

# A systematic review of methods to measure menstrual blood loss

## SUPPLEMENTAL TABLE 3

### Overview of types of validation performed, practicalities, and limitations of methods.

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
<b>AH</b>				
Original AH method [1]	<ul style="list-style-type: none"> <li>Iron isotope activity</li> </ul>	<ul style="list-style-type: none"> <li>Recovery of blood from sanitary pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Simple, accurate, convenient, no complaints of odor (samples sent by mail)</li> <li>Towels and tampons can be combined in assay</li> <li>Well established as a clinical assay and in the research setting</li> </ul>	<ul style="list-style-type: none"> <li>Towel/tampon color can affect assay</li> </ul>
Original AH method (increased incubation time) [2]		<ul style="list-style-type: none"> <li>Discrimination of HMB</li> <li>Recovery of blood from towels and tampons (Modess<sup>®</sup>, Kotex<sup>®</sup>), tampons (Tampax<sup>®</sup>), or cotton sponges (Rondic<sup>®</sup>)</li> <li>Internal consistency</li> </ul>	<ul style="list-style-type: none"> <li>Reliable and simple</li> <li>Good accuracy down to 0.1 mL</li> <li>Satisfactory recovery of blood can be achieved with different brands/types of sanitary product</li> <li>Participants using their customary method of sanitary protection are more likely to cooperate</li> <li>Soiled products may be stored for <math>\leq 1</math> month</li> </ul>	<ul style="list-style-type: none"> <li>It is not known if storage of soiled products for <math>&gt;1</math> month results in hemoglobin degradation</li> <li>The reason for poorer blood recovery from one brand (Kotex<sup>®</sup> towels) tested is unknown</li> </ul>
Modified AH method (Stomacher <sup>®</sup> blender, automation) [3]		<ul style="list-style-type: none"> <li>Recovery of blood from towels (Kotex<sup>®</sup> Simplicity low bulk, Dr White's<sup>®</sup> Maternity high bulk, Kotex<sup>®</sup> New Freedom, Libresse<sup>®</sup> Comfort, Boots<sup>®</sup> Femina, Nikini<sup>®</sup>, Lilia<sup>®</sup>) and tampons (Tampax<sup>®</sup> Regular, Tampax<sup>®</sup> Super, Lil-Lets<sup>®</sup> Regular, Lil-Lets<sup>®</sup> Super, Lil-Lets<sup>®</sup> Super-plus)</li> <li>Internal consistency</li> </ul>	<ul style="list-style-type: none"> <li>Rapid (15 min for stable eluate)</li> <li>Many blood samples can be analyzed at low cost and within a short period of time</li> <li>Minimizes exposure of technicians to discomfort</li> <li>Suitable for routine laboratory use, even in the tropics</li> </ul>	<ul style="list-style-type: none"> <li>Towel/tampon color can affect assay</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
Modified AH method (Stomacher® blender, automation) [4]	<ul style="list-style-type: none"> <li>AH method [2]</li> </ul>	<ul style="list-style-type: none"> <li>Recovery of blood from four towels (Skylark®, Carefree®, Comfit®, and Stayfree®)</li> <li>External validation (Indian sanitary pads)</li> <li>Intracycle consistency</li> </ul>	<ul style="list-style-type: none"> <li>Quick (15 min per extraction)</li> <li>Practical for use in India with various sanitary pads</li> <li>Can be used to assess the effect of sterilization, intrauterine devices, and oral contraceptives on MBL</li> </ul>	
Modified AH method (Stomacher® blender, and modified equation for calculation of MBL including a mean “blank” absorbency for different brands of sanitary products) [5]		<ul style="list-style-type: none"> <li>Recovery of blood from towels (Kotex® Maxi) and tampons (Tampax® Super)</li> <li>Analysis of blanks</li> <li>Internal consistency</li> <li>Validation of discriminatory power</li> </ul>	<ul style="list-style-type: none"> <li>Accurate, convenient, minimal odor (fume hood)</li> <li>Avoids manual squeezing of sanitary wear and shortens the AH procedure</li> <li>All patients agreed that it was “not too much bother”</li> <li>Assessors agreed that the measurement was “not more unpleasant to perform than many other routine laboratory procedures in urine or feces”</li> <li>Can be performed as a routine laboratory procedure and is suitable for clinical use</li> </ul>	<ul style="list-style-type: none"> <li>Blank values of each type of towel or tampon must be determined and used in the calculation of MBL</li> </ul>
Modified AH method (volumetric test; non-caustic chemicals used for extraction of hemoglobin; standard curves produced) [6]		<ul style="list-style-type: none"> <li>Recovery of blood from towels (Stayfree® Maxi Regular or Thin and Mini) and tampons (Tampax® or OB®)</li> <li>Validation of discriminatory power</li> </ul>	<ul style="list-style-type: none"> <li>Better than long, cumbersome methods using radioisotopes</li> <li>Simple, rapid (2 h for extraction and measurement), accurate, reliable, no unpleasant odors, only small volumes of caustic solution</li> <li>Can aid the diagnosis and evaluation of treatment of dysfunctional uterine bleeding</li> </ul>	<ul style="list-style-type: none"> <li>Extraction efficiency varies with product (standard curves required for each product used)</li> <li>With high MBL, samples need to be diluted for measurement</li> </ul>
Modified AH method (detergent extraction; photometric analysis; calibration factor applied for specific brands of feminine products) [7]		<ul style="list-style-type: none"> <li>Recovery of blood from towels (Kotex® Simplicity Super) and tampons (Tampax® Super Plus)</li> <li>Internal consistency</li> <li>Validation of discriminatory power</li> </ul>	<ul style="list-style-type: none"> <li>Rapid extraction (&lt;30 min) of a complete collection of sanitary material</li> <li>Clear, simple instructions (89% of women collected products)</li> <li>A single measurement is sufficient for diagnosis of HMB (a second MBL measurement can be used in cases of obvious methodological problems)</li> </ul>	<ul style="list-style-type: none"> <li>High cooperation rates might not be achieved outside a research study</li> </ul>
