

Real-world treatment and outcomes for heavy menstrual bleeding from large electronic health records results from the CHAracterization and treatMent Pathways of HMB (Champion-HMB) study

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Background

- Heavy menstrual bleeding (HMB) occurs in an estimated 30% of women and affects their health and quality of life yet delays in diagnosis and treatment are widespread.¹⁻⁵
- 54% of women with HMB have never been diagnosed or treated.⁶
- HMB clinical care guidelines have been published in several countries in Europe and globally.^{5,9-12} Levonorgestrel-based intrauterine devices (LNG-IUDs) are an effective therapeutic option for HMB recommended by clinical guidelines such as those published by UK NICE⁷ and by the Society of Obstetricians and Gynecologists of Canada.²
- Extensive real-world population-based studies of HMB are lacking. Despite the availability of non-invasive therapeutic options including LNG-IUDs, invasive treatments are common.
- We describe the early findings of a multi-country network study that used standardized data from electronic health records (EHR) across databases from France, Germany, and insurance claims data from the USA.

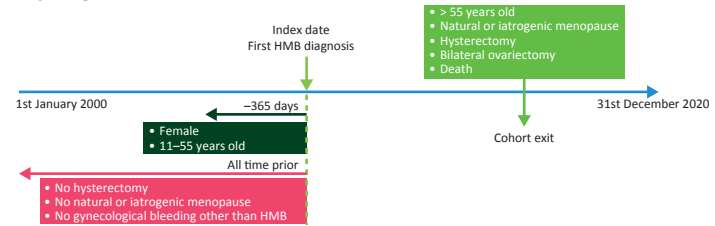
Aims

- To describe the incidence rates of women diagnosed with HMB per year and over the entire study period, and the proportion of women receiving a diagnosis of HMB from 2000–2020.
- To characterize women with a diagnosis of HMB in terms of demographics, parity, reproductive history, comorbidities, and procedures, in order to better understand the clinical characteristics of patients.
- To describe the treatment pathways of multiple therapeutic options for women with HMB, including LNG-IUDs.
- To estimate the frequency of invasive treatment (such as endometrial ablation and hysterectomy).

Methods

- Design:** retrospective cohort study.
- Study period:** from January 1st, 2000 to December 31, 2020.
- Data sources:** four observational healthcare data sources: LPD France, DA Germany, OPTUM Clinformatics and IBM MarketScan US.
 - Data were accessed as part of the OHDSI Research Network, and converted to the OMOP Common Data Model (OMOP CDM v4 or 5, <http://omop.org/cdm>; <https://github.com/OHDSI/CommonDataModel>). This model harmonizes data structure and maps coding systems to a standardized set of concepts.
- Covariates:** Demographics; underlying causes of HMB starting anytime before or after HMB diagnosis; therapies.

Study design



- Measures:** the proportion of women with HMB out of women at risk, and HMB diagnosis incidence per 1000 person-years.
- Proportion definition:**
$$\frac{\text{Sum of } N \text{ women with } \geq 1 \text{ HMB occurrence during the entire study period}}{\text{Total } N \text{ of eligible women in the data source}}$$

*note: women with multiple occurrences of HMB will be counted once.
- Incidence rate definition:**
$$\text{Incidence rate} = \frac{N \text{ of new cases of HMB in a given time period}}{\text{Total person-time of the at-risk population}}$$

where N of new cases in a given time period corresponds to the total number of individuals in the study population, and total person-time of the at-risk population corresponds to the sum of the time at risk spent by individuals within the study.
- A descriptive analysis of the study population was performed using the ATLAS function ‘Characterization’ which provides counts and proportions (i.e. frequency distributions) according to the covariates (<https://github.io/TheBookOfOhdsi/Characterization.html>, last accessed Nov 18, 2021).

