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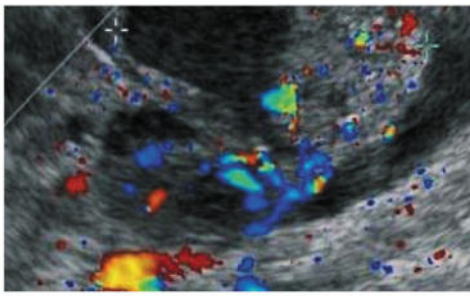

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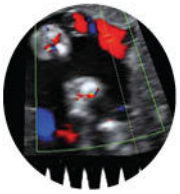

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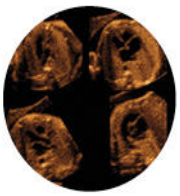

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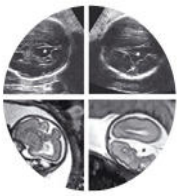

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How thick is too thick? When endometrial thickness should prompt biopsy in postmenopausal women without vaginal bleeding

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KEYWORDS: endometrial cancer; incidental findings; screening; transvaginal; transvaginal ultrasound

ABSTRACT

Objective *Transvaginal sonography (TVS) is routinely performed as part of a pelvic sonogram in postmenopausal women, and images of the endometrium are frequently obtained. In women without vaginal bleeding, the threshold separating normal from abnormally thickened endometrium is not known. The aim of this study was to determine an endometrial thickness threshold that should prompt biopsy in a postmenopausal woman without vaginal bleeding.*

Methods *This was a theoretical cohort of postmenopausal women aged 50 years and older who were not receiving hormone therapy. We determined the risk of cancer for a postmenopausal woman with vaginal bleeding when the endometrial thickness measures > 5 mm, and then determined the endometrial thickness in a woman without vaginal bleeding that would be associated with the same risk of cancer. We used published and unpublished data to determine the sensitivity and specificity of TVS, the incidence of endometrial cancer, the percentage of women symptomatic with vaginal bleeding, and the percentage of cancer that occurs in women without vaginal bleeding. Ranges for each estimate were included in a sensitivity analysis to determine the impact of each estimate on the overall results.*

Results *In a postmenopausal woman with vaginal bleeding, the risk of cancer is approximately 7.3% if her endometrium is thick (> 5 mm) and < 0.07% if her endometrium is thin (≤ 5 mm). An 11-mm threshold yields a similar separation between those who are at high risk and those who are at low risk for endometrial cancer. In postmenopausal women without vaginal bleeding, the risk of cancer is approximately 6.7% if the endometrium is thick (> 11 mm) and 0.002% if the endometrium is thin (≤ 11 mm). The estimated risk of cancer was sensitive to the percentage of cancer cases that were estimated to occur in women without vaginal bleeding. For the base case we estimated that 15% of cancers occur in women without vaginal bleeding. When we changed the estimate to project that only 5% of cancers occur in women without vaginal bleeding, the projected risk of cancer with a thick measurement was only 2.2%, whereas when we estimated that 20% of endometrial cancers occur in women without bleeding, the projected risk of cancer with a thick measurement was 8.9%. As a woman's age increases, her risk of cancer increases at each endometrial thickness measurement. For example, using the 11 mm threshold, the risk of cancer associated with a thick endometrium increases from 4.1% at age 50 years to 9.3% at age 79 years. Varying the other estimates used in the decision analysis within plausible ranges had no substantial effect on the results.*

Conclusions *In a postmenopausal woman without vaginal bleeding, if the endometrium measures > 11 mm a biopsy should be considered as the risk of cancer is 6.7%, whereas if the endometrium measures ≤ 11 mm a biopsy is not needed as the risk of cancer is extremely low.* Copyright © 2004 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Postmenopausal vaginal bleeding is a common complaint and is associated with a 1–10% risk of endometrial cancer, depending on age and risk factors[1,2]. Because the risk of cancer is relatively high, the clinical standard of care requires diagnostic evaluation to exclude malignancy[2,3]. Until the 1980s, fractional dilation and