Modified AH method (Stomacher® blender and absorbance at A <sub>564</sub> to measure hemoglobin instead of AH; combined with menstrual diary)		<ul style="list-style-type: none"> <li>Recovery of blood from towels (Libresse® Good Night and Invisible Super) and tampons (OB® Fleur Plus and Extra Plus)</li> </ul>	<ul style="list-style-type: none"> <li>A measurement kit with detailed instructions, sanitary protection, and storage bags resulted in a 99% acceptance rate, but this could also be because of the clinical trial setting and the inclusion of only women with HMB</li> <li>Combining a diary with a pictorial chart test (and this AH test) would give the best accuracy</li> </ul>	<ul style="list-style-type: none"> <li>AH test alone does not measure all fluid content of the menstrual discharge</li> <li>AH test gives no details of bleeding pattern</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
[8]				
Modified AH method (for SAP-c towels) [9]		<ul style="list-style-type: none"> <li>Recovery of a range of simulated menstrual fluid volumes from SAP-c towels (Always Ultra with Wings Normal, Long, Night)</li> </ul>	<ul style="list-style-type: none"> <li>Accurate, minimal odor</li> <li>Samples may be stored for 3 weeks at all tested temperatures without loss of recovery</li> <li>Towels can be processed individually/in batches</li> <li>Does not need specialized laboratory facilities</li> <li>Can be readily used in the clinical research setting</li> </ul>	
Modified AH method (rapid AH technique for SAP-c towels) [10]	<ul style="list-style-type: none"> <li>A manual reference method for blood extraction from towels</li> </ul>	<ul style="list-style-type: none"> <li>Recovery of a range of simulated menstrual fluid volumes from SAP-c towels (Always Ultra with Wings Normal, Long, Night)</li> </ul>	<ul style="list-style-type: none"> <li>Reliable, accurate</li> <li>Rapid (a Stomacher® could process 16 towels/h)</li> <li>Reduced handling of caustic sodium hydroxide</li> <li>Direct measurement of hemoglobin levels</li> <li>Samples could be stored for 3 weeks at 4°C without loss of recovery</li> <li>Can be readily used in the clinical research setting</li> </ul>	<ul style="list-style-type: none"> <li>Conversion factors are required for each product used</li> </ul>
MFL and menstrual cups				
MFL [11]	<ul style="list-style-type: none"> <li>AH method [3]</li> <li>PBAC</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Validated for towels (Kotex® Simplicity 2) and tampons (Tampax® Super)</li> </ul>	<ul style="list-style-type: none"> <li>MFL is possibly of more relevance than MBL to women (who may be more concerned about flooding than whether discharge is blood or fluid)</li> <li>Strong correlation between change in total MFL and MBL suggests that total MFL measurement could be used as an assessment of HMB, while being much easier to perform</li> </ul>	
Regression estimation of MBL from MFL [12]	<ul style="list-style-type: none"> <li>AH method [1,3]</li> </ul>	<ul style="list-style-type: none"> <li>Inter-cycle consistency</li> <li>Validated for regular or super towels without wings and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Provides an accurate estimate of MBL in women with moderate to very heavy losses and appears to be more accurate than PBAC</li> <li>MBL classification can be made from the measured total MFL directly without having to calculate blood loss</li> <li>Self-sealing plastic bags for storage eliminated odor</li> <li>Total MFL is much easier to ascertain than MBL, only requiring weighing of sanitary products before and after use, and a commercial pack for this purpose would be inexpensive and simple</li> <li>The tool is not subject to behavioral distortion, as was the number of menstrual hygiene products needed, or perceptual bias</li> <li>For most clinical purposes, the estimate of MBL could be made ignoring the hygiene product type (sanitary pad or tampon)</li> </ul>	<ul style="list-style-type: none"> <li>Women have to collect all menstrual loss meticulously including “clots”</li> </ul>
MFL		<ul style="list-style-type: none"> <li>Validation of</li> </ul>	<ul style="list-style-type: none"> <li>MFL may be a simple alternative to PBAC and the AH</li> </ul>	<ul style="list-style-type: none"> <li>Overlap of MFL data existed</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
(for SAP-c towels) [13]		discriminatory power <ul style="list-style-type: none"> <li>Validated for Always Ultra towels</li> <li>External validation</li> </ul>	method in women without urinary incontinence <ul style="list-style-type: none"> <li>Can be used to measure the effect of medical intervention on MFL</li> </ul>	between bleeding categories
Gynaeseal [14]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>		<ul style="list-style-type: none"> <li>95% of women found Gynaeseal easy to insert; one required assistance in removing the Gynaeseal; one parous women was unable to insert the device</li> <li>60% of women with normal MBL required no supplementary sanitary wear</li> <li>“Change the Gynaeseal only once per day” (women with normal loss, n = 6)</li> <li>“Ability to have sexual intercourse during menstruation” (n = 3)</li> </ul>	<ul style="list-style-type: none"> <li>All women with HMB who tried to aspirate menstrual fluid from the lower chamber of the Gynaeseal reported spillage of menses</li> <li>Only five of 22 women submitted written measurements of menstrual volume</li> <li>All women with HMB said they preferred the standard method of menstrual fluid collection because menstrual spillage was unpleasant</li> <li>Compared with standard sanitary wear: the seal was “messy to remove” (n = 16; 73%); the odor of the latex was “offensive” (n = 2); and the device was not disposable by lavatory flush (n = 5)</li> </ul>
Mooncup [15]	<ul style="list-style-type: none"> <li>Sanitary pads and tampons</li> </ul>		<ul style="list-style-type: none"> <li>Mooncup was changed, on average, less frequently than tampons AND pads</li> <li>From follow-up questionnaire: “less leakage during activity”</li> </ul>	<ul style="list-style-type: none"> <li>Greater reported frequency of leakage compared with pads AND tampons</li> <li>It was changed, on average, 2.3 times more frequently than pads</li> <li>From questionnaire: “difficult to remove”; “painful”; “uncomfortable on insertion and when in situ”; “frequent emptying and leakage”; “unhappy having to clean it in the kitchen” (hygiene reasons); “having to change the Mooncup in public toilets where facilities are limited”</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
