

# Vaccines are underused in pregnancy: what about knowledge, attitudes and practices of providers?

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**Summary.** *Introduction.* To investigate actual knowledge of official recommendations towards seasonal influenza (SID), and Tetanus-diphtheria acellular-pertussis (Tdap) vaccines in obstetrics/gynecologists (OB-GYN). *Methods.* PubMed and EMBASE databases were searched. A meta-analysis was performed to calculate odds ratio (OR) and 95% confidence interval (CI) among case controls, cross-sectional studies, either questionnaire or laboratory exams based. *Results.* A total of 6 studies met inclusion criteria, including 1323 OBGYN from 5 different countries. Overall, around 99% of sampled professionals were aware that official recommendations towards SID in pregnancy do exist, compared to 92% for Tdap, with significant heterogeneity ( $I^2 > 95\%$ ,  $p < 0.001$ ). Concerns about vaccine safety was reported by 10% of respondents for Tdap, and by 6.0% for SID, but again available studies were substantially heterogenous ( $I^2 = 86.7\%$  and  $86.0\%$ ,  $p < 0.001$ ). Eventually, 93% of respondents actively recommended SID in pregnancy, compared to 88% for Tdap ( $I^2 98.8\%$  and  $I^2 95.9\%$ , respectively  $p < 0.001$ ). The evidence of significant publication bias was initially subjectively identified from the funnel plot, and then objectively confirmed through the regression test for all analyses. *Conclusions.* These results suggest an appropriated understanding of official recommendation among sampled OBGYN, with high shares of professionals actively promoting vaccination practices among their patients. Despite the high heterogeneity and the significant publication bias we identified, our results also hint towards extensive knowledge gaps of OBGYN, and particularly regarding unmotivated concerns about vaccine safety. As a consequence, appropriate information and formation campaigns should be appropriately tailored. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** vaccination, pregnancy, influenza vaccines, Pertussis vaccine, Diphtheria-Tetanus-Pertussis Vaccine

## Introduction

Pregnant women and infants under 6 months are at higher risk for adverse outcomes from seasonal influenza (SID) and pertussis (1–6) and opinions concerning potential barriers to immunization, among obstetrician-gynecologists. Methods: In 2007, surveys

were sent to Collaborative Ambulatory Research Network members, a representative sample of practicing Fellows of the American College of Obstetricians and Gynecologists; 394 responded (51.2%). Therefore, maternal immunization has been proposed as an evidence based strategy to prevent or mitigate the severity of infections in pregnant women and their newborn in-

fants through transplacental antibody transfer (7,8). However, CDC have recently reported that around 65% of American women do not receive influenza Tetanus-diphtheria acellular-pertussis (Tdap) vaccines, as otherwise recommended by available guidelines since 2011 (9).

Root cause analyses for inappropriate vaccination rates usually focus on knowledge, attitudes and practices (collectively, KAPs) of the target populations (ie pregnant women) (10–12), but also knowledge gaps and misbeliefs of healthcare providers may actively contribute (13–15). In particular, a certain base of evidence points towards the lack of understanding of obstetrics-gynecologists (OBGYN) of official recommendations for SID/Tdap vaccines, that associated with their potential overstating of potential health effects of immunizations, may collectively contribute to restrain pregnant women from appropriate vaccinations (14–16).

Therefore, this systematic review will assess the available base of evidence about KAP of OBGYN towards SID/Tdap vaccines.

## Materials and Methods

This systematic review has been conducted following the PRISMA (Prepared Items for Systematic Reviews and Meta-Analysis) guidelines (17). We searched into two different databases (PubMed and Embase) for relevant studies published from 2011 (ie inclusion of SID/Tdap among recommended vaccinations for pregnant women) to 31/12/2019, without any chronological restriction. The search strategy was a combination of the following keywords (free text and Medical Subject Heading [MeSH] terms): “*knowledge, attitudes, practices*”, “*obstetric\**”, “*gynecologist\**”, “*vaccin\**”, “*immunization*” (Figure 1). Records were handled using a references management software (Mendeley Desktop Version 1.19.5, Mendeley Ltd 2019), and duplicates were removed.

Articles eligible for review were original research publications available online or through inter-library loan. Articles had to be written in Italian, English, German, French or Spanish, the languages spoken

by the investigators. Studies included were national and international reports, case studies, cohort studies, case-control studies and cross-sectional studies. Only articles reporting the actual number of OBGYN included in the study, and deliberately assessing knowledge of official recommendations towards Tdap and/or SID, were eligible for the full review. Articles were excluded if: (1) full text was not available; (2) articles were written in a language not understood by reviewers; (3) reports lacked significant timeframe (ie the year of study); (4) reports including OBGYN alongside other healthcare providers lacked discrete figures for OBGYN.

