

## Appendix: Tables

Model (M1): Evaluation of blood loss

Let

$Hb_{ik}$	Hemoglobin [g/dl] of patient $i$ at day $k$ (imputed by linear interpolation)
$Fe_{ik}$	Serum-ferritin [ng/ml] of patient $i$ at day $k$ , (imputed by linear interpolation)
$H_{ik}$	Number of days with HEAVY bleeding during the episode of interest of patient $i$ with respect to day $k$
$H_{ik}^1$	Number of days with HEAVY bleeding during the preceding episode of patient $i$ with respect to day $k$
$H_i^I$	Occurrence [0=no, 1=yes] of HEAVY bleeding during the complete available diary of patient $i$
$N_{ik}^{MW}$	Mean number of days with NORMAL bleeding of all episodes of the last 30 days of patient $i$ with respect to day $k$
$N_i^{BI}$	Number of days with NORMAL bleeding during the second heaviest episode during baseline of patient $i$
$N_{ik}^I$	Occurrence of NORMAL bleeding during the episode of interest of patient $i$ with respect to day $k$
$L_i^{BI}$	Number of days with LIGHT bleeding during the second heaviest episode during baseline of patient $i$
$L_{ik}^I$	Occurrence of LIGHT bleeding during the episode of interest of patient $i$ with respect to day $k$
$S_{ik}^I$	Occurrence of SPOTTING during the episode of interest of patient $i$ with respect to day $k$
$Age_i$	Age of patient $i$ [years],

then we get the following equations for the estimation of the MBLV according (M1) based on the BI given in the diary of patient  $i$  at day  $k$

if day $k$ was a day with SPOTTING	if day $k$ was a day with LIGHT bleeding
$  \begin{aligned}  MBLV_{Spotting\ ik} &= \exp (2.5712 \\  &-0.1008 Hb_{ik} + 0.002255 Fe_{ik} \\  &+ 0.0236 H_{ik} - 0.02189 H_{ik}^{-1} + 0.0863 H_i^I \\  &+ 0.01507 N_{ik}^{MW} - 0.04875 N_i^{Bl} \\  &- 0.04017 L_i^{Bl} - 0.02261 L_{ik}^I \\  &- 0.02386 S_{ik}^I \\  &+ 0.00535 Age_i) - 1  \end{aligned}  $	$  \begin{aligned}  MBLV_{light\ ik} &= \exp (3.19185 \\  &-0.1008 Hb_{ik} - 0.002133 Fe_{ik} \\  &+ 0.01273 H_{ik} - 0.02221 H_{ik}^{-1} - 0.2687 H_i^I \\  &+ 0.01507 N_{ik}^{MW} - 0.04875 N_i^{Bl} \\  &- 0.04017 L_i^{Bl} + 0.05601 L_{ik}^I \\  &+ 0.10104 S_{ik}^I \\  &+ 0.01387 Age_i) - 1  \end{aligned}  $
if day $k$ was a day with NORMAL bleeding	if day $k$ was a day with HEAVY bleeding
$  \begin{aligned}  MBLV_{normal\ ik} &= \exp (4.16355 \\  &-0.1008 Hb_{ik} - 0.00327 Fe_{ik} \\  &- 0.03281 H_{ik} + 0.03253 H_{ik}^{-1} - 0.4811 H_i^I \\  &+ 0.01507 N_{ik}^{MW} - 0.04875 N_i^{Bl} \\  &- 0.04017 L_i^{Bl} + 0.14008 L_{ik}^I \\  &+ 0.02943 S_{ik}^I \\  &+ 0.02837 Age_i) - 1  \end{aligned}  $	$  \begin{aligned}  MBLV_{heavy\ ik} &= \exp (5.01735 \\  &-0.1008 Hb_{ik} - 0.00437 Fe_{ik} \\  &- 0.05434 H_{ik} + 0.04494 H_{ik}^{-1} - 0.4811 H_i^I \\  &+ 0.01507 N_{ik}^{MW} - 0.04875 N_i^{Bl} \\  &- 0.04017 L_i^{Bl} + 0.05601 L_{ik}^I \\  &- 0.02386 S_{ik}^I \\  &+ 0.03026 Age_i) - 1  \end{aligned}  $