• High dropout rate				
<b>Measurement of iron/labelled red blood cells</b>				
Radioactive iron ( $Fe^{59}$ ) [16]		<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Internal consistency</li> <li>Validated for “sanitary napkins” and Tampax® tampons</li> </ul>	<ul style="list-style-type: none"> <li>Highly accurate</li> </ul>	<ul style="list-style-type: none"> <li>Requires collection of soiled radioactive products</li> </ul>
Radioactivity counting dome ( $Cr^{51}$ ) [17]		<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Accuracy</li> <li>Validated for bespoke pads</li> </ul>	<ul style="list-style-type: none"> <li>Simple, accurate technique</li> <li>Eliminates count rate errors due to geometric irregularity of the sample</li> </ul>	<ul style="list-style-type: none"> <li>Quite technical</li> <li>Requires specialist bespoke equipment</li> <li>Patients had to use bespoke pads throughout the study and have blood labelled with <math>Cr^{51}</math></li> </ul>
$Fe^{59}$ whole body counting [18]		<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> </ul>	<ul style="list-style-type: none"> <li>Relatively simple</li> <li>No need for collection of menses or pads</li> <li>Of great value for routine clinical investigation of anemias where HMB or some other form of blood loss is suspected</li> </ul>	<ul style="list-style-type: none"> <li>Not as accurate as some techniques (an error of 20–40 mL per period may not be unusual)</li> </ul>
Atomic and chemical analysis of iron recovery [19]	<ul style="list-style-type: none"> <li>Chemical analysis</li> <li>Atomic analysis</li> </ul>	<ul style="list-style-type: none"> <li>Reproducibility</li> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Estimation of menstrual iron losses are similar for both methods but atomic absorption avoids the necessity of preparing special glassware, is quicker, and helps to reduce errors that may occur during dilution</li> <li>Does not use derivatives of hemoglobin which may be destroyed by bacterial action, or colorimetric reactions that might suffer from interference by contaminants</li> </ul>	<ul style="list-style-type: none"> <li>Final estimates of iron may differ by as much as 6 mg between techniques</li> </ul>
Menstrual iron loss [20]	<ul style="list-style-type: none"> <li>MFL</li> </ul>	<ul style="list-style-type: none"> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>The first time iron losses have been directly measured from menstrual fluid</li> <li>Can be used to ascertain abnormal MBL before iron-deficient erythropoiesis has developed</li> </ul>	
<b>PBAC</b>				
Original PBAC method [21]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Agreement between participant and investigator</li> <li>Validated for Tampax®/Kotex® Fems Super Plus tampons; Kotex® Simplicity 2 towels</li> </ul>	<ul style="list-style-type: none"> <li>Simple, reasonably accurate</li> <li>In general, patients found the charts easy to use</li> <li>Superior to using counts of towels/tampons (not biased by extreme cases of towel/tampon use)</li> <li>Could be of value to both clinical practitioners and research workers, especially if it is not possible to measure MBL objectively</li> </ul>	<ul style="list-style-type: none"> <li>Not as accurate as AH method</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
PBAC [22]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validated for customary sanitary wear</li> </ul>	<ul style="list-style-type: none"> <li>Suitable for use in women complaining of heavy MBL; however, it should not replace the use of the AH method as the “gold standard”</li> </ul>	<ul style="list-style-type: none"> <li>Discriminatory power is only intermediate for detecting heavy MBL</li> </ul>
Modified PBAC (modified icons) [23]	<ul style="list-style-type: none"> <li>AH method [1,3,5]</li> </ul>	<ul style="list-style-type: none"> <li>Agreement between participant and investigator</li> <li>Validated for Kotex<sup>®</sup> Maxi Long pads; Tampax<sup>®</sup> Super tampons</li> </ul>	<ul style="list-style-type: none"> <li>Superior to subjective assessment of MBL at predicting HMB, even if performed only once</li> <li>None of the participants found the chart too difficult to complete</li> <li>No need to collect sanitary wear</li> <li>Can be used to make therapy more adequate and rational</li> </ul>	<ul style="list-style-type: none"> <li>Does not give a measure of MBL in milliliters</li> </ul>
PBAC [24]		<ul style="list-style-type: none"> <li>External validation (general community)</li> <li>Validated for unspecified pads and tampons with same absorbency as original study</li> </ul>		<ul style="list-style-type: none"> <li>PBAC may overestimate MBL in the general community</li> </ul>
Modified PBAC (revised icons and rating system) [25]		<ul style="list-style-type: none"> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Appropriate for measuring any apparent change in MBL</li> </ul>	
Modified PBAC (simplified, but with additional questions) [26]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validated for unspecified products</li> </ul>	<ul style="list-style-type: none"> <li>Probably the best available tool to health workers in developing countries for managing abnormal blood loss in girls</li> </ul>	<ul style="list-style-type: none"> <li>Required simplification for a poorly educated population</li> <li>Should be used with a dysmenorrhoea questionnaire</li> </ul>
PBAC [27]	<ul style="list-style-type: none"> <li>AH method (reference not given)</li> </ul>	<ul style="list-style-type: none"> <li>Validated for Tampax<sup>®</sup> Super; Kotex<sup>®</sup> Simplicity 2</li> </ul>	<ul style="list-style-type: none"> <li>Simple</li> </ul>	<ul style="list-style-type: none"> <li>Inaccurate and therefore does not appear to be of clinical value</li> </ul>
