Total	**381(100)**

Table 3 - The pregnancy categories are helpful for you in making the decision to prescribe/dispense a medication to a pregnant woman.

Pregnancy category	To a great extent	Somewhat	Very little	Not at all
Category A	85	9	4	2
Category B	65	28	5	2
Category C	32	43	19	6
Category D	39	19	20	22
Category X	54	8	4	34

Data are expressed as percentage

Table 2 - Resources used to check pregnancy safety information by study participants.

Source	Always	Usually	Sometimes	Rarely	Never
Product leaflet/insert	11	10	25.5	25.5	28
Specialized reference for pregnancy	20	21	24.0	16.0	19
Hospital formulary	21	21	22.0	17.0	18
Micromedex®	42	13	16.0	11.0	18
Lexi Comp® (Uptodate)	33	14	17.0	14.0	22
British National Formulary	19	15	23.0	22.0	21
Regulatory agencies websites (FDA)	22	11	25.0	23.0	19
Drug and Poison Information Centre	29	15	25.0	17.0	14
Expert healthcare provider	20	16	31.0	18.0	15

Data are expressed as percentage. FDA - Food and Drug Administration

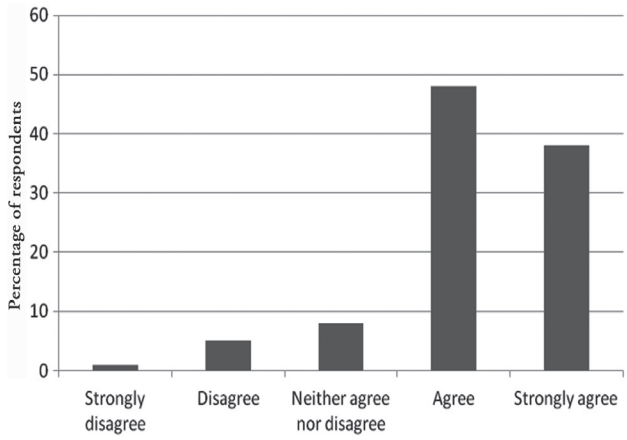

Figure 2 - Food and Drug Administration pregnancy risk classification system for pregnancy safety information (n=347).

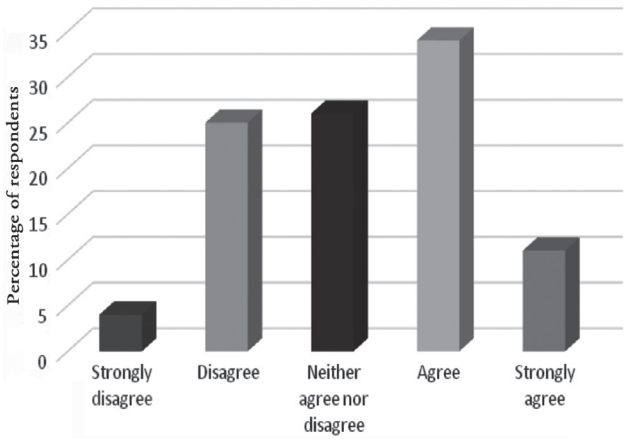

Figure 3 - European Medicine Agency description for pregnancy safety information (n=349).

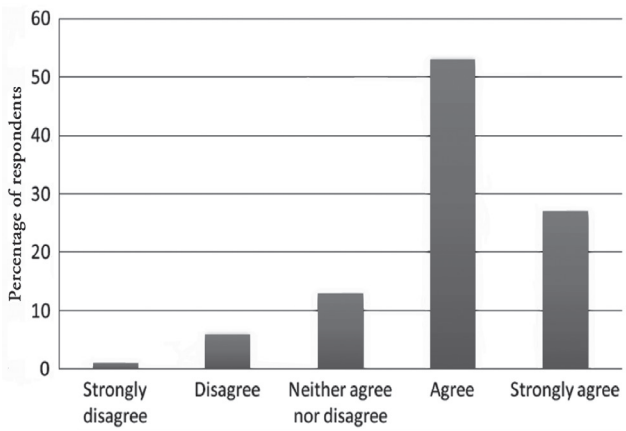

Figure 4 - Food and Drug Administration pregnancy risk classification system and the European Medicine Agency description for pregnancy safety information (n=344).

