

### C. Contribution to Science

1. My research career has had two foci within the realm of women's health: women's reproductive health and intimate partner violence. Because of my interest in disease prevention, my earliest work in women's reproductive health investigated various factors in relation to ectopic pregnancy risk. This research provided important new clinically relevant information about the impact of induced abortion and tubal sterilization procedures on risk of the disease. Later investigations of this topic in which I was involved as co-investigator focused on determining the magnitude of the current problem; our findings indicated that contrary to prevailing opinion, the incidence of ectopic pregnancy in the US did not decrease after the peak of the epidemic in the 1980s. This finding is clinically relevant, providing information for clinicians about the likelihood of the diagnosis of ectopic pregnancy diagnosis in general. In addition, our research emphasizes the importance of continued etiologic investigations of the disease.
  - a. Holt VL, Chu J, Daling JR, Stergachis A, Weiss NS (1991). Tubal sterilization and subsequent ectopic pregnancy: a case-control study. *JAMA*, 266, 242-6.
  - b. Holt VL, Daling JR, Stergachis A, Voigt LF, Weiss NS (1991). Results and effect of refusal recontact in a case-control study of ectopic pregnancy. *Epidemiology* 1991, 2:375-379.
  - c. Trabert B, Holt VL, Yu O, Grafter J, Yarbrow P, Wehnes L, Scholes D (2011). Population-based ectopic pregnancy trends - 1993-2007. *Am J Prev Med*, 40, 556-60. PMC 3093105.
  - d. Scholes D, Yu O, Raebel M, Trabert B, Holt VL (2011). Improving automated case-finding for ectopic pregnancy using a classification algorithm. *Hum Reprod*, 26, 3163-8. PMC 3196880.
  
2. Another focus of my reproductive health research portfolio has been the study of oral contraceptives (OCs). Two aspects of OC use have been investigated: impact on ovarian cysts and likelihood of OC failure. My findings on the former aspect provided clinically relevant information that low-dose OC use has little or no effect on functional ovarian cyst likelihood, in contrast to previous research on higher dose OCs. This finding has implications for the likely ineffectiveness of OC treatment for cyst prophylaxis. My research on risk factors for OC failure has focused on the impact of high body weight or obesity. The important findings from these studies, for which I was the principal investigator, were that both of these factors increase the likelihood of a woman becoming pregnant while taking OCs. These findings have spawned further research by others on the impact of obesity on drug effectiveness in general.
  - a. Holt VL, Daling JR, McKnight B, Moore D, Stergachis A, Weiss NS (1992). Functional ovarian cysts in relation to the use of monophasic and triphasic oral contraceptives. *Obstet Gynecol*, 79, 529-33.
  - b. Holt VL, Cushing-Haugen K, Daling JR. Oral contraceptives, tubal sterilization, and functional ovarian cyst risk (2003). *Obstet Gynecol*, 102, 252-8.
  - c. Holt VL, Cushing-Haugen K, Daling JR (2002). Body weight and risk of oral contraceptive failure. *Obstet Gynecol*, 99, 820-7.
  - d. Holt VL, Scholes D, Wicklund KG, Cushing-Haugen KL, Daling JR (2005). Body mass index, weight, and oral contraceptive failure risk. *Obstet Gynecol*, 105, 46-52.
  
3. The third focus of my reproductive health research has been the study of female reproductive system diseases, most notably endometriosis. This research has had both methodologic and practical importance. My publication on the design of epidemiologic studies provided a novel framework within which to determine and define the disease entity that has been cited and utilized by numerous other investigators. My research on risk factors for endometriosis has focused both on genetic and environmental factors, with particular emphasis on the effect of environmental chemical exposures such as organochlorine pesticides, polychlorinated biphenyls, and Bisphenol A. These findings have increased our knowledge not only of contributors to endometriosis risk but also have led to a broader understanding of the mechanism of action of these chemicals as endocrine disruptors.
  - a. Holt VL, Weiss NS (2000). Recommendations for the design of epidemiologic studies of endometriosis. *Epidemiology*, 11, 564-9.
  - b. Holt VL, Trabert B, Upson K (2012). Endometriosis. In "Women and Health, Second Edition", Goldman MB, Editor. Academic Press, San Diego CA.
  - c. Trabert B, Schwartz SM, Peters U, De Roos AJ, Chen C, Scholes D, Holt VL (2011). Genetic variation in the sex hormone metabolic pathway and endometriosis risk: an evaluation of candidate genes. *Fertil Steril*, 96, 1401-06. PMC 3228888.