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curettage was the procedure most often used. Dilation and curettage is invasive, and is associated with a 1–2% complication rate, thus less invasive endometrial biopsy techniques are increasingly favored for evaluating these women[3]. More recently, transvaginal sonography (TVS)[4,5] has been advocated as the initial test in the evaluation of postmenopausal bleeding. TVS is attractive as it is minimally invasive, has a high cancer detection rate[6,7], and the cost is similar to biopsy[8]. If the endometrium is thin by TVS, most commonly defined as a thickness of ≤ 5 mm[4,5], the risk of cancer is sufficiently low that a biopsy may be deferred.

Because most women with endometrial cancer are symptomatic with vaginal bleeding, the risk of endometrial cancer is very low among women without vaginal bleeding. It is therefore impractical to use TVS as a screening test to detect endometrial cancer in asymptomatic postmenopausal women[3,9–12]. However, TVS is performed as part of a pelvic sonogram in postmenopausal women referred for a variety of symptoms, such as suspicion of a pelvic mass, and images of the endometrium are frequently obtained. Although concern regarding endometrial pathology may not have been the indication for the test, it is difficult for the interpreting and referring physician to know how to manage an incidental finding of a thickened endometrium. In clinical practice this leads to large numbers of biopsies because of an incidental finding.

In postmenopausal women without vaginal bleeding (and thus at a low risk for endometrial cancer), the threshold that separates normal from pathologically thickened endometrium is not known, and there is no consensus regarding what constitutes a 'thickened endometrial stripe' in these women[13]. If an endometrial thickness threshold cut-off of > 5 mm was used to define an abnormal test result, as is used in women with vaginal bleeding, the number of false-positive test results would far outnumber the true-positive test results. However, at some endometrial thickness measurements the risk of cancer is sufficiently high that additional evaluation with endometrial biopsy is warranted, even in a woman without vaginal bleeding. The thickness cut-off that should be considered abnormal in a postmenopausal woman without bleeding has not been standardized.

We sought to determine an endometrial thickness measurement that should be considered abnormal and therefore prompt biopsy in a postmenopausal woman without vaginal bleeding. Our aim was to determine the endometrial thickness threshold at which the risk of cancer in a woman without bleeding would be similar to the risk of cancer in a woman with bleeding, when the endometrium measures > 5 mm. We thought it appropriate that if a certain risk of cancer prompts biopsy in a woman with vaginal bleeding, that a similar risk of cancer (albeit at a greater thickness threshold) should prompt biopsy for a woman without vaginal bleeding.

METHODS

We performed a decision analysis to determine the endometrial thickness threshold that should be considered abnormal in asymptomatic postmenopausal women (Figure 1). We used as our benchmark the risk of cancer that prompts biopsy in women who are symptomatic with vaginal bleeding, and sought to determine the endometrial