Discussion. We studied the knowledge and attitude of HCPs toward the medication pregnancy category systems and medication use during pregnancy in Saudi Arabia. The rationale of this study related to the fact that these pregnancy category systems have been available for many years; however, data on their usefulness is sparse. Furthermore, there are no data on HCPs' knowledge of and attitude toward using both the FDA pregnancy category system and the European pregnancy category system in the Saudi Arabian context.

A high number of the HCPs participating in this study have prescribed or dispensed a drug that may lead to teratogenicity, from which we can speculate there may be alarming indications that medication use by pregnant women is a serious issue in Saudi Arabia. In Saudi Arabia, it has been found that physicians and pharmacists have lower compliance with the recommendations of proper use of drugs during pregnancy.[7,8] Another alarming indicator of a lack of awareness regarding the importance of checking medications' teratogenicity information is that only 30% of participating HCPs check the teratogenicity information for the drug that will be dispensed or prescribed to their patients. This increases the risk, as pharmacists often do not check this information, considering that it is the responsibility of the treating physician.

Micromedex® is the most regularly used reference to check pregnancy information, followed by Lexicomp® and the Drug and Poison Information Centers. With respect to Lexicomp®, these results were quite similar to those of a study performed by Mountford et al,[9] investigating the quality, and usability of common drug information databases; they found that Lexicomp® was the most preferred reference. However, Micromedex® was the least preferred reference, whereas it was the most used reference in our study.

Most HCPs are aware of the FDA pregnancy category system and believe this system to be of a great value to them during their daily practice. However, a study drawing comparisons between 3 category systems: the USFDA, the Australian Drug Evaluation Committee (ADEC), and the Swedish Catalogue of Approved Drugs (FASS), found that only 25% of the medications have the same pregnancy category.[3] This could create confusion and difficulty in interpreting information related to the use of medicines during pregnancy. Another study[10] compared the drug teratogenicity information in the FDA category system with the Teratogen Information System (TERIS). The authors found discrepancies in the teratogenicity information between the 2 systems, for instance, 20 drugs have no, minimal, or an unlikely risk, while the FDA categorized

17 of them as class C and 3 as D or X. Thus, in the context of deciding the benefit/risk balance for using a drug during pregnancy, it is important to be aware of some of the differences among the pregnancy category systems available. A study found that 21% of pregnant women have been prescribed medications with a teratogenicity risk.[11] Another Finnish study had similar results.[12] A systematic review examining outpatient drug use among pregnant women found that in some countries, such as France, approximately 59% of pregnant women had received drugs with teratogenicity risk.[13] However, it is also important to mention that even if there is teratogenicity risk from a specific drug, patients should not discontinue it without consulting their physician, since this might affect negatively the patient's disease state, as in case of some psychiatric diseases.[14]

It was anticipated that it would be easier for HCPs to balance benefits and risks of drugs based on the A, B, and X categories. One of the least useful categories was C; this could be due to the fact that this category does not allow for a clear judgment on whether to use the drug or not. This result could be cause for alarm, because more than 60% of medications are classified as category C.[15] Similar results were found by Bertoldi et al,[16] as they found that approximately 52% of the participated mothers in the study have used at least one drug with unknown fetal risk, most of which are classified as category C by the FDA category system.

In terms of use of the pregnancy category systems, we found firstly that respondents used the FDA category system, indicating this to be the most commonly used system in Saudi Arabia. This could be attributed to its ease of use, especially for categories A, B, D, and X; 2) the information they are seeking is only available in the FDA category system; or 3) their educational background was influenced by the American system. To a lesser extent some respondents used both (US and Europe) pregnancy category systems, which may be for a number of reasons: 1) HCPs like to use one system and then double-check against the other; 2) HCPs had used one system and did not find a conclusive answer, and therefore decided to use the other; and 3) the narrative system was used to give more details about the drug teratogenicity risk. Finally, some respondents - again, fewer than in the other 2 groups - use only the narrative system, which could be due to several reasons: 1) HCPs like to get more detailed information about the drug risk, rather than only using the letter system; 2) the medication's pregnancy category risk may only be available through the narrative system, especially if the drug is manufactured and available in a European country such as the United Kingdom.[4]

Limitations of this study include that although study participants claim they are aware of the pregnancy category systems; we were not able to assess the reported knowledge. Our findings might not be generalizable to other setting, such as primary care where most of the medicines are prescribed, and could not be generalized to other cities in Saudi Arabia as the practice standards may vary.