Results

Data sources

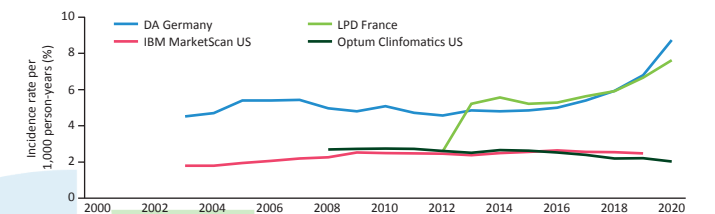
Data source	Source population	Sample size	Data type	Data collection period	Study period*	Percentage population covered
Disease Analyser (DA) Germany	Ambulatory	38.5M ^b	Electronic health records	1992 onwards	2003 to 2020	46%
Longitudinal Patient Data (LPD) France	Ambulatory	17.9M	Electronic health records	1994 onwards	2012 to 2020	27%
OPTUM Clinformatics US	Closed claims	69.39M	Claims data	2007 onwards	2008 to 2020	19% ^c
IBM MarketScan US	Closed claims	164.78M	Claims data	2002 onwards	2003 to 2019	NA

*The study period differed across data sources due to differences in data availability at the time of study implementation. Overall study data collection was from January 1st, 2000 to December 31, 2020. ^bMillion. ^cIn 2014, US Optum data covered a population of approximately 19% of the US population in commercial health plans and 19% of those in Medicare.

HMB proportion

- The proportion of women diagnosed with HMB was 2.21% (out of 2,276,641 women) in France, 2.6% (out of 5,080,352) in Germany, and 5.51% (out of 1,981,152, MarketScan) and 5.13% (out of 648,491 women, Optum) in the USA.

Incidence of heavy menstrual bleeding by year



*LPD France incidence 2012 outlier may be due to an exception in data recording. DA: Disease Analyser; LPD: Longitudinal Patient Data; OHDSI: Observational Health Data Sciences and Informatics; OMOP: Observational Medical Outcomes Partnership

Underlying organic causes

- Of the women with HMB, the proportion with diagnosed **underlying organic causes** (including leiomyoma, polyps, endometrial hyperplasia, or endometrial malignancy) was 1.42% (France), 27.92% (Germany), 35.18% (USA, MarketScan), and 34.63% (USA, Optum).
- The proportion of women with HMB and **underlying ovulatory dysfunction** was 6.00% (France), 36.28% (Germany), 28.78% (USA, MarketScan), and 30.13% (USA, Optum).

HMB subgroup* n (%)	France (N=39,565)	Germany (N=118,885)	US MarketScan (N=1,981,152)	US Optum (N=686,491)
Polyps	254 (0.64)	5,165 (4.34)	16,1107 (8.13)	56,939 (8.29)
Leiomyoma	305 (0.77)	27,815 (23.40)	532,625 (26.88)	179,787 (26.19)
Malignancy and endometrial hyperplasia	2 (0.01)	214 (0.18)	3,304 (0.17)	1,062 (0.15)
Coagulopathy	79 (0.20)	2,359 (1.98)	40,922 (2.07)	15,683 (2.28)
Ovulatory dysfunction	2,374 (6.00)	43,126 (36.28)	570,128 (28.78)	20,6843 (30.13)
Endometrial dysfunction	279 (0.71)	9,250 (7.78)	64,014 (3.23)	21,605 (3.15)
Total ^a	3,293 (8.33)	87,929 (73.98)	1,372,100 (69.28)	481,919 (70.21)

*Each subgroup describes women diagnosed with a specific comorbidity anytime before or after HMB diagnosis. ^aThis is the total of underlying causes, as women may have had more than 1 underlying cause diagnosed.