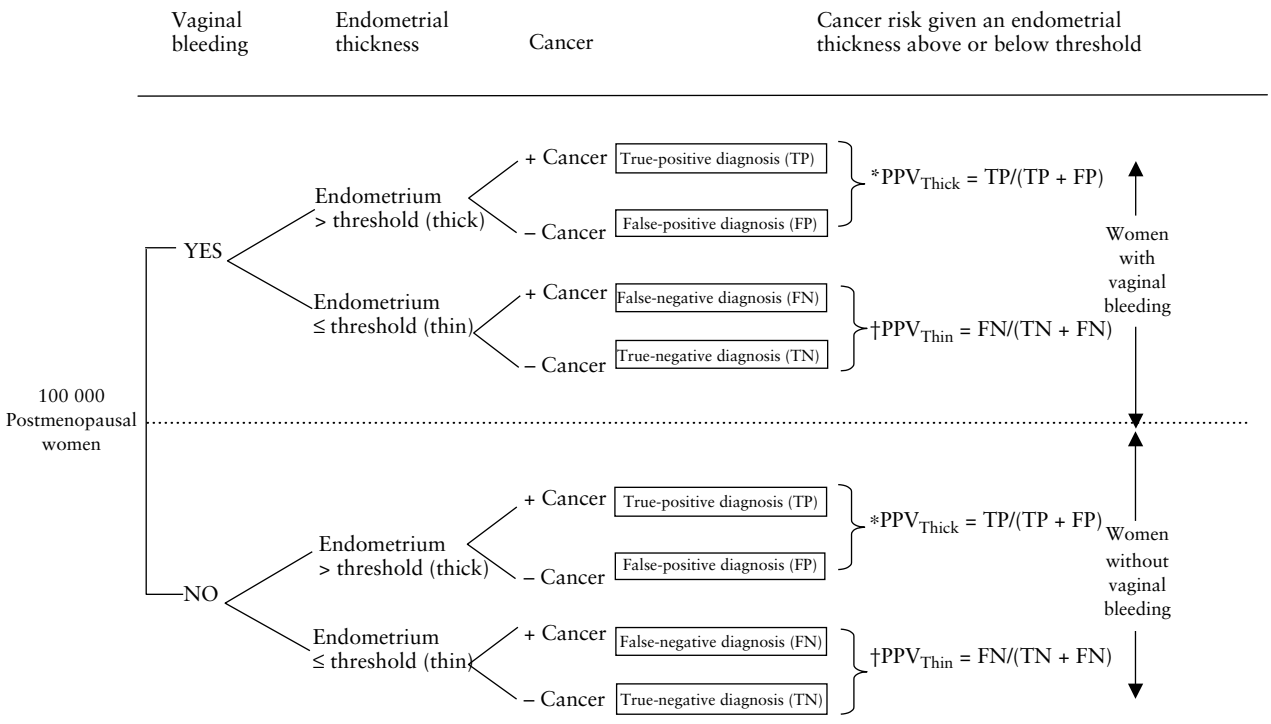

Figure 1 Decision tree used to determine the endometrial thickness threshold that should be considered abnormal in asymptomatic postmenopausal women. *PPV$_{Thick}$, risk of cancer if the endometrium measures above a threshold. †PPV$_{Thin}$, risk of cancer if the endometrium measures at or below a threshold. PPV$_{Thin}$ equals 1 – negative predictive value. PPV, positive predictive value.

thickness that would be associated with a similar cancer risk in women without vaginal bleeding. We collected data from several published and non-published sources. Estimates and ranges for the key assumptions are provided in Table 1. We used conservative assumptions for each estimate in order to maximize the detection of occult cancer. For each endometrial thickness threshold we defined a measurement at or below that threshold as normal, and defined a measurement above that threshold as abnormal.

Vaginal bleeding

Vaginal bleeding is a common complaint and accounts for the majority of presenting complaints for gynecological visits in postmenopausal women. Based on the results of the Women's Health Initiative[14], we estimated that 7% of postmenopausal women are symptomatic with vaginal bleeding, and included a range of 4–10%[3,15].

Incidence of endometrial cancer in women without vaginal bleeding

Most cases of endometrial cancer occur in women with vaginal bleeding[2,3,16]. Nonetheless, there is likely a preclinical phase during which some cancers might be detectable prior to the development of symptoms (and thus the rationale for considering biopsy in a woman who is not experiencing vaginal bleeding). In addition, some cancers do not present with bleeding until they have progressed beyond Stage I. We used two sources to estimate the percentage of cancer cases that occur in women without vaginal bleeding. First, Hofmeister reviewed 20 677 endometrial biopsies, including 187 cases of endometrial cancer[16], and reported that 17% of the cases of endometrial cancer occurred in women without vaginal bleeding; and in the most recent subset of data analyzed, 15% of cases occurred in women without vaginal bleeding. This study is widely cited as evidence that most cases of endometrial cancer occur in women with vaginal bleeding[3]. Second, we looked at the distribution of endometrial cancer, by stage, in the National Surveillance Epidemiology and End Results (SEER) program, the national cancer registry[17]. Among women older than 50 years diagnosed with endometrial cancer, 23% presented with Stage II or higher and, as an extreme possibility, it may be that all cancers diagnosed beyond Stage I did not bleed while at an earlier stage and thus might be detectable in women without vaginal bleeding. Adopting the Hofmeister data, we estimated that 15% of endometrial cancers occur in women without vaginal bleeding[16], with a plausible range of 5–20%, which we included in the sensitivity analysis.