**Table 1 Detailed description of model (M1)**

<b>Model (M1)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
Intercept		4.6027	0.2535	4.1055	5.0999
BI	Spotting	-2.4673	0.2738	-3.0044	-1.9302
BI	light	-1.9143	0.2138	-2.3336	-1.4950
BI	normal	-0.9745	0.1552	-1.2790	-0.6701
BI	heavy	0	.	.	.
$H_{ik}$		-0.1008	0.01042	-0.1212	-0.08034
$Fe_{ik}$		-0.00437	0.001062	-0.00645	-0.00229
$Fe_{ik} * BI$	Spotting	0.006625	0.001694	0.003305	0.009946
$Fe_{ik} * BI$	light	0.002237	0.001273	-0.00026	0.004733
$Fe_{ik} * BI$	normal	-0.00110	0.000973	-0.00301	0.000804
$Fe_{ik} * BI$	heavy	0	.	.	.
$H_{ik}$		-0.05434	0.01261	-0.07906	-0.02962
$H_{ik} * BI$	Spotting	0.07794	0.02101	0.03675	0.1191
$H_{ik} * BI$	light	0.06707	0.01720	0.03336	0.1008
$H_{ik} * BI$	normal	-0.02153	0.01771	-0.05623	0.01318
$H_{ik} * BI$	heavy	0	.	.	.
$H_{ik}^{-1}$		0.04494	0.01221	0.02102	0.06887
$H_{ik}^{-1} * BI$	Spotting	-0.06683	0.02065	-0.1073	-0.02635
$H_{ik}^{-1} * BI$	light	-0.06715	0.01743	-0.1013	-0.03297
$H_{ik}^{-1} * BI$	normal	0.01241	0.01756	-0.02200	0.04682
$H_{ik}^{-1} * BI$	heavy	0	.	.	.
$H_i^I$		-0.4811	0.09601	-0.6693	-0.2929
$H_i^I * BI$	Spotting	0.5674	0.1202	0.3317	0.8031
$H_i^I * BI$	light	0.2124	0.08462	0.04656	0.3783
$H_i^I * BI$	normal	0	.	.	.
$H_i^I * BI$	heavy	0	.	.	.
$N_{ik}^{MW}$		0.01507	0.004575	0.006104	0.02404
$N_i^{BI}$		-0.04875	0.01562	-0.07936	-0.01814
$L_i^{BI}$		-0.04017	0.009837	-0.05945	-0.02089
$L_{ik}^I$		0.05601	0.04037	-0.02311	0.1351
$L_{ik}^I * BI$	Spotting	-0.07862	0.05267	-0.1819	0.02462
$L_{ik}^I * BI$	light	0	.	.	.
$L_{ik}^I * BI$	normal	0.08407	0.05242	-0.01867	0.1868
$L_{ik}^I * BI$	heavy	0	.	.	.
$S_{ik}^I$		-0.02386	0.03135	-0.08532	0.03759
$S_{ik}^I * BI$	Spotting	0	.	.	.

<b>Model (M1)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
$S_{ik}^I * BI$	light	0.1249	0.03947	0.04751	0.2022
$S_{ik}^I * BI$	normal	0.05329	0.03915	-0.02346	0.1300
$S_{ik}^I * BI$	heavy	0	.	.	.
$Age_i$		0.03026	0.004714	0.02102	0.03950
$Age_i * BI$	Spotting	-0.02491	0.006427	-0.03751	-0.01231
$Age_i * BI$	light	-0.01639	0.005060	-0.02630	-0.00647
$Age_i * BI$	normal	-0.00189	0.003664	-0.00908	0.005288
$Age_i * BI$	heavy	0	.	.	.

**Table 2 Model (M1), fixed effects**

<b>Model (M1)</b>	Patient		Residual Error	
Random Effects: Variance	Estimate	Standard Error	Estimate	Standard Error
Spotting	0.3238	0.03171	0.5478	0.01310
light	0.2658	0.02177	0.7411	0.01162
normal	0.3002	0.02514	0.7705	0.01437
heavy	0.3561	0.03092	0.4732	0.01240

