Comparison of Menstrual Pictogram Scoring to the Validated Alkaline Hematin Assay as Techniques for Measuring Blood Loss on Feminine Hygiene Products

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INTRODUCTION

To invalidate Menstural Pictograms (MP) for measurement of menstrual blood loss (MBL) on feminine hygiene products.

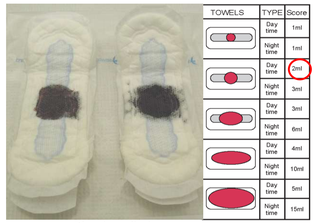
Prospective experimental analysis
Control Samples: Measured volumes of blood were applied to Kotex Regular Maxi Pads or Tampax Super Tampons. The MP (G. Warrilow et al. *The Obstetrician and Gynecologist* 2004; **6**:88-92) score was recorded and compared to actual volumes applied.

Clinical Samples: Patient feminine hygiene samples were scored using the MP and results were compared to a fully validated alkaline hematin (AH) assay, proven accurate and precise.

CONTROL SAMPLES

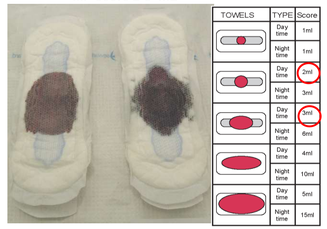
Control Samples: Measured blood volumes applied with serological pipet to Kotex Maxi Pads or Tampax Tampons, Vs MP scores recorded.

MP score 2 mL



Blood applied
10 mL **20 mL**

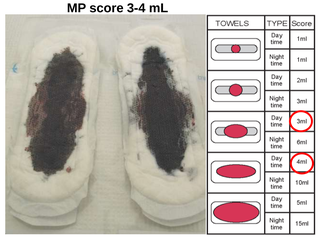
MP score 2-3 mL



Same pads after compression

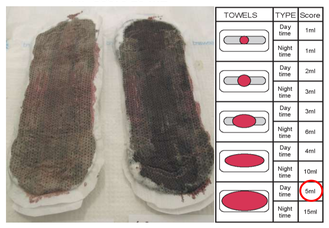
Pictogram scores under-estimate actual volumes applied by up to 10 fold, sometimes more.

MP score 3-4 mL



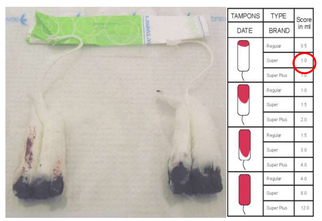
Blood applied
30 mL **40 mL**

MP score 15 mL



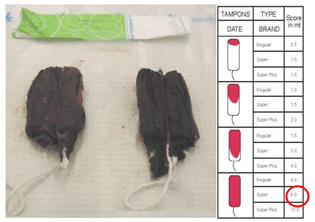
Blood applied, Pads compressed
40 mL **60 mL**

MP score 1 mL



Blood applied
3 mL **6 mL**

MP score 8 mL



Blood applied
12 mL **20 mL**

CLINICAL SAMPLES

Menstrual Pictogram: Is the Maximum Score Realistic?

For 166 patients in a clinical trial undergoing MBL measurement by alkaline hematin, actual average volumes measured on samples consisting of pads only or tampons only were compared to the pictogram maxima (12 mL- Tampon; 15 mL-Pad).

Samples = Tampons only (1-8/sample): 173	
Of these, # assayed below LLOQ:	67 (38.7%)
# assayed >LLOQ & ≤12.0 mL/tampon:	63 (36.4%)
# assayed >12.1 mL & ≤25.0 mL/tampon:	27 (15.6%)
# assayed >25.0 mL/tampon:	6 (9.2%)

Samples = Pads only (1-4/sample):	1347
Of these, # assayed below LLOQ:	233 (17.3%)
# assayed >LLOQ & ≤15.0 mL/pad:	753 (55.9%)
# assayed >15.1 mL & ≤25.0 mL/pad:	248 (18.4%)
# assayed >25.1 & ≤50.0 mL/pad:	103 (7.6%)
# assayed >50.0 mL/pad:	10 (0.7%)

Approximately 25% of assayed tampon samples and 27% of assayed pad samples averaged more than the maximum respective MP scores.