PBAC [11]	<ul style="list-style-type: none"> <li>AH method [3]</li> <li>MFL</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Validated for Tampax<sup>®</sup> Super; Kotex<sup>®</sup> Simplicity 2</li> </ul>	<ul style="list-style-type: none"> <li>Easy to use</li> </ul>	<ul style="list-style-type: none"> <li>Care should be taken in interpreting PBAC scores (relationship between PBAC and MBL/MFL is not direct)</li> </ul>
PBAC [28]		<ul style="list-style-type: none"> <li>External validation (Turkish women)</li> <li>Validation of discriminatory power</li> <li>Validated for</li> </ul>	<ul style="list-style-type: none"> <li>Simple, non-laboratory method, semi-objective</li> <li>Number and size of any clots passed are taken into account and scored</li> <li>PBAC is recommended for the diagnosis of HMB and evaluation of treatment outcomes</li> </ul>	<ul style="list-style-type: none"> <li>Validity of PBAC has been debated</li> <li>Not gold standard</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
		unspecified pads and tampons		
PBAC (for SAP-c towels) [29]	<ul style="list-style-type: none"> <li>AH method [1,2]</li> </ul>	<ul style="list-style-type: none"> <li>Validated for Always Ultra towels</li> </ul>	<ul style="list-style-type: none"> <li>Simple, accurate</li> <li>Could be used in clinical practice to aid decisions about treatment and follow-up</li> </ul>	
Modified PBAC (revised icons and used to estimate volume loss vs a score) [30]		<ul style="list-style-type: none"> <li>External validation (Iranian women)</li> <li>Discriminatory power</li> <li>Validated for unspecified products</li> </ul>	<ul style="list-style-type: none"> <li>All women completed the PBAC</li> </ul>	<ul style="list-style-type: none"> <li>Subject to recall bias</li> </ul>
PBAC [31]		<ul style="list-style-type: none"> <li>External validation (adolescents)</li> <li>Validation of discriminatory power</li> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Quick (&lt;10 min to complete)</li> </ul>	<ul style="list-style-type: none"> <li>Subject to recall bias</li> </ul>
Modified PBAC (revised icons) [32]	<ul style="list-style-type: none"> <li>Subjective assessment of MBL</li> </ul>	<ul style="list-style-type: none"> <li>Reliability</li> <li>Validated for women's own choice of sanitary items</li> </ul>	<ul style="list-style-type: none"> <li>Quicker and less expensive than AH method</li> <li>Does not require collection of sanitary material</li> <li>A low PBAC score may be used to define treatment endpoints for clinical use or in trials</li> </ul>	<ul style="list-style-type: none"> <li>Less accurate than AH method</li> </ul>
e-PBAC e-BQ [33]		<ul style="list-style-type: none"> <li>External validation (bleeders vs non-bleeders, oral contraceptive users vs non-users)</li> <li>Validated for unspecified products</li> </ul>	<ul style="list-style-type: none"> <li>Facilitated collection of menstrual data in real time</li> <li>Easy and straightforward to complete</li> <li>Patients prefer electronic methods to paper methods</li> <li>Electronic methods aid data collection/analysis and potentially reduce the chance of errors resulting from manual calculation of bleeding scores</li> <li>Combination of e-BQ and e-PBAC to assess or screen bleeding in women in the general female population is recommended</li> </ul>	
<b>Menstrual pictogram</b>				
Original menstrual pictogram [34]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validated for Tampax<sup>®</sup> Regular, Super, Super Plus; Kotex<sup>®</sup> Maxi Super, Maxi Night-time towels</li> </ul>	<ul style="list-style-type: none"> <li>Includes extraneous blood loss (clots and in bowl)</li> <li>Simple, effective</li> <li>Provides a semi-quantitative estimate of extraneous blood loss in milliliters</li> <li>More accurate than the original PBAC, probably owing to a</li> </ul>	

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
			<ul style="list-style-type: none"> <li>wider range of icons/absorbency levels</li> <li>• Could easily be used in primary and secondary care to diagnose HMB, and thus improve clinical treatment decisions and outcomes</li> <li>• Could be used in studies to determine total objective MBL in a normal population</li> </ul>	
Menstrual pictogram as part of a Symptometrics device [35]	<ul style="list-style-type: none"> <li>• AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>• Agreement with paper charts</li> <li>• Validated for unspecified sanitary pads</li> </ul>	<ul style="list-style-type: none"> <li>• Fast (mean time to measure, analyze, and transfer to the computer: one set of paper-based data, 118 min; data from the Symptometrics device, 5 min)</li> <li>• 48% of participants preferred the Symptometrics device to the paper equivalent (36%) to collect data</li> <li>• Instant display of symptom data makes diagnosis and management more precise and appropriate</li> <li>• Could revolutionize clinical and research practice of menstrual cycle disorders</li> </ul>	
Modified menstrual pictogram (excluding extraneous MBL and revised icons) [36]	<ul style="list-style-type: none"> <li>• AH method [1,3]</li> </ul>	<ul style="list-style-type: none"> <li>• External validation (North American treated population)</li> <li>• Validation of discriminatory power</li> <li>• Validated for Tampax® Regular, Super, Super Plus; Kotex® Maxi Super, Maxi Night-time towels</li> </ul>	<ul style="list-style-type: none"> <li>• Simple</li> <li>• Avoids need to collect soiled products</li> <li>• Could be useful in clinical practice to determine whether the patient-reported HMB meets the criteria for HMB and to help to decide if surgical intervention is necessary</li> <li>• Can be used in clinical trials to detect endpoints in response to treatments for MBL</li> </ul>	<ul style="list-style-type: none"> <li>• The agreement between menstrual pictogram and AH scores was weaker when there was heavy staining of towels</li> </ul>