Ultrasound thickness of the endometrium in asymptomatic postmenopausal women who do not have endometrial cancer

For the decision analysis we needed to know the normal range of endometrial thickness measurements in

Table 1 Baseline estimates and ranges for key assumptions used in the decision analysis

Variable	*Best estimate*	*Range*	*Sources*
Percentage of postmenopausal women symptomatic with vaginal bleeding	7%	4–10%	WHI[14], PEPI[15], Disaia and Creasman[3]
Percentage of endometrial cancer that occurs in women without vaginal bleeding	15%	5–20%	Hofmeister[16], SEER[17]
Mean endometrial thickness in postmenopausal women with endometrial cancer	20 mm	SD 6 mm	Smith-Bindman *et al.*[7]
Sensitivity of transvaginal ultrasound at detecting cancer at each thickness threshold	Based on results from meta-analyses. Sensitivity varies from 98% (at 3 mm) to 50% (at 20 mm)	Sensitivity reduced 20% in women without bleeding as compared to women with bleeding at each endometrial thickness threshold	Smith-Bindman *et al.*[7], Tabor *et al.*[6]
Mean endometrial thickness, and distribution of endometrial thickness measurements, and false-positive rate at each endometrial thickness measure, in postmenopausal women without cancer and without vaginal bleeding	3.5 mm	Endometrial thickness was calculated using data describing 2016 women. False-positive rates for each endometrial thickness measurement were calculated using these data	Fleischer *et al.*[10,19], GlaxoSmithKline (unpublished data)
Incidence of endometrial cancer*	75.6/100 000	45.8–109.1/100 000, corresponding to the risk of cancer in women aged 50–79 years	SEER[17]

*Adjusted to account for the high rate of hysterectomy (40%) in postmenopausal women[20]. PEPI, Postmenopausal Estrogen/Progestin Interventions Trial; SEER, Surveillance Epidemiology and End Results Program; WHI, Women's Health Initiative.

postmenopausal women without bleeding and who do not have endometrial cancer, so that we could determine the false-positive rate of TVS at each endometrial thickness cut-off. The mean endometrial thickness in postmenopausal women without vaginal bleeding has been reported to vary between 3 and 5 mm[11,13,18,19], however most published studies have been too small to empirically determine accurate percentile cut-offs far from the mean value. The largest study of the appearance of the endometrium in asymptomatic postmenopausal women described baseline measurements in women considering participating in a trial of idoxifene, a selective estrogen receptor modulator drug[10,19]. This study reported that most women (1833/1926) had an endometrial measurement ≤ 5 mm. However, the published data from these studies excluded women whose endometria measured > 10 mm. Therefore, to determine the normal distribution of endometrial thickness in postmenopausal women without bleeding we obtained unpublished data from this trial, describing a total of 2016 women (1926 women previously reported plus an additional 90 women previously unreported), and calculated empirical percentile cut-offs using these data. For inclusion in this trial, women had to have no history of endometrial or breast cancer, and no use of hormone therapy within the 6 months prior to enrolling in the study. Additionally, follow-up information regarding subsequent diagnoses of endometrial cancer was performed. We then calculated for each value from 3 to 20 mm the fraction of postmenopausal women without endometrial cancer who have an endometrial thickness above this value, and thus the false-positive rates of TVS at each thickness threshold from 3 to 20 mm.