- d. Upson K, Sathyanarayana S, De Roos AJ, Koch HM, Scholes D, Holt VL (2014). A population-based case-control study of urinary Bisphenol A concentrations and risk of endometriosis. *Hum Reprod.* 29, 2457-64.
4. I also have participated in a number of perinatal epidemiologic studies, primarily as a faculty mentor of master's and doctoral students. One notable aspect of this focus was my work with a doctoral student, Mona Lydon-Rochelle, on maternal pregnancy outcomes after perinatal procedures. The findings related to uterine rupture risk among women with a prior cesarean delivery who underwent a trial of labor rather than a scheduled cesarean delivery were of particular interest to the obstetrical community, and resulted in changes to clinical protocols for this subset of women. Additional work as part of this focus has concerned adverse pregnancy outcome likelihood after experiencing injury during pregnancy and risk of adverse neonatal outcome among women with psychiatric disorders. Both of these topics have implications for public health prevention activities.
    - a. Lydon-Rochelle M, Holt VL, Martin DP, Easterling TR (2001). Risk of uterine rupture during labor among women with a prior cesarean delivery. *New England J Med*, 345, 3-8.
    - b. Lydon-Rochelle M, Holt VL, Martin DP, Easterling TR (2001). Cesarean delivery and postpartum mortality among primiparas in Washington State, 1987-1996. *Obstet Gynecol*, 97, 169-74.
    - c. Schiff MA, Holt VL (2002). The Injury Severity Score in pregnant trauma patients: Predicting placental abruption and fetal death. *J Trauma*, 53, 946-9.
    - d. Kelly RH, Russo J, Holt VL, Danielsen BH, Zatzick D, Walker E, Katon W (2002). Psychiatric and substance use disorders as risk factors for low birth weight and preterm delivery: A population-based study. *Obstet Gynecol*, 100, 297-304.
  5. A final focus of my research has been intimate partner violence (IPV). My externally-funded research in this field has involved the relationship between the justice system and IPV, with a landmark study of the effect of civil protection orders on subsequent IPV between that couple. These findings have been cited by prosecutor's offices and victim advocates in their efforts to promote more extensive use of protection orders among abused women. I have also mentored graduate students who have investigated the effect of IPV on adverse pregnancy outcomes, the findings of which have informed public policy in favor of increased IPV risk identification and intervention.
    - a. Holt VL, Kernic MA, Lumley T, Wolf ME, Rivara FP (2002). Civil protection orders and risk of subsequent police-reported violence. *JAMA*, 288, 589-94.
    - b. Holt VL, Kernic MA, Wolf ME, Rivara FP(2003). Do protection orders affect the likelihood of future partner violence and injury? *Am J Prev Med*, 24, 16-21.
    - c. Lipsky S, Holt VL, Critchlow CW, Easterling TR (2003). Impact of police-reported intimate partner violence during pregnancy on neonatal health outcomes. *Obstet Gynecol*, 102, 557-64.
    - d. Janssen PA, Holt VL, Sugg NK, Emanuel I, Critchlow CM, Henderson AD (2003). Intimate partner violence and adverse pregnancy outcomes: A population-based study. *Am J Obstet Gynecol*, 188, 1341-7.

**Complete List of Published Work in MyBibliography:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1ToWp06GJtSQc/bibliography/47886133/public/?sort=date&direction=ascending>