Modified menstrual pictogram (for SAP-c towels) [37]	<ul style="list-style-type: none"> <li>• AH method [9]</li> </ul>	<ul style="list-style-type: none"> <li>• Internal consistency</li> <li>• Validated for Always Ultra with Wings Normal, Long, Night</li> </ul>	<ul style="list-style-type: none"> <li>• Women found the pictogram easy and quick to use and no one reported any difficulty in matching towel stains to pictogram icons</li> <li>• Can easily be carried in a normal-sized handbag, although a more robust format is required for routine use</li> <li>• Obviates the need to send towels to a laboratory for assessment</li> <li>• The tool would be suitable for testing in a clinical trial</li> </ul>	<ul style="list-style-type: none"> <li>• Not as accurate as the AH method or soiled towel weight (volume assignment is by five discrete images)</li> <li>• In the clinical setting, feminine towels (and hence stain spread) would be affected by mechanical pressures of the wearer</li> </ul>
Modified menstrual pictogram (for SAP-c towels, correcting for change in blood fraction with	<ul style="list-style-type: none"> <li>• AH method [10]</li> <li>• MFL</li> </ul>	<ul style="list-style-type: none"> <li>• Participant vs investigator agreement</li> <li>• Validated for Always Ultra with Wings Normal, Long, Night</li> </ul>	<ul style="list-style-type: none"> <li>• In general, the menstrual pictogram was easy to use with respect to towel color codes, the scorecard, and icon matching</li> <li>• Storing the towels and using the pictogram under everyday conditions were considered satisfactory</li> <li>• Avoids the inconvenience of collecting used feminine</li> </ul>	<ul style="list-style-type: none"> <li>• Excludes extraneous blood loss</li> <li>• Icon assignment difficult when the towel stain differs from depictions</li> <li>• Individual perception and</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
volume) [38]			<ul style="list-style-type: none"> <li>• products for laboratory assessment</li> <li>• The scoring environment was not considered to be a problem</li> <li>• A simple means of measuring MBL in the clinical setting</li> <li>• Ideally suited to clinical trials to screen women for HMB and to assess clinical improvement during the investigation of new treatment regimens</li> </ul>	<ul style="list-style-type: none"> <li>• interpretation of stain areas or incorrectly recorded data may result in inconsistencies</li> <li>• Assigned scores may be inappropriate for non-validated products</li> </ul>
<b>Questionnaire</b>				
Postal questionnaire (grading MBL as light, moderate, heavy, or very heavy) [39]			<ul style="list-style-type: none"> <li>• High response rate</li> </ul>	
Menorrhagia multi-attribute utility assessment scale, (considers practical difficulties, effects on social life, psychological effects, physical health, interruption to work, and effects on family life) [40]		<ul style="list-style-type: none"> <li>• Face and content validation</li> </ul>	<ul style="list-style-type: none"> <li>• Allows assessment of the impact of both the actual disease process and interventions to alleviate it</li> <li>• Intended to have clinical relevance in that it is designed to allow clinicians to assess a woman's current perception of her health, using a simple to administer clinical scale</li> <li>• Might be used longitudinally to monitor the change in health of a patient during a series of interventions</li> </ul>	
Menstrual record (function of reported saturation and absorbency of each product)  Menstrual recall (function of number of products used, absorbency, and number of heavy/light days) [41]	<ul style="list-style-type: none"> <li>• MFL</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• Validated for unspecified sanitary pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>• Non-invasive; quick to administer and analyze; has a low respondent burden (does not require a high level of participant motivation); takes into account different products used in clinical practice</li> <li>• The Menstrual recall method is preferable in an epidemiological setting to the Menstrual record and MFL methods, and is ideal in population studies requiring discrimination between heavy and normal MBL</li> </ul>	<ul style="list-style-type: none"> <li>• Recall method does not give precise measure of MBL and relies on memory</li> <li>• Record method is time-consuming for the participant and the information is difficult to collect and analyze</li> <li>• Could result in the misclassification of participants' MBL and is not an accurate means of diagnosing HMB in the clinical setting</li> </ul>
Menstrual score questionnaire (self-perceived debility)			<ul style="list-style-type: none"> <li>• Semi-objective</li> </ul>	<ul style="list-style-type: none"> <li>• 60.6% response rate</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
in terms of dysmenorrhoea, heavy days, frequency of changing products, clots, flooding, time off work, and duration of the problem) [42]				
Electronic calendar (self-assessment of bleeding as none, spotting, normal, or heavy) [43]		<ul style="list-style-type: none"> <li>• Comparison with paper version</li> </ul>	<ul style="list-style-type: none"> <li>• Requires less time for data entry and cleaning of data compared with paper forms</li> <li>• Can include a large amount of information because data entry can be simplified with pull-down screens, icons, and the programming of complicated skip patterns into the software</li> <li>• Error checks are built in</li> <li>• Results of an evaluation survey suggest a general acceptance of the electronic calendar by women</li> </ul>	<ul style="list-style-type: none"> <li>• Data entry has an average lag time of 2 days</li> </ul>
Interview to determine flow (number of products/cycle) over the previous 5 years [44]		<ul style="list-style-type: none"> <li>• Validated for unspecified pads and tampons</li> </ul>		<ul style="list-style-type: none"> <li>• Recall bias</li> <li>• The clinical importance of very small menstrual cycle changes may not represent a substantial public health concern</li> </ul>
Questionnaire assessing self-perceived changes in MBL (lighter, same, heavier, more variable, stopped) over 12 months [45]			<ul style="list-style-type: none"> <li>• Self-reporting of heavier MBL as a marker for menstrual dysfunction is subjective but is in keeping with usual clinical methods</li> </ul>	<ul style="list-style-type: none"> <li>• Respondents were asked about a change in MBL rather than if they actually had HMB</li> <li>• Wording of the questions affects accuracy</li> <li>• Subject to recall bias</li> </ul>