Ultrasound thickness of the endometrium in women with endometrial cancer

The endometrium is thicker in women with endometrial cancer compared with those without endometrial cancer, as described in a large number of primary studies as well as two meta-analyses[6,7]. In the larger meta-analysis of 35 studies describing 759 women diagnosed with endometrial cancer between 1992 and 1996[7], endometrial cancer was associated with a mean endometrial thickness of 20 mm (SD 6 mm) compared with 4 mm (SD 1 mm) in women with normal endometria. This systematic review provides the most stable estimate of the thickness of endometrial cancer and the true-positive and false-negative rate of TVS at each thickness threshold. Because there are no studies describing the ultrasound appearance of endometrial cancer in women without vaginal bleeding, for our initial estimate we assumed that the appearance of endometrial cancer is similar among women with and without vaginal bleeding. As endometrial cancer may be thinner when it occurs in women without bleeding as compared to women with bleeding, for the sensitivity analysis we estimated that TVS may detect 20% fewer cancers at each endometrial thickness cut-off in asymptomatic, as compared with symptomatic, women.

Incidence of endometrial cancer

The SEER data provide the most accurate estimates of the population risk of endometrial cancer[17]. Among women age 50 years and older, 75.6 cases of endometrial cancer are diagnosed annually per 100 000 women, and this ranges from 45.8/100 000 for women aged 50–54 years to 109.1/100 000 for women aged 75–79 years. Since the SEER data include all women, the SEER estimated incidence of endometrial cancer was adjusted upwards to account for the large number of postmenopausal women who have undergone hysterectomies, estimated at 40%[20].

Analysis

For the decision analysis we assumed a population of 100 000 postmenopausal women aged 50 years and older, none of whom was taking hormone therapy or had undergone hysterectomy, who underwent a TVS examination that captured adequate images of the endometrium. For each endometrial thickness threshold we calculated the risk of cancer for women with an endometrial thickness less than or equal to that cut-off (thin) vs. above that cut-off (thick), stratified by whether they were symptomatic or asymptomatic with vaginal bleeding (Figure 1). We dichotomized endometrial thickness, so that an endometrial thickness equal to or below a certain cut-off should be considered 'normal', and an endometrial thickness above a certain cut-off should be considered 'abnormal', as this seemed practical in terms of clinical management. The risk of cancer for women who have an endometrium less than or equal to a cut-off (the positive predictive value (PPV) thin), corresponding to (1− the negative predictive value) was defined as the false-negatives (1− sensitivity) divided by the sum of the false-negatives plus the true-negatives. This is the risk of cancer among women with a thin endometrium. The risk of cancer for women with an endometrial thickness greater than a cut-off (the PPV thick) was defined as the true-positives divided by the sum of the true-positives plus the false-positives. This is the risk of cancer among women with a thick endometrium. An illustration of how the numbers were calculated is provided in the Appendix. Among postmenopausal women with vaginal bleeding, an endometrial thickness ≤ 5 mm is generally considered normal, while thicknesses > 5 mm are considered abnormal[4,5]. We estimated the risk of cancer associated with a thickened endometrium in women with vaginal bleeding, and then determined the corresponding endometrial thickness in women without vaginal bleeding that results in a similar risk of cancer. Additionally, some investigators have considered an endometrial thickness ≤ 4 mm to be normal[7]. Therefore we also estimated the risk of cancer in women with vaginal bleeding associated with this definition of a thick endometrium, and determined the corresponding endometrial thickness in women with vaginal bleeding that results in a similar threshold.

The potential impact of each of the estimates on the cancer risk was determined with a one-way sensitivity

analysis that systematically varied each of the assumptions listed in Table 1 throughout its range of values.