**Table 3 Model (M1), random effects**

<b>Model (M2)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
Intercept		3.9210	0.2332	3.4637	4.3783
BI	Spotting	-2.0222	0.2581	-2.5283	-1.5160
BI	light	-1.7589	0.2021	-2.1552	-1.3626
BI	normal	-0.9576	0.1553	-1.2621	-0.6530
BI	heavy	0	.	.	.
$H_{ik}$		-0.1011	0.01048	-0.1217	-0.08060
$Fe_{ik}$		-0.00452	0.001066	-0.00661	-0.00243
$Fe_{ik} * BI$	Spotting	0.006538	0.001699	0.003207	0.009869
$Fe_{ik} * BI$	light	0.002414	0.001273	-0.00008	0.004909
$Fe_{ik} * BI$	normal	-0.00098	0.000978	-0.00290	0.000937
$Fe_{ik} * BI$	heavy	0	.	.	.
$H_{ik}$		-0.04743	0.01243	-0.07179	-0.02307
$H_{ik} * BI$	Spotting	0.06983	0.02028	0.03009	0.1096
$H_{ik} * BI$	light	0.04835	0.01652	0.01598	0.08073
$H_{ik} * BI$	normal	-0.01346	0.01682	-0.04642	0.01950
$H_{ik} * BI$	heavy	0	.	.	.
$N_{ik}^I$		0.03505	0.01647	0.002759	0.06734
$L_{ik}^I$		0.06246	0.04039	-0.01671	0.1416
$L_{ik}^I * BI$	Spotting	-0.09965	0.05286	-0.2033	0.003948
$L_{ik}^I * BI$	light	0	.	.	.
$L_{ik}^I * BI$	normal	0.07293	0.05253	-0.03003	0.1759
$L_{ik}^I * BI$	heavy	0	.	.	.
$S_{ik}^I$		-0.02252	0.03140	-0.08407	0.03902
$S_{ik}^I * BI$	Spotting	0	.	.	.
$S_{ik}^I * BI$	light	0.1278	0.03951	0.05037	0.2052
$S_{ik}^I * BI$	normal	0.04854	0.03928	-0.02844	0.1255
$S_{ik}^I * BI$	heavy	0	.	.	.
$Age_i$		0.03285	0.004761	0.02352	0.04218
$Age_i * BI$	Spotting	-0.02394	0.006447	-0.03658	-0.01131
$Age_i * BI$	light	-0.01659	0.005044	-0.02648	-0.00670
$Age_i * BI$	normal	-0.00201	0.003683	-0.00923	0.005207
$Age_i * BI$	heavy	0	.	.	.

**Table 4 Model (M2), fixed effects**

<b>Model (M2)</b>	<b>Patient</b>		<b>Residual Error</b>	
<b>Random Effects: Variance</b>	<b>Estimate</b>	<b>Standard Error</b>	<b>Estimate</b>	<b>Standard Error</b>
Spotting	0.3261	0.03189	0.5476	0.01310
light	0.2897	0.02338	0.7416	0.01163
normal	0.3337	0.02730	0.7739	0.01443
heavy	0.3761	0.03278	0.4746	0.01243

**Table 5 Model (M2), random effects**

<b>Model (M3)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
Intercept		5.1672	0.1336	4.9052	5.4291
BI	Spotting	-2.9475	0.05658	-3.0585	-2.8365
BI	light	-2.2335	0.04349	-2.3188	-2.1482
BI	normal	-0.9132	0.03158	-0.9752	-0.8513
BI	heavy	0	.	.	.
$Hb_{ik}$		-0.1008	0.01055	-0.1215	-0.08009
$Fe_{ik}$		-0.00479	0.001086	-0.00691	-0.00266
$Fe_{ik} * BI$	Spotting	0.006537	0.001713	0.003179	0.009895
$Fe_{ik} * BI$	light	0.002459	0.001286	-0.00006	0.004979
$Fe_{ik} * BI$	normal	-0.00080	0.000980	-0.00272	0.001121
$Fe_{ik} * BI$	heavy	0	.	.	.