General Health Questionnaire and women's perception of the heaviness of MBL questionnaire [46]			<ul style="list-style-type: none"> <li>• 76% response rate</li> </ul>	<ul style="list-style-type: none"> <li>• Psychological distress may increase the self-reporting of gynecological physical symptoms in a community sample</li> </ul>
MVJ (6-point Likert scale based on the frequency of required changes of defined absorbency)	<ul style="list-style-type: none"> <li>• MFL</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• Validated using 87 different brands of towels/tampons</li> </ul>	<ul style="list-style-type: none"> <li>• Simple and practical</li> <li>• Particularly sensitive when estimating moderate to heavy bleeding (three periods should be assessed)</li> <li>• A practical and inexpensive method for clinicians to use with midlife/perimenopausal patients (group most vulnerable to</li> </ul>	<ul style="list-style-type: none"> <li>• Based on the perception of total MFL</li> <li>• Does not measure MBL (can use to estimate MBL)</li> <li>• Some participants did not</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
products) [47]			worry and/or interventions when HMB is incorrectly diagnosed) <ul style="list-style-type: none"> <li>An MVJ score of 6 may indicate a bleeding volume of some concern</li> </ul>	understand how to use the MVJ correctly <ul style="list-style-type: none"> <li>Did not work well in “light bleeders”</li> </ul>
MEQ (includes questions on subjective heaviness of period, type and number of products used, and clots) [48]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Validated for towels (Bodyform® Ultra Super and Super Plus sizes) and tampons (Tampax® Regular and Super)</li> <li>Inter-cycle consistency</li> </ul>	<ul style="list-style-type: none"> <li>Validated with real-life data</li> <li>First study to ask whether the period for which blood was collected was representative of periods as reported</li> <li>Provides a moderately good prediction of patients with an MBL &gt; 80 mL</li> </ul>	<ul style="list-style-type: none"> <li>More than one cycle should be analyzed</li> </ul>
Postal questionnaire on menstrual symptoms (i.e., heaviness, duration, if problematic) [49]		<ul style="list-style-type: none"> <li>Focus group discussions to check suitability for women in a community setting</li> </ul>	<ul style="list-style-type: none"> <li>Missing responses for questionnaire items were never more than 2.3%</li> <li>Women may be better served by a broader clinical assessment of the impact of periods on QoL and closer attention to the aspects of periods they find problematic</li> </ul>	<ul style="list-style-type: none"> <li>Does not include all factors that contribute to perception of periods</li> <li>Exact wording of the questionnaire is important</li> <li>Response rate of 61.5% (women with HMB are more likely to respond)</li> <li>Discrepancies in use of the terms “symptom” or “problem” in questionnaires vs in clinical practice</li> </ul>
Questionnaire assessing MBL (number of pads used; if physician was consulted) [50]		<ul style="list-style-type: none"> <li>Questionnaires were pretested in one school before they were used in the field</li> <li>External validation (Malaysian adolescents)</li> <li>Validated for unspecified pads</li> </ul>	<ul style="list-style-type: none"> <li>May help to meet the need for routine screening for dysmenorrhoea in school health programmes</li> </ul>	<ul style="list-style-type: none"> <li>Self-reporting</li> <li>Certain survey questions were not answered (some students may not have understood the questions)</li> <li>Those who had left school were not surveyed, so the results cannot be generalized to all female adolescents</li> </ul>
Questionnaire assessing changes in MBL including number of pads used and QoL [51]		<ul style="list-style-type: none"> <li>Validated for unspecified pads</li> </ul>		<ul style="list-style-type: none"> <li>Relies on subjective perception of reduction in MBL</li> <li>6/23 patients did not answer the questionnaire</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
Free-text questionnaire and follow-up qualitative interviews in patients with HMB [52]		<ul style="list-style-type: none"> <li>• Face validity (coding schemes checked with two other researchers)</li> <li>• The analysis used constant comparison to check for the presence of each coding theme in respondents' accounts and to seek counter examples</li> </ul>	<ul style="list-style-type: none"> <li>• Free text allowed the collection of responses in women's own terms, without prejudgment</li> <li>• The breadth of data from a large number of women given the questionnaire complemented the greater depth of information from a smaller number of qualitative interviewees</li> <li>• The community setting allowed exploration of concerns about menstrual symptoms among a population whose concerns were previously under-explored; most studies are carried out among patients referred to secondary care</li> </ul>	<ul style="list-style-type: none"> <li>• Categorization of free-text answers was difficult; it was subject to interpretation</li> <li>• Distinction between symptoms on questionnaire vs those reported in consultation</li> <li>• Responders (61.5%) may differ from non-responders (e.g., in motivation to complete the questionnaire or in literacy); this limits the generalizability of the questionnaire</li> <li>• Response bias (more missing free-text data than answers to fixed choice questions)</li> </ul>
QoL questionnaire (adapted from adult QoL questionnaires about perceptions, symptoms, and family history of bleeding problems) [53]	<ul style="list-style-type: none"> <li>• PBAC [21]</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• External validation (adolescents)</li> </ul>		
MIQ (health-related QoL) [54]	<ul style="list-style-type: none"> <li>• AH method (reference not given)</li> </ul>		<ul style="list-style-type: none"> <li>• Considers the importance and meaningfulness of MBL changes to women</li> </ul>	<ul style="list-style-type: none"> <li>• Further studies are needed to establish a minimally important change in MBL in women with and without HMB</li> </ul>