RESULTS

In a postmenopausal woman with vaginal bleeding, the risk of endometrial cancer is approximately 0.07% if her endometrium is thin (≤ 5 mm) and 7.3% if her endometrium is thick (> 5 mm) (Table 2). In a postmenopausal woman without vaginal bleeding, an 11 mm threshold yields a similar separation between women who are at high risk and low risk for endometrial cancer (Table 2). In a postmenopausal woman without vaginal bleeding, the risk of cancer is approximately 0.002% if her endometrium is thin (≤ 11 mm) and 6.7% if the endometrium is thick (> 11 mm). In a woman without bleeding, if the definition of a normal endometrial thickness is lowered from 11 to 7 mm (so that a measurement of 8 mm or greater would be considered abnormal), the cancer risk in a woman with a 'thick endometrium' is only 2.1%. By decreasing the cut-off from 11 to 7 mm, the cancer detection rate would increase slightly (from 87% to 95%) but the false-positive rate would nearly quadruple (from 0.25% to 0.90%). Some investigators[7] have advocated that a threshold of '≤ 4 mm' should be considered normal in postmenopausal women with vaginal bleeding, and '5 mm or greater' should be considered abnormal. The risk of cancer is approximately 4.6% in postmenopausal women with vaginal bleeding if the endometrium measures 5 mm or greater (see upper arrow, Table 2). In women without vaginal bleeding, a threshold of 10 mm (i.e. ≤ 10 mm is considered normal) is associated with a similar cancer risk (see lower arrow, Table 2).

These results varied depending on the percentage of cancers that were estimated to occur in women without vaginal bleeding (Figure 2). We estimated that 15% of cancers occur in women without vaginal bleeding. When we decreased the rate to posit that only 5% of cancers occur in women without vaginal bleeding, the risk of cancer associated with a thickness threshold of 11 mm was only 2.2%. When we increased the rate to posit that 20% of cancers occur in women without vaginal bleeding, the risk of cancer associated with the thickness threshold of 11 mm rose to 8.9%. As a woman's age increases, her risk of cancer increases at each endometrial thickness measurement. Using the 11 mm threshold, the risk of cancer increased from 4.1% at age 50 years to 9.3% at age 79 years (Figure 2). Varying the other estimates used in the decision analysis within plausible thickness ranges had no substantial effect on the results.

DISCUSSION

The interpretation and clinical management of an incidentally noted thick endometrium has not been standardized[13]. Endometrial cancer is usually associated with vaginal bleeding and the risk of cancer is very low in women without bleeding. Therefore, in asymptomatic women the index of suspicion for underlying cancer should be extremely high to warrant an invasive endometrial biopsy on the basis of imaging findings alone. An endometrial thickness > 11 mm in a postmenopausal woman without vaginal bleeding carries a risk of cancer of approximately 6.7%, and is similar to that of a postmenopausal woman with bleeding and an endometrial thickness > 5 mm. Conversely, the risk of cancer is quite low among asymptomatic women whose endometrial thickness measures ≤ 11 mm. If a cut-off of 11 mm is used as the threshold to prompt biopsy, biopsies would occur in only a small percentage of women (0.25%), and yet most cases of occult endometrial cancer

Table 2 The risk of endometrial cancer at various endometrial thickness measurements in women who are symptomatic or asymptomatic with vaginal bleeding

Threshold to define a normal endometrium (mm)	*Women with vaginal bleeding: cancer risk (%) if the endometrium*		*Women without vaginal bleeding: cancer risk (%) if the endometrium*	
	≤ Threshold	*> Threshold*	*≤ Threshold*	*> Threshold*
≤ 4	0.07	4.6 ⇦	0.00	0.2
≤ 5	0.07	7.3	0.00	0.4
≤ 6	0.08	7.7	0.00	1.5
≤ 7	0.09	10.8	0.00	2.1
≤ 8	0.12	12.7	0.00	2.9
≤ 9	0.14	15.1	0.00	3.6
≤ 10	0.18	16.6	0.00	5.8 ⇦
≤ 11	0.21	40.3	0.00	6.7
≤ 12	0.25	42.1	0.00	10.3
≤ 13	0.30	48.2	0.00	10.9
≤ 14	0.36	52.2	0.00	12.0
≤ 15	0.42	53.5	0.01	13.1
≤ 16			0.01	14.9
≤ 17			0.01	16.8
≤ 18			0.01	19.6
≤ 19			0.01	30.9