Two independent reviewers reviewed titles, abstracts, and articles. Titles were screened for relevance to the subject. Any articles reporting original studies, which did not meet one or more of the exclusion criteria, were retained for full-text review. The investigators independently read full-text versions of eligible articles. Disagreements were resolved by consensus between the two reviewers; where they did not reach consensus, input from a third investigator (MR) was obtained. Further studies were retrieved from reference lists of relevant articles and consultation with experts in the field.

Data abstracted included:

1. Total number of OBGYN participating into the study;
2. Settings of the study, including the characteristics of the sampling strategy and whether a power analysis had been preventively performed in order to ascertain the appropriate sample size;
3. Share of respondents aware of official recommendations towards Tdap and/or SID vaccinations in pregnancy;
4. Share of respondents exhibiting concerns towards Tdap and/or SID vaccinations in pregnancy;
5. Share of respondents reportedly recommending Tdap and/or SID vaccinations in pregnancy.

We first performed a descriptive analysis to report the characteristics of the included studies. The pooled prevalence of the reported KAP were initially calculated, and  $I^2$  statistic was then calculated to quantify the amount of inconsistency between included studies; it estimates the percentage of total variation across

studies that is due to heterogeneity rather than chance.  $I^2$  values ranging from 0 to 25% were considered to represent low heterogeneity, from 26% to 50% as moderate heterogeneity and above 50% as substantial heterogeneity, being pooled using a fixed-effects model because of the reduced number of samples eventually included. To investigate publication bias, contour-enhanced funnel plots were generated, and regression test for funnel plot asymmetry were ultimately performed with calculation of correspondent Z value with their p value. All calculations were performed by means of *metafor* package with R (version 3.4.3) and RStudio (version 1.1.463) software.

## Results

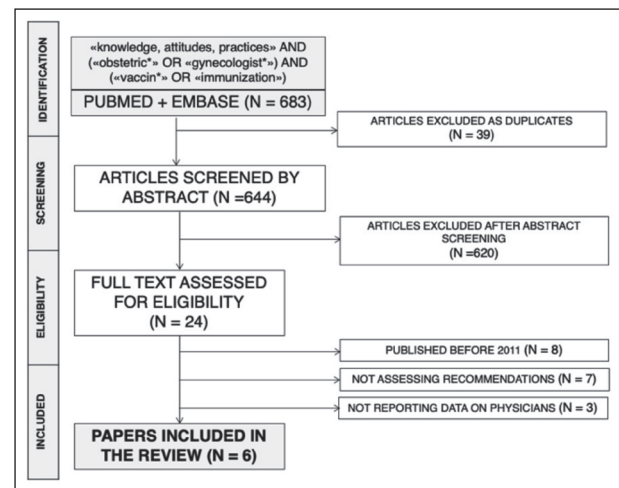
Initially, 683 entries were identified. After applying the inclusion and exclusion criteria (Figure 1), 6 articles were included in the analyses and summarized (Table 1).

The studies reported KAP of obstetrics and gynecologist from USA (2 studies) (2,18), Italy (in table 1, 14 was reported), Lebanon (19), Israel (20), and Germany (21), for a pooled population of 1323 health-care providers, and 65.53% of them were from a single German study (21).

As shown in Table 1, in 5 studies, sampling was performed by convenience (2,15,18,19,21), and only in three cases a preventive power analysis was performed (19–21). Even though 4 studies were reportedly multicenter ones, only three of them eventually included pro-

fessionals from various geographical areas (19–21). All studies employed a structured questionnaire, that in the majority of cases was self-administered (2,15,18,19,21), also as online surveys (15,21), while in 1 study it was compiled through a face-to-face interview.

Based on the fixed-effect model, as shown in Figure 2, around 99% (95%CI 98-99%) of professionals were aware that official recommendations towards SID in pregnancy do exist (range 57 to in figure 2, 99 was reported), compared to 92% for Tdap (range 24% to 95%), with  $I^2$  of 96.4% ( $p < 0.001$ ) and 98.9% ( $p < 0.001$ ). Interestingly enough, excluding the study of Böhm et al (21) from the pooled analyses, the respective shares would drop to 78.3% and 65.8%.