MIQ (health-related QoL) [55]	<ul style="list-style-type: none"> <li>• MIQ item 6c</li> <li>• AH method (reference not given)</li> </ul>	<ul style="list-style-type: none"> <li>• Construct and convergent validation</li> <li>• Validation of discriminatory power</li> <li>• Test-retest evaluation</li> <li>• Reliability of individual items</li> <li>• Assessment of the respondent burden</li> </ul>	<ul style="list-style-type: none"> <li>• Quick (2 min to complete)</li> <li>• Able to differentiate for each MIQ item the degree of change that women with HMB perceived as being clinically meaningful</li> <li>• Not limited by a proof of robustness vs other analytical tools because it uses "meaningful change"</li> <li>• If the observation period is short, a 1-point positive change in scores may be considered a desirable and easily interpretable outcome</li> <li>• The respondent burden is minimal and appropriate for diagnostic and clinical research settings</li> </ul>	

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
SF-36 (general health status; Portuguese version) [56]	<ul style="list-style-type: none"> <li>• PBAC</li> <li>• Hemo-globin levels</li> </ul>	<ul style="list-style-type: none"> <li>• External validation (Portuguese population)</li> </ul>	<ul style="list-style-type: none"> <li>• Practical</li> <li>• Can be useful to guide efforts to improve clinical assistance</li> </ul>	<ul style="list-style-type: none"> <li>• The presence of other factors such as poor diet, undernourishment, and depression can be reflected in the physical/mental scores</li> </ul>
Electronic daily uterine fibroid symptom diary (patient-reported outcomes in the form of 11 items: five addressing menstrual bleeding or spotting; one each related to cramping [distinct from other pain], fatigue, and bloating; and three addressing other fibroid-related pain) [57]		<ul style="list-style-type: none"> <li>• Face and content validation</li> </ul>	<ul style="list-style-type: none"> <li>• Concept saturation was achieved, indicating that the eight items contained in the diary were relevant to women with uterine fibroids and consistent with how they viewed their symptoms</li> <li>• Every symptom addressed in the diary was endorsed by at least two-thirds of the participants, resulting in a succinct questionnaire appropriate for daily administration</li> <li>• Average time for completing the full diary was 1–2 min per day</li> <li>• Most participants reported that the questions were “straightforward,” “applicable,” and captured the most bothersome symptoms associated with their uterine fibroids</li> <li>• Participants understood how to answer the diary questions and most participants stated that they could distinguish fibroid-related symptoms</li> <li>• It is expected that total MBL can be estimated as a function of the daily ratings on the bleeding item, the presence of clots, and sanitary product use</li> </ul>	<ul style="list-style-type: none"> <li>• The diary is not ideal for evaluating symptom changes or treatment response in the small minority of women with uterine fibroids who have no bleeding symptoms</li> <li>• Owing to the size of the screen of the handheld device, and because it was felt that participants could report the number of saturated sanitary products used more reliably than estimating the portion of saturation on the basis of a picture, the PBAC was not incorporated</li> <li>• Diagnostic utility, as well as known groups, criterion and concurrent validity require assessment</li> </ul>
Hospital for Sick Children bleeding questionnaire (question on heaviness of bleeding during period) and PBAC [58]	<ul style="list-style-type: none"> <li>• Subjective assessment (initial questionnaire)</li> </ul>	<ul style="list-style-type: none"> <li>• External validation (adolescents)</li> </ul>	<ul style="list-style-type: none"> <li>• A combined PBAC and Hospital for Sick Children bleeding questionnaire approach detected more cases of HMB in adolescents than a single question</li> <li>• Development of screening programs for HMB in adolescents in schools using both a bleeding questionnaire and a PBAC would improve detection and treatment of HMB</li> </ul>	<ul style="list-style-type: none"> <li>• High dropout rate</li> <li>• Difficult to perform research on HMB in adolescents</li> </ul>
Health Utilities Index questionnaire (assesses health-related QoL based on eight attributes: vision, hearing, speech, ambulation, dexterity, emotion, cognition, and	<ul style="list-style-type: none"> <li>• Clinical History Assessment Tool</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• External validation (women with von Willebrand disease)</li> </ul>	<ul style="list-style-type: none"> <li>• Differences in mean utility scores <math>\geq 0.03</math> for health-related QoL, and <math>\geq 0.05</math> for single attributes, are considered to be clinically important</li> </ul>	

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
pain) [59]				
Web-based questionnaire including disease-specific questions, on the perceptions of MBL [60]	<ul style="list-style-type: none"> <li>• SF-36</li> <li>• Quality of daily life</li> </ul>		<ul style="list-style-type: none"> <li>• Accurately predicted the prevalence of HMB</li> <li>• Response rate was sufficient for power requirements</li> </ul>	<ul style="list-style-type: none"> <li>• 4% of returned questionnaires were excluded because the question about perception of MBL was not answered</li> </ul>
Postal questionnaire to calculate bleeding score (sum of daily ratings of blood loss) and health-related QoL [61]				<ul style="list-style-type: none"> <li>• The numbers of women returning questionnaires (69.1%) failed to meet power requirements</li> </ul>
MBL score (based on number and absorbency of products used and self-perceived "heavy" days) [62]	<ul style="list-style-type: none"> <li>• Ferritin</li> <li>• Platelet count</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• Internal consistency</li> <li>• Validated for pads (mini, normal, super, night/superplus) and tampons (mini, regular, super, superplus); brand not specified</li> </ul>	<ul style="list-style-type: none"> <li>• Easy, practical, simple, feasible</li> <li>• Highly reliable</li> <li>• Does not rely on participant's memory</li> </ul>	<ul style="list-style-type: none"> <li>• Generalizability unknown</li> </ul>