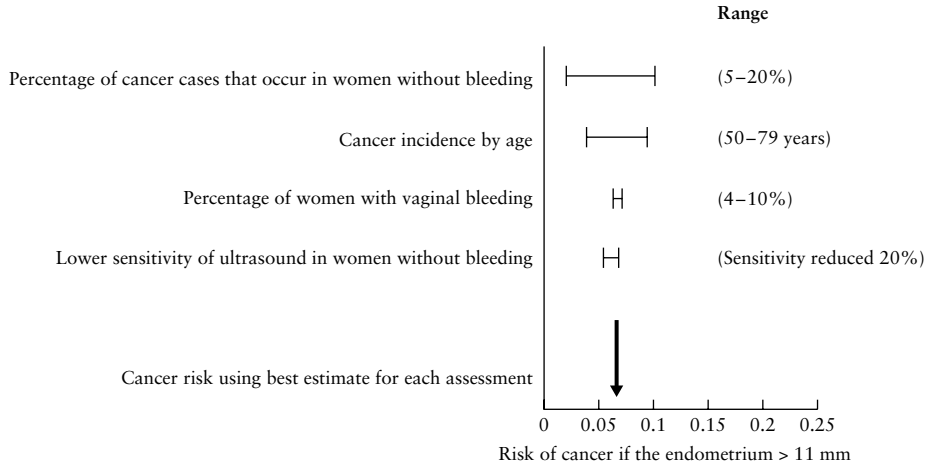

Figure 2 Impact of each of the point estimates used in the decision analysis on the estimated cancer risk in postmenopausal women without vaginal bleeding when the endometrium measures > 11 mm.

would be detected (87%). If this threshold was lowered to 10 mm (so that 10 mm is considered normal and 11 mm is abnormal), the percentage of women who undergo biopsy would increase from 0.25% to 0.39%, 89% of cancers would be detected, and the risk of cancer in a woman with a 'thick' measurement would be 5.8% (see lower arrow, Table 2). This is similar to the risk of cancer among women who are bleeding when a threshold of ≤ 4 mm is considered normal (see upper arrow, Table 2). The results of this analysis remained robust across broad changes in the assumptions described in Table 1.

Several investigators have suggested that an even thinner endometrial measurement should prompt biopsy in asymptomatic women, and in clinical practice a biopsy is often recommended even at a measurement of only 8 mm[21]. The recommendation to biopsy a woman with an incidentally noted endometrial measurement of 8 mm does not take into account the low risk of endometrial cancer among women without vaginal bleeding. Based on our analysis, if this threshold is used as a cut-off, then biopsy would be prompted in asymptomatic women with a lower risk of endometrial cancer (2.1%) than is currently used to trigger biopsy in women with vaginal bleeding. Furthermore, if an 8 mm thickness were considered abnormal in postmenopausal women without vaginal bleeding, it would lead to biopsies in nearly 1% of normal postmenopausal women. This seems inappropriate for the evaluation of a disease that most often presents with symptoms, and does so while still at a curable stage. No cut-off is perfect, and cancer will be missed no matter what cut-off is used. However, using a cut-off of 10 or 11 mm seems to provide an acceptable trade-off between cancer detection and unnecessary biopsies prompted by an incidental finding.

Because of this grouping of endometria below and above that threshold, the risk of cancer in women with a thick endometrium is very high, and the risk of cancer in women with a thin endometrium is very low. In actual practice there is a continuum of risk, and no abrupt change in cancer risk occurs at 10 or 11 mm.

Our analysis does not take into account individual patient risk for endometrial cancer. A woman with known risk factors for endometrial cancer (such as diabetes, which increases the risk of endometrial cancer three-fold; obesity, which increases the risk of cancer 10-fold; the use of unopposed estrogen or tamoxifen, which increases the risk two-fold; or age > 70 years)[3] will have a higher risk of cancer than one without such risk factors, even with the same endometrial thickness measurement. Thus, it is important to take into account individual patient risk when deciding how to manage imaging findings. We considered only endometrial thickness, and no other components of endometrial appearance such as homogeneity, nodularity and Doppler flow characteristics. There are insufficient data on these characteristics to determine how they should be used in screening for endometrial cancer.