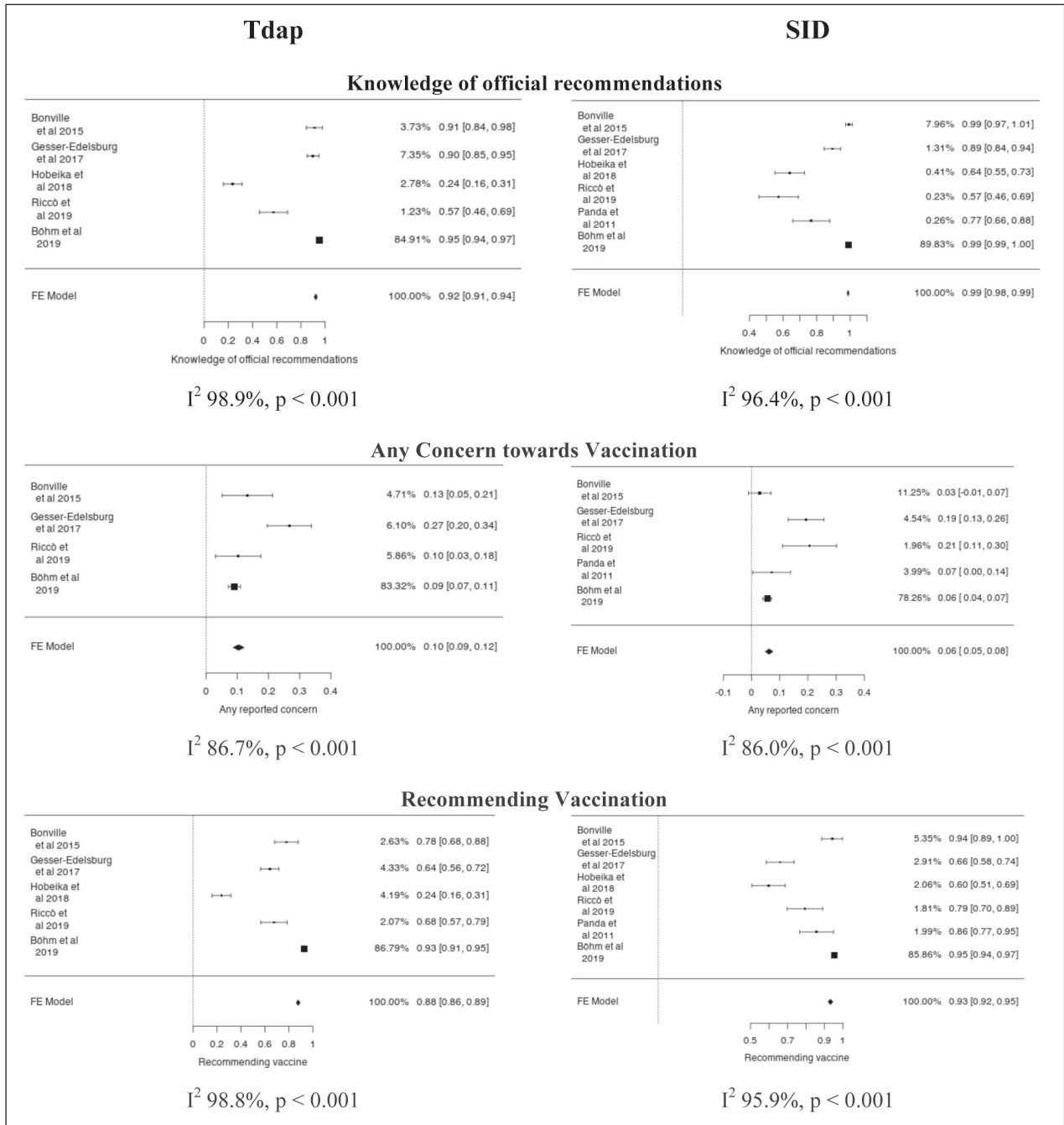
**Figure 1.** PRISMA flow diagram including keywords employed for the inquiry (ie «knowledge, attitudes, practices» AND («obstetric\*» OR «gynecologist\*») AND («vaccin\*» OR «immunization\*»).

**Table 1.** Summary of reported evidence about knowledge, attitudes and practices of obstetrics-gynecologists towards diphtheria-tetanus-pertussis (Tdap) and influenza (Flu) vaccine in pregnant women.