Menorrhagia-specific QoL questionnaire, PBAC, and SF-36 (Iranian version) [63]		<ul style="list-style-type: none"> <li>• External validation (Iranian population)</li> <li>• Validated for medium-sized Panberes sanitary towels</li> </ul>		<ul style="list-style-type: none"> <li>• Limitations in assessing some problems that patients with HMB may experience</li> </ul>
Internet-based survey (about predefined symptoms of HMB, consultation with physician, and effect on daily life) [64]		<ul style="list-style-type: none"> <li>• Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>• Internet-based and paper surveys conducted when people do not have the same access to information technology give similar outcomes; thus, it is unlikely that the internet-based medium affected the results</li> </ul>	<ul style="list-style-type: none"> <li>• Information was only from the patient's perspective not from that of the healthcare professional</li> </ul>
MBQ (scores on heaviness, pain, irregularity, and QoL)	<ul style="list-style-type: none"> <li>• SF-36</li> </ul>	<ul style="list-style-type: none"> <li>• Validation of discriminatory power</li> <li>• Internal consistency</li> <li>• Content validation</li> </ul>	<ul style="list-style-type: none"> <li>• Covers a range of symptoms, the amount and regularity of bleeding, and the impact of symptoms on women's lives, specifically on the fear of social embarrassment based on focus group studies</li> </ul>	<ul style="list-style-type: none"> <li>• Generalizability unknown</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
[65]		<ul style="list-style-type: none"> <li>Validation of 1-month recall</li> </ul>	<ul style="list-style-type: none"> <li>A systematic process was used to develop the questionnaire using real input from women with HMB across a range of patient experiences</li> <li>Accurately summarizes the experiences of participants prospectively catalogued over 1 month</li> <li>Could improve the evaluation of women with self-reported HMB in clinical practice</li> <li>Could facilitate interpretation of data on treatment effectiveness and facilitate comparison and summation of results across studies</li> </ul>	
Female Health Questionnaire, online and paper versions – based on Fraser et al., 2015 (36) [66]			<ul style="list-style-type: none"> <li>Mixed mode (online and paper) strategy used to limit bias</li> </ul>	<ul style="list-style-type: none"> <li>Subject to recall bias</li> <li>Online survey more likely to be completed by females with menstrual cycle issues</li> <li>Presence of illness or the use of medication not recorded; these could increase HMB diagnosis</li> </ul>
<b>Additional methods involving self-perception</b>				
Subjective complaint of HMB [67]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> </ul>		
Subjective assessment of MBL [68]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Quick</li> </ul>	<ul style="list-style-type: none"> <li>Does not take clots into account</li> <li>Many women are not good judges of the volume of their MBL</li> </ul>
Subjective complaint and clinical history of HMB, and subjective daily assessment of MBL on a 4-point scale [69]	<ul style="list-style-type: none"> <li>AH method [3]</li> <li>Duration of menstruation</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> </ul>		<ul style="list-style-type: none"> <li>May result in large numbers of hysterectomies for HMB that cannot be objectively confirmed</li> <li>Not as accurate as AH method</li> </ul>
Subjective and objective clinical parameters [70]	<ul style="list-style-type: none"> <li>AH method [1]</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>Validated for unspecified pads and tampons</li> </ul>	<ul style="list-style-type: none"> <li>Hemoglobin levels fall with increasing blood loss, although the relationship is insufficiently precise for this to be a diagnostic test for objective HMB</li> </ul>	<ul style="list-style-type: none"> <li>It is difficult to establish the volume of MBL with certainty without an objective assessment</li> <li>There was substantial variation in the number of sanitary items used</li> <li>For the hemoglobin test, HMB</li> </ul>

Study (reference)	Concurrent validation (reference)	Other validation	Advantages	Disadvantages
				<p>can coexist with a hemoglobin level well within the normal range, so it should not be relied on as a screening test to deny treatment</p> <ul style="list-style-type: none"> <li>The relationship between objective MBL and height is weak and of doubtful clinical importance</li> </ul>
Mixed linear model (menstrual diary and laboratory parameters) [71]	<ul style="list-style-type: none"> <li>AH method [3]</li> </ul>	<ul style="list-style-type: none"> <li>Validation of discriminatory power</li> <li>External validation (similar study population)</li> </ul>	<ul style="list-style-type: none"> <li>Simple and accurate</li> <li>A menstruation diary could be a better descriptor of blood loss measurements than the AH method</li> <li>The specificity and sensitivity make this technique suitable for clinical use and counselling</li> <li>Can be used to estimate MBL in clinical studies</li> </ul>	<ul style="list-style-type: none"> <li>Does not give a precise MBL measure; in studies where MBL is the primary efficacy outcome, the AH method will remain the gold standard (although it does not account for MBL outside sanitary protection)</li> <li>Further studies are required to test reproducibility and generalizability</li> </ul>

AH = alkaline hematin; BQ = bleeding questionnaire; HMB = heavy menstrual bleeding; MBL = menstrual blood loss; MBQ = Menstrual Bleeding Questionnaire; MEQ = Menstrual Evaluation Questionnaire; MFL = menstrual fluid loss; MIQ = Menorrhagia Impact Questionnaire; MVJ = Mansfield-Voda-Jorgensen Menstrual Bleeding Scale; PBAC = pictorial blood loss assessment chart; QoL = quality of life; SAP-c = superabsorbent polymer-containing; SF-36 = Medical Outcomes Study Short 36-item Short Form Health Survey.

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