**Table 6 Model (M3), fixed effects**

<b>Model (M3)</b>	Patient		Residual Error	
Random Effects: Variance	Estimate	Standard Error	Estimate	Standard Error
Spotting	0.3314	0.03244	0.5484	0.01311
light	0.3074	0.02453	0.7421	0.01164
normal	0.3939	0.03133	0.7762	0.01446
heavy	0.4423	0.03730	0.4771	0.01249

**Table 7 Model (M3), random effects**

<b>Model (M4)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
Intercept		4.4280	0.1244	4.1840	4.6721
BI	Spotting	-3.2645	0.1330	-3.5253	-3.0036
BI	light	-2.4975	0.09408	-2.6821	-2.3130
BI	normal	-1.0739	0.06642	-1.2042	-0.9437
BI	heavy	0	.	.	.
$H_{ik}$		-0.05295	0.01258	-0.07760	-0.02829
$H_{ik} * BI$	Spotting	0.08038	0.02096	0.03929	0.1215
$H_{ik} * BI$	light	0.07200	0.01719	0.03830	0.1057
$H_{ik} * BI$	normal	-0.02199	0.01771	-0.05671	0.01273
$H_{ik} * BI$	heavy	0	.	.	.
$H_{ik}^{-1}$		0.04963	0.01225	0.02561	0.07365
$H_{ik}^{-1} * BI$	Spotting	-0.06633	0.02067	-0.1068	-0.02582
$H_{ik}^{-1} * BI$	light	-0.06457	0.01747	-0.09882	-0.03033
$H_{ik}^{-1} * BI$	normal	0.01485	0.01764	-0.01972	0.04943
$H_{ik}^{-1} * BI$	heavy	0	.	.	.
$H_i^I$		-0.4375	0.1074	-0.6480	-0.2270
$H_i^I * BI$	Spotting	0.5229	0.1269	0.2742	0.7717
$H_i^I * BI$	light	0.1898	0.08808	0.01713	0.3624
$H_i^I * BI$	normal	0	.	.	.
$H_i^I * BI$	heavy	0	.	.	.
$N_{ik}^{MW}$		0.01856	0.004583	0.009574	0.02754
$N_i^{BI}$		-0.05796	0.01714	-0.09156	-0.02435
$L_i^{BI}$		-0.04800	0.01089	-0.06934	-0.02666
$L_{ik}^I$		0.05539	0.04050	-0.02400	0.1348
$L_{ik}^I * BI$	Spotting	-0.07872	0.05275	-0.1821	0.02466
$L_{ik}^I * BI$	light	0	.	.	.
$L_{ik}^I * BI$	normal	0.07913	0.05259	-0.02394	0.1822
$L_{ik}^I * BI$	heavy	0	.	.	.
$S_{ik}^I$		-0.02250	0.03148	-0.08421	0.03921
$S_{ik}^I * BI$	Spotting	0	.	.	.
$S_{ik}^I * BI$	light	0.1290	0.03957	0.05147	0.2066
$S_{ik}^I * BI$	normal	0.05629	0.03932	-0.02078	0.1334
$S_{ik}^I * BI$	heavy	0	.	.	.

**Table 8 Model (M4), fixed effects**



<b>Model (M4)</b>	Patient		Residual Error	
Random Effects: Variance	Estimate	Standard Error	Estimate	Standard Error
Spotting	0.3623	0.03455	0.5458	0.01303
light	0.3136	0.02489	0.7437	0.01166
normal	0.3983	0.03193	0.7727	0.01441
heavy	0.4545	0.03809	0.4747	0.01244

**Table 9 Model (M4), random effects**

<b>Model (M5)</b>					
Fixed Effects	BI	Estimate	Standard Error	LCL	UCL
Intercept		2.5439	0.1977	2.1561	2.9317
BI	Spotting	-1.8872	0.2594	-2.3959	-1.3785
BI	light	-1.5478	0.2019	-1.9438	-1.1517
BI	normal	-0.8546	0.1457	-1.1403	-0.5689
BI	heavy	0	.	.	.
Age <sub>i</sub>		0.03411	0.005078	0.02416	0.04406
Age <sub>i</sub> *BI	Spotting	-0.02476	0.006677	-0.03785	-0.01167
Age <sub>i</sub> *BI	light	-0.01702	0.005185	-0.02718	-0.00686
Age <sub>i</sub> *BI	normal	-0.00203	0.003729	-0.00934	0.005280
Age <sub>i</sub> *BI	heavy	0	.	.	.

**Table 10 Model (M5), fixed effects**

<b>Model (M5)</b>	Patient		Residual Error	
Random Effects: Variance	Estimate	Standard Error	Estimate	Standard Error
Spotting	0.3592	0.03418	0.5465	0.01306
light	0.3335	0.02618	0.7448	0.01168
normal	0.4059	0.03203	0.7794	0.01453
heavy	0.4431	0.03755	0.4789	0.01255

**Table 11 Model (M5), random effects**