Reference	Country	Sampled practitioners, No./TOT, %	Sampling strategy	Multicenter?	Multiple area?	Preventive Power Analysis?	Self-administered questionnaire?
Bonville et al. (2)	USA	68, 5.14%	Convenience	YES	NO	NO	YES
Gesser-Edelsburg et al. (20)	Israel	150, 11.34%	Quantitative multistage	YES	YES	YES	NO
Hobeika et al. (19)	Lebanon	114, 8.62%	Convenience	YES	YES	YES	YES
Panda et al. (18)	USA	56, 4.23%	Convenience	NO	NO	NO	YES
Riccò et al. (14)	Italy	68, 5.14%	Convenience	NO	NO	NO	YES
Böhm et al. (21)	Germany	867, 65.53%	Convenience	YES	YES	YES	YES
<b>POOLED</b>		1323, 100%		4, 66.67%	3, 50.00%	3, 50.00%	5, 83.33%

A certain degree of concern about vaccine safety was reported by 10% of respondents for Tdap (95%CI 9-12%; range 9 to 27%), and by 6.0% for SID (95% 5-8%; range 3 to 21%). In both cases, available studies were substantially heterogenous ( $I^2 = 86.7\%$  and  $86.0\%$ ,

$p < 0.001$  for both analyses). Still, exclusion from the pooled analyses the single German study would nearly double the share of respondents exhibiting concerns towards assessed immunization (ie 14.3% for SID and 21.1% for Tdap).



**Figure 2.** Forest plots reporting raw proportions with correspondent 95% confidence intervals (95%CI) of participants aware of official recommendations for Tdap and/or SID vaccine in pregnancy, reporting any concern towards Tdap and/or SID, and recommending Tdap and/or SID in pregnant women

Eventually, 93% of respondents actively recommended SID in pregnancy (95%CI 92-95), compared to 88% for Tdap (95%CI 86-89%). Again, the reports were strikingly heterogeneous, with rates ranging from 24% to 93% for Tdap ( $I^2$  98.8%,  $p < 0.001$ ), and from 60% to 95% for SID ( $I^2$  95.9%,  $p < 0.001$ ). However, as better shares for both SID and Tdap were again referred from the German study of Böhm et al (21), eliding such report would shrink average figures to 73.3% for SID and 55.5% for Tdap.

The presence of publication bias was evaluated using contour-enhanced funnel plots and regression test for funnel plot asymmetry. Each point in funnel plots represents a separate study and asymmetrical distribution indicates the presence of publication bias. First, studies' effect sizes were plotted against their standard errors and the visual evaluation of the funnel plot suggested a significant publication bias, as all the 6 graphs appeared largely asymmetrical (**Figure 3**). The subjective evidence from the funnel plot was objectively confirmed using the regression test.

## Conclusions

Despite a growing interest towards immunization KAPs in gynecologists/obstetrics, few studies of inconsistent quality have actually inquired their understanding of official recommendations for Tdap and/or influenza vaccines in pregnancy. More interestingly, only 4 studies have been performed in high-income countries, and 2 of them are USA based. Unfortunately, not only available studies are mostly underpowered, with around 65.53% of participants from a single research (21), but participants are often sampled by convenience (eg participant to conferences/formation courses; members of a certain health center), with subsequent concern on their actual representativity (20). Moreover, only three studies collected participants at a national level (19-21): as a consequence, results are doubtfully generalizable.