We did not make separate calculations based on the use of hormone therapy. The most common hormone therapy regimens use a combination of estrogen and progesterone, which do not alter endometrial thickness very much, if at all[11], and thus would not be expected to alter the results reported here. Additionally, since hormone therapy will, if anything, tend to increase the endometrial thickness, 11 mm remains a conservative threshold, as it will lead to additional, rather than fewer, biopsies. We obtained data gathered from healthy volunteers enrolled in a clinical trial in order to estimate the normal appearance of the endometrium in women without vaginal bleeding. These results describing the normal appearance of the endometrium were similar to previous reports based on smaller datasets[21]. While we believe these data can be generalized, it is possible that these women may have systematic differences in their endometrial thickness compared with women who might not have been included. We intentionally limited the critical outcome of interest to the detection of endometrial cancer, rather than other benign endometrial abnormalities such as polyps or hyperplasia, as it is not clear if these benign processes require treatment in asymptomatic women.

Diagnostic tests are typically interpreted as positive or negative based on imaging findings alone, and this does not take into account underlying patient risk of disease. This is not ideal, as the same radiological finding has a very different likelihood of reflecting actual disease depending on patient risk factors. In the context of a cancer screening test (such as TVS used in postmenopausal women without vaginal bleeding) it is important to consider the low risk of cancer when deciding how to manage an incidental finding, and it is not reasonable to simply decide to biopsy a certain percentage of women with the thickest endometrial stripes. Based on this analysis, and in comparison with the threshold that is widely accepted in women with bleeding, an endometrial thickness measurement of ≥ 11 mm provides a reasonable cut-off to prompt biopsy in postmenopausal women without vaginal bleeding.

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APPENDIX

We calculated the risk of cancer at each endometrial thickness among women with and without vaginal bleeding using the estimates provided in Table 1. To illustrate the method, we have shown how we calculated the risk of cancer associated with an endometrial thickness of ≥ 8 mm, in a woman with and a woman without vaginal bleeding. In the cohort of 100 000 postmenopausal women, 60% will have a uterus, and 756 cases of endometrial cancer will occur in these women and are assigned to the women with a uterus. Overall, 7% of the women will have vaginal bleeding, and 85% of cancer cases will occur in the women who are symptomatic with bleeding. If an endometrial thickness of ≥ 8 mm is considered abnormal, 0.9% of women without cancer and without bleeding and 12% of women without cancer and with bleeding will have endometrial measurements above this threshold, and 95% of women with cancer will have endometrial measurements above this threshold.

Women with vaginal bleeding

$$PPV_{Thick} = \frac{Tp = \text{number of women with cancer with an endometrium} \geq 8\text{ mm}}{(TP + FP) = \text{number of women with and without cancer with an endometrium} \geq 8\text{ mm}}$$

TP = (75.6/0.6 cancers) × (85% of cancer occurs in women with bleeding) × (95% of cancer cases have ≥ 8 mm endometrium)
= 101.7

FP = (100 000 women) × (7% are symptomatic with bleeding) × (12% of women without cancer, but with bleeding, have an endometrium ≥ 8 mm)
= 840.0

$PPV_{Thick} = (TP)/(TP + FP) = .108$

Women without vaginal bleeding

$$PPV_{Thick} = \frac{Tp = \text{number of women with cancer with an endometrium} \geq 8\text{ mm}}{(TP - FP) = \text{number of women with and without cancer with an endometrium} \geq 8\text{ mm}}$$

TP = (75.6/0.6 cancers) × (15% of cancer occurs in women without bleeding) × (95% of cancer cases have an endometrium ≥ 8 mm)
= 18.0

FP = (100 000 women) × (93% do not have vaginal bleeding) × (0.9% of women without cancer, and without vaginal bleeding, have ≥ 8 mm) GlaxoSmithKline
= 837.0

$PPV_{Thick} = (TP)/(TP + FP) = .021$

FP, false-positive diagnosis; TP, true-positive diagnosis; PPV, positive predictive value; PPV_{Thick}, risk of cancer if the endometrium measures above a threshold.