23 Patients, 102 Cycle Days
MP Volume (mL) Vs AH Assay Volume (mL)

MP Vol.	5	1	1	0	2	2	1	2	1	4
AH Vol.	<5.00	<2.50	<2.50	<2.50	<2.50	<2.50	<2.50	<2.50	<2.50	<2.50
MP Vol.	3	3	4	3	0	3	6	4	2	3
AH Vol.	<2.50	<2.50	<2.50	<2.50	<2.50	2.57	2.98	3.44	3.46	4.00
MP Vol.	6	3	7	17	5	3.5	5	4	3	5
AH Vol.	4.06	4.21	4.38	5.25	5.43	5.47	6.07	6.20	6.71	6.83
MP Vol.	5.5	13	18	15	20	15	7	9	18	10
AH Vol.	8.21	8.74	10.6	11.8	13.4	14.1	15.7	15.7	16.4	17.4
MP Vol.	14	12	19	12	14	19	16	22	10	9
AH Vol.	18.0	18.1	18.3	19.0	19.0	20.3	20.9	21.4	22.3	22.7
MP Vol.	20	35	13	8	14	14	17	15	16	17
AH Vol.	23.4	23.8	23.8	25.3	26.0	27.9	30.6	30.9	38.1	33.2
MP Vol.	21	37	41	25	27	18	40	18	17	30
AH Vol.	35.2	39.7	43.2	43.4	43.4	46.8	47.0	47.3	51.3	51.9
MP Vol.	50	21	34	30	70	15	29	56	37	34
AH Vol.	52.8	56.4	57.3	57.8	63.6	64.4	64.6	66.4	69.1	69.3
MP Vol.	42	33	29	22	65	59	31	25	18	30
AH Vol.	70.7	71.9	78.9	81.0	81.9	83.0	83.1	85.4	90.6	95.8
MP Vol.	60	91	70	68	100	54	59	100	83	162
AH Vol.	132	143	164	164	167	171	173	196	212	212
MP Vol.	106	91								
AH Vol.	280	311								

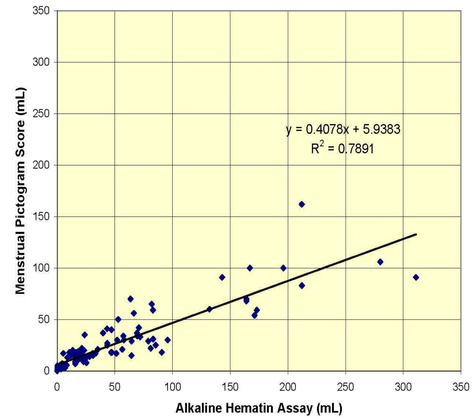
% Diff = (MP Vol - AH Vol) / (Mean, AH & MP Vols)

Table shows data points in increasing order of AH volume, left to right, top to bottom row
Colors depict whether alkaline hematin and MP volumes are within 15% of each other (green).

AH Vol BQL, MP Vol Consistent with this:	MP Vol "Accurate":	MP Over-Estimated Vol:	MP Under-Estimated Vol:
10 data points (9.8%)	within ±15% of AH Vol 12 data points (11.8%)	> 15% bias Vs AH Vol 16 data points (15.7%)	> 15% bias Vs AH Vol 64 data points (62.7%)

78% of pictogram scores are ***inaccurate*** by bio-assay ± 15% standard

Menstrual Pictogram Score Vs Alkaline Hematin Assay: Individual Collection Days (102)



Pictogram Method Shortcomings:

- **Lack of clinically relevant accuracy**
  - Vastly different blood volumes appear the same and produce the same pictogram score.
  - Pictogram-estimated blood volumes are inaccurate
  - Volumes are under-estimated at higher (more clinically relevant) volumes
- **Clinically relevant ceiling effect (lack of dynamic range)**
- **Pictogram can't be validated to current FDA ±15% accuracy and precision standards**

CONCLUSION

•Photographs clearly show that it is very difficult to distinguish between different amounts of blood on the same pad or tampon, leading to incorrect MP scoring.

•The pictogram does not meet established bio-assay accuracy standards (± 15% of nominal), with greater degree of under-estimation at higher volumes more relevant to establishing menorrhagia.

•The pictogram leads to a substantial number of mainly false negatives (sometimes false positives) using either 80 mL or 160 mL as the blood loss threshold for inclusion in a clinical study, most likely increasing the number of subjects to screen.

We propose a validated alkaline hematin method should be the method of choice when measuring blood loss in a clinical trial of menorrhagic conditions.

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