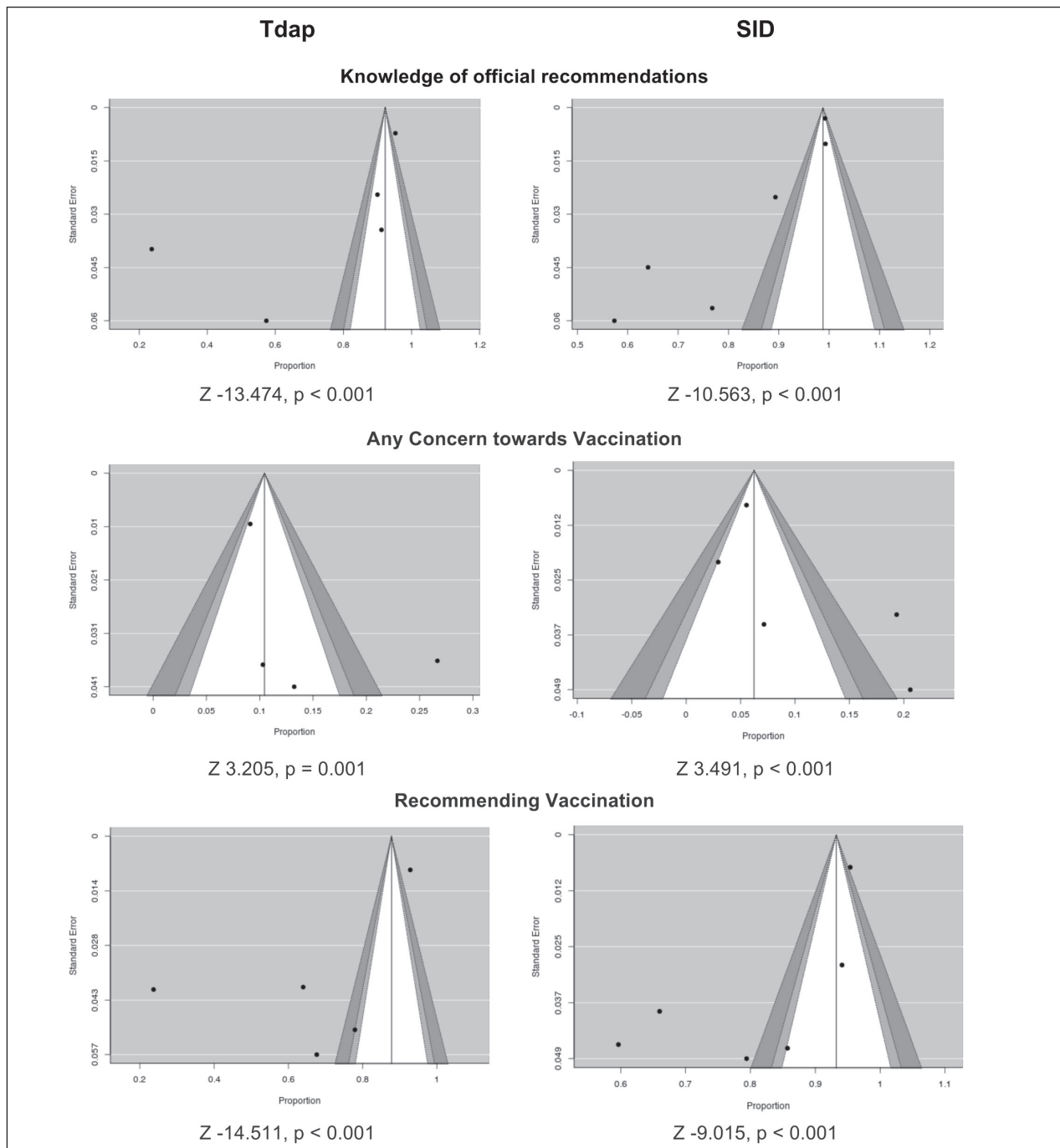
Actually, even though available evidence seemly suggests that OBGYN are extensively aware of official recommendations towards SID and Tdap, the heterogeneity among available studies means that significant uncertainties and knowledge gaps are actually reported

for both immunizations, and particularly for Tdap, with actual figures that may peak to 42.6% (15) and 76.3% (19), respectively.

Interestingly, while the majority of sampled OBGYN recommended Tdap and/or SID, a significant share of sampled medical professionals still reported unmotivated concerns on vaccine safety, particularly on Tdap. As a consequence, available estimates are only limitedly compatible with the usual health belief model, in which a particular protective action is directly influenced by the perceived susceptibility to a health threat, its severity, and perceived benefits and/or barriers (22-24). More probably, our results suggest that OBGYN, while formally coping with official recommendations, still harbor significant and unsolved misconceptions towards Tdap / SID (13,14): similarly to similar reports in vaccinations performed by General Practitioners (25,26), in the school settings (13,27) attitudes and practices of STs towards vaccination are otherwise lacking. Objectives. The aim of this study was therefore to evaluate knowledge and attitudes of STs regarding vaccinations in a sample from North Italy. Material and methods. In this cross sectional study, 154 STs from Lombardy region (Northern Italy, and in the occupational settings (14,16,28-32)Legislative Decree n.81/2008, it is reasonable that such uncertainties in critical providers may contribute in compromising vaccination rates subjects referring to them for information and counseling, as pregnant women for OBGYN (9).

In summary, while patients and their possible vaccine hesitancy are usually identified as the main target for specifically targeted tailored information campaigns (12,33-35)even though immunization is recommended since many years and still remains the fundamental tool for its prevention. Healthcare workers (HCWs, our results suggest that also healthcare providers, and more specifically OBGYN should be specifically targeted in order to overcome the significant share of concerns and misconceptions they otherwise exhibited, eventually improving the safety profile of both mothers and children (1-4, 36-37).

**Conflict of interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article



**Figure 3.** Contour-enhanced funnel plots of the participants aware of official recommendations for Tdap and/or SID vaccine in pregnancy, reporting any concern towards Tdap and/or SID, and recommending Tdap and/or SID in pregnant women.

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- Received: 15 February 2020  
Accepted: 15 March 2020  
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