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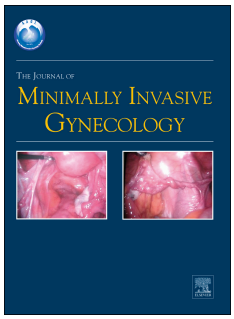

Hysteroscopic Essure Inserts for Permanent Contraception: Extended Follow-Up Results of a Phase III Multicenter International Study

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Letter to the Editor
The Journal of Minimally Invasive Gynecology

Hysteroscopic Essure Inserts for Permanent Contraception: Extended Follow-Up Results of a Phase III Multicenter International Study

July 10, 2015

To the Editor:

We read the article by Drs. Chudnoff, Nichols, and Levie with great interest and applaud their publication of Phase III data on 5 year follow-up after hysteroscopic sterilization [1]. However, we are concerned about their focus on perfect use, rather than real world use. Specifically, their evaluation of effectiveness was based on "women with successful bilateral placement of Essure inserts," rather than women who attempted Essure. For example, the study excluded 4 women who became pregnant before undergoing a hysterosalpingogram (HSG), 15 women who underwent hysterectomy, 1 woman who missed her 6 month follow-up HSG, 1 woman who was incarcerated, 1 woman who had unsatisfactory device placement, and 1 woman with leukemia from the "intention to treat" analysis. By removing these participants from the study's denominator, the proportion of successful procedures appears higher than it really is. In addition, 30% of enrolled women did not complete 5 year follow-up, and these women may have had more problems than women who completed follow-up.

We agree with the authors' hypothesis that some women may not consider laparoscopic sterilization due to the need to have the procedure in the operating room, receive general anesthesia or miss work. Yet the authors do not report how many of the procedures they studied were done in the office versus operating room, information about anesthesia used, or days of missed work.

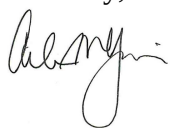
While we appreciate the authors' reference to our previous publications on the topic, we feel that our results were misrepresented, perhaps due to a misunderstanding of our methodology [2,3]. Our Markov models incorporated all relevant data available in the published literature, including data from the manufacturer of Essure. We also performed extensive sensitivity analyses in both studies to assess the impact on our findings when varying the value of key variables over plausible ranges, rather than relying on single parameter assumptions. Moreover, we disagree with the statement that our "models accentuate poor HSG follow-up with hysteroscopic sterilization" [1]. Based on published data that were available at the time of publication on the proportion of women completing HSG follow-up while considering the study size to ensure that findings from a small study do not "count" as much as findings from larger studies, we estimated that on average 79% (range 13-94%) of women returned for the recommended HSG at 3 months [3]. Similarly, our "projected pregnancy rates" are based on published data reported in the literature, including pregnancies reported by the manufacturer on their website [4]. Indeed, data from Chudnoff et al. [1] support findings from our studies. For example, Chudnoff et al report that 81% (421/518) of women were able to rely on the procedure at 3 months

post-procedure [1]. This finding confirms our first Markov model which predicted that approximately 85% of women undergoing attempted hysteroscopic sterilization would be able to rely on the procedure for contraception at 3 months post-procedure [2].

In addition, the authors incorrectly state that our models do not include complication rates. Both major and minor complications related to hysteroscopic and laparoscopic sterilization were incorporated in the first Markov model [2], and we found no significant difference in complications between the two procedures based on the data available at that time [2]. In contrast, inherent in Chudnoff et al's discussion of complications is the assumption that there are fewer complications with hysteroscopic than laparoscopic sterilizations. Although Chudnoff, et. al., discuss 457 adverse events related to hysteroscopic sterilization with Essure reported on the Manufacturer and User Facility Device Experience (MAUDE) database, the FDA recently updated this number to 5093 adverse events reported since the 2002 approval [5]. This increase in adverse events has prompted the FDA to convene a public meeting of its Obstetrics and Gynecology Devices Panel on September 24, 2015 to discuss data regarding Essure's safety and effectiveness.

As 750,000 women have undergone hysteroscopic sterilization worldwide since 2001, evaluating the safety and effectiveness of hysteroscopic sterilization is of great importance. We still lack data about the short and long-term side effects, safety, need for further surgery including hysterectomy, and risk of pregnancy in women who attempt Essure, not just a subset of those that have successful placement and receive follow-up with confirmation of tubal blockage. Women and their physicians need this essential information to truly make informed decisions regarding choice of sterilization procedure.

Sincerely,



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