In conclusion, it may be concluded that HCPs in Saudi Arabia are aware of the FDA and EMA medication pregnancy category systems, with more familiarity to the former. Moreover, there is a preference for using the FDA over the European system. Notable, there are a large proportion of Saudi physicians and pharmacists had either prescribed or dispensed a teratogenic medications to their patients, which emphasizes the necessity of checking medicine pregnancy safety information to ensure safe use. Further studies exploring other settings and expanding geographical coverage will allow better understanding of the use of information on pregnancy exposure in Saudi Arabia.

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Appendix A - Health care professionals practice toward information for the use of medicines during pregnancy.

Dear participant:
The aim of this questionnaire is to provide insight about the practice of healthcare providers on the source and the type of safety information about medicines when using medications for pregnant women.
Please be advised that all information in this survey will be dealt with in strict confidence and will be used for research purposes only.
Thank you for participating in this study.

Please mark the appropriate box next to your answer choice with an "x". Please answer all of the questions to the best of your ability

1. How frequent do you prescribe/dispense a medication to pregnant women?

☐ On daily basis ☐ On weekly basis ☐ On monthly basis ☐ Never

2. Do you have any experience of using medications during pregnancy that caused teratogenicity?

☐ Yes ☐ No

3. I check for updates concerning the safety information for medicines when deciding to prescribe/dispense a medication to pregnant women

☐ Always ☐ Usually ☐ Sometimes ☐ Rarely ☐ Never

4. When I need to check pregnancy safety information for a medicine I will use: (please fill all sources you use)

Source	Always	Usually	Sometimes	Rarely	Never
Product leaflet/insert					
Specialized reference for pregnancy					
Hospital formulary					
Micromedx					
Lexi Comp (up to date)					
British National Formulary					
Regulatory agencies websites (Food and Drug Administration [FDA])					
Drug and poison information center					
Expert healthcare provider					
Other (specify)					

5. Are you aware of the FDA pregnancy classification (A, B, C, D or X)?

[ ] Yes [ ] No If no please go to question number 10

PLEASE CONTINUE OVERLEAF

6. The FDA classification system (A, B, C, D, or X) is very helpful and practical for decision making when there is a need to prescribe/dispense a medication to a pregnant woman

☐ Strongly agree ☐ Agree ☐ Neither agree nor disagree ☐ Disagree ☐ Strongly disagree

7. To what extent the pregnancy categories is helpful for you to make decision to prescribe/dispense a medication to a pregnant woman? (please answer all categories)

Pregnancy Category	To a great extent	Somewhat	Very little	Not at all
Category A				
Category B				
Category C				
Category D				
Category X				

8. For pregnancy safety information I only use the FDA pregnancy risk classification system (A, B, C, D, or X)

☐ Strongly agree ☐ Agree ☐ Neither agree nor disagree ☐ Disagree ☐ Strongly disagree

9. For pregnancy safety information I will use both pregnancy risk classification letter (A, B, C, D, or X) and the narrative description (for example teratogenic effect)

☐ Strongly agree ☐ Agree ☐ Neither agree nor disagree ☐ Disagree ☐ Strongly disagree

For pregnancy safety information I only use the narrative description (for example: teratogenic effect)

☐ Strongly agree ☐ Agree ☐ Neither agree nor disagree ☐ Disagree ☐ Strongly disagree

11. Participant Demographic Information

Gender	Male	Female
Age		
Experience		
Health specialty		

Appendix B - United States Food and Drug Administration Pregnancy Category System.[17] *Adapted from US Federal Agency (FDA). Federal Register. Department of Health and Human Services. Food and Drug Administration. 2008/Vol. 73, No. 104. 21 CFR Part 201*

Pregnancy category	Explanation
A	Adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus in the first trimester of pregnancy
B	Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women. Or animal reproduction studies have shown an adverse effect (other than decrease in fertility), but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus during the first trimester of pregnancy.
C	Animal reproduction studies have shown an adverse effect on the fetus, but there are no adequate and well-controlled studies of humans. The benefits from the use of the drug in pregnant women might be acceptable despite its potential risks. Or animal studies have not been conducted and there are no adequate and well-controlled studies of humans
D	There is positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experience or studies of humans, but the potential benefits from the use of the drug in pregnant women might be acceptable despite its potential risks
X	Studies in animals or humans have demonstrated fetal abnormalities or there is positive evidence of fetal risk based on adverse reaction reports from investigational or marketing experience, or both. The risk involved in the use of the drug in pregnant women clearly outweighs any possible benefits