

Public Comments & Responses

Ultrasonography (Ultrasound) in Pregnancy

Health Technology Assessment

Date: September 22nd, 2010

Hayes, Inc. Report on Ultrasonography (Ultrasound) in Pregnancy**Response to Public Comments**

Hayes Inc. is an independent vendor contracted to produce evidence assessment reports for the WA HTA program. For transparency, all comments received during the comments process are included in this response document. Comments related to program decisions, process, or other matters not pertaining to the evidence report are acknowledged through inclusion only.

This document responds to comments from the following parties:

- Medical Imaging & Technology Alliance (MITA) (letter from Executive Directory Dave Fisher)
- Society for Maternal-Fetal Medicine (SMFM) (letter from President Joshua Copel, MD)
- Association for Medical Ultrasound (AIUM) (letter from President Harvey L. Nisenbaum, MD)

Medical Imaging & Technology Alliance (MITA)*Comment Process*

MITA requests that the Washington HTA process allow 30 days rather than 2 weeks for comments and that the public meeting precede preparation of the final evidence report.

Evidence Related to TVU/Preterm Birth, Early Screening in Low-Risk Patients, and Late Screening in Low-Risk Patients

MITA requests consideration of numerous additional articles. With one exception, these studies, narrative reviews, and editorials do not meet the inclusion criteria for the report, i.e., systematic reviews or studies with control groups that evaluated the effect of US scanning on change in patient management; frequency of Cesarean section and abortion; or maternal and fetal health outcomes, including frequency of preterm birth. None of the recommended articles addressed clinical utility in these terms. Generally, these articles addressed the issue of accurate prediction, which is a necessary but not sufficient condition for clinical utility. Furthermore, the suggested articles generally presented data pertaining to statistical associations between US findings and conditions or future outcomes rather than sensitivity, specificity, or other actual measures of diagnostic accuracy.

One recommended study (“A Randomized Trial Using Ultrasound to Identify the High-Risk Fetus in a Low-Risk Population” by McKenna et al. [2003]) *did* meet the inclusion material for the HTA report and was included in the selected systematic review and meta-analysis by Bricker et al. (2008).

Other Points

The letter points out that that some fetuses with unknown anomalies will be carried to term, with the result of neonatal death or birth followed by life-altering disabilities. The letter refers to the value patients might attach

to the information that US detection would provide. This is a good point that might have policy implications but does not relate to the health and management outcomes implied by the key questions defined for the evidence report.

Society for Maternal-Fetal Medicine (SMFM)

Limitations of the RADIUS Trial

This trial (Ewigman et al., 1993) was included in two selected systematic reviews with meta-analyses, one review of routine US screening in early pregnancy (Whitworth et al., 2010) and one review of routine US screening in late pregnancy (Bricker et al., 2008). The RADIUS trial also served as the basis for sensitivity and utilization estimates in the selected cost-effectiveness study by (Vintzileos et al., 2000). The letter makes several criticisms:

“The discussion about the impact of routine ultrasound is based in large part on the RADIUS study,” While the RADIUS study was by far the largest of the studies included in the two systematic reviews, it was only one of several studies, accounting for somewhat more or somewhat less than half of patients included in pooled estimates for the key outcomes of perinatal mortality and perinatal morbidity.

“...which relied mainly on complications of prematurity for its composite [perinatal adverse] outcome,” Many of the outcomes that were used to define the composite outcome (Table 2 in the article) could be caused by circumstances other than premature birth. Examples include spinal cord injury, presumed neonatal sepsis, necrotizing enterocolitis, intraventricular hemorrhage, or bone fracture. The letter from SMFM does not specify any perinatal outcomes that might be prevented by US screening but were omitted from the composite outcome definition.

“... was underpowered to detect any change in morbidity or mortality due to birth defects” The study was powered to detect a 20 percent relative difference in the incidence of adverse perinatal outcome. Power calculations were based on an assumption of a 5% incidence in the control group. Thus, the study was powered to detect a significant difference if the control group incidence had been 5% and the US group incidence had been in the range of 4% to 6%. The observed incidences were 4.9% in the control group and 5.0% in the US group, an absolute difference of 0.1 percentage points and a relative difference of only 2%. The study was not large enough to show this difference to be significant, but the result favored the control group, and the magnitude of the difference was of doubtful clinical importance. Incidence differences when broken down by fetal death, neonatal death, severe morbidity, and moderate morbidity were 0 to 0.1 percentage point.

“... and contained erroneous cost assumptions.” In the Discussion section of the RADIUS study article, the authors estimated cost savings based on trial results and an assumption of \$200 per US scan (the study was published in 1993). The source of the price assumption was not identified. Given the price data available from later sources (\$200 to \$400), it is possible that \$200 is an overestimate of the cost of US for the time period represented by the RADIUS study. However, the evidence report draws no conclusions from the cost data supplied by the RADIUS authors.

“This problem also makes the ICSI guideline unreliable.” The ICSI guideline cites several studies in addition to the RADIUS trial and concludes “An overall assessment of the existing evidence does not support the use of routine ultrasound examination in low-risk pregnancies as there currently is no proof of improved perinatal outcome.”

Omission of a Study of Progesterone for Treatment of Short Cervix (Fonseca et al., 2007)

This study assesses the effectiveness of progesterone, not the effectiveness of US. It compares outcomes between women who did and did not receive progesterone; all women were identified as being at high risk of preterm birth on the basis of transvaginal US (TVU) determination of cervical length. An appropriate assessment of the effectiveness of TVU, taking the availability of progesterone into account, would compare patients treated with progesterone on the basis of TVU results with patients treated with progesterone on the basis of obstetric history. Such a study (Simcox et al., 2009) was included in the evidence report. Simcox et al. found no effect on the rate of preterm birth even though use of TVU increased the used of progesterone.

Unclear Quality Ratings in Table 2

These ratings apply to the overall body of evidence for the corresponding outcomes, which is the level of quality assessment defined by the GRADE system. See Quality Assessment in the METHODS section of the evidence report.

This is a summary table only. Outcome-specific information about individual study quality and references for individual studies contributing to key outcomes appear in Appendices III and IV. In the narrative text that describes findings (LITERATURE REVIEW), specific reasons for quality ratings are given in the summary sections. These reasons include multiple factors in addition to individual study quality. Clarifying statements have been added to Tables 2-4.

Absence of References and Appropriateness of Recommendations in Table 5

Table 5 is also a summary table, but there is no corresponding Appendix. References have been added. The comments in the last column of Table 5 refer to factors taken into account in translating study findings into conclusions about cost implications and cost-effectiveness. These same factors are also mentioned in the context of the discussion of findings and the summary for Cost Implications and Cost-Effectiveness in the LITERATURE REVIEW.

Cost Conclusion

The letter expresses support for a portion of the report’s conclusion statement regarding cost implications and cost-effectiveness.

American Institute of Ultrasound in Medicine (AIUM)

AIUM supports the comments sent by the Society of Maternal-Fetal Medicine.