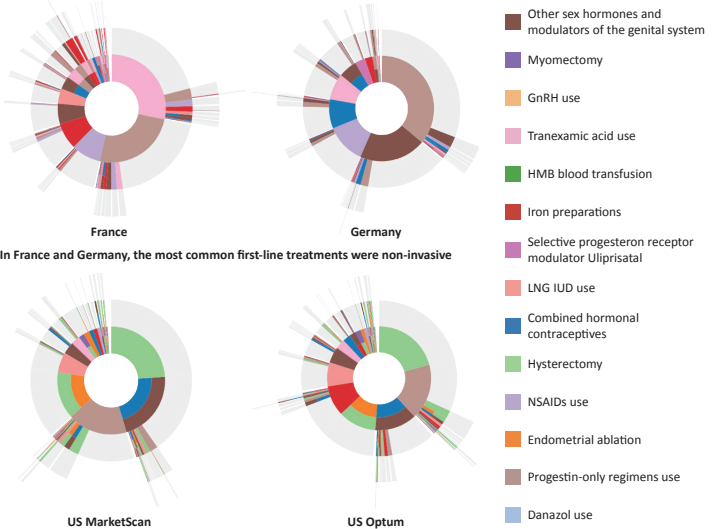
Surgery

- The proportion of women with HMB having surgery (hysterectomy or endometrial ablation) was 0.11% (France) and ranged from 11.84% (endometrial ablation, USA, MarketScan) to 25.62% (hysterectomy, USA, Optum).

n (%)	LPD France (N=39,565)	DA Germany (N=118,885)	US MarketScan (N=1,981,152)	US Optum (N=686,491)
Endometrial ablation	0	0	234,561 (11.84)	66,668 (9.71)
Hysterectomy	44 (0.11)	0	586,055 (29.58)	175,904 (25.62)
Total ^a	44 (0.11)	0	820,616 (41.42)	242,572 (35.34)

*Data are numbers of women with intervention after date of HMB diagnosis (index date). One woman can have more than one intervention.

Treatment pathways for HMB



In the US, hysterectomy was the most common first-line treatment

Sunburst plot of treatment pathways for women with HMB. The inner ring depicts the first line treatment. Subsequent outer rings depict the second and third-line treatments.

Discussion

- This study included more than 3 million women with HMB in the largest multinational cohort of women with HMB studied to date. Advanced network analytics allowed us to generate standardized, timely, real-world evidence into the incidence, proportion, and patient journeys of women with HMB from diverse populations, countries, and datasets.
- The incidence and proportion of HMB were low across the three countries compared to prior studies,^{13,14} suggesting delayed or under-diagnosis of HMB. These results agree with other published studies.⁶
- The results show country-specific differences in HMB diagnosis, management, and variation in capture by setting (primary or specialist ambulatory care only, including inpatient care). In the USA, hysterectomy was the most common first-line treatment. In France, tranexamic acid and progesterin-only regimens were most common. Progesterin-only regimens were also most common in Germany. European surgical data were heavily underestimated because primary care databases did not capture hospital interventions.

Conclusion

- HMB is widely under-diagnosed in the three countries in this study (USA, France and Germany). Country-specific differences in HMB diagnosis and management may reflect differences in health systems, including access to specialists and variation in data capture by setting.
- The next step is to include additional countries within the European Health Data & Evidence Network to provide more real-world insights into HMB and its management.

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Disclosures
Kristina Gemzell-Danielsson is an investigator in trials sponsored by Bayer, Mithra and NIH; has consulted for: Bayer, Gedeon-Richter, Exeltis, Natural Cycles, Dailly, MedinCell, Circle, Obvivo, Mithra, Vifor, has received honorariums for lectures on contraception and fibroid care from Bayer, Gedeon-Richter, Exeltis, Nordic Pharma, Natural Cycles, Mithra, Organon. Oskari Heikinheimo serves on advisory boards for Bayer AG and Gedeon-Richter, and has planned and lectured at educational events organized by these companies. Ronald Herrera, Carsten Moeller, Federica Pisa, Gabriele Schuhmann-Giampieri, and Marco Serrani are all employees of Bayer AG, Berlin, Germany. Juliane Schoendorf is employed by Bayer OY, Helsinki, Finland. Bruno Imthurn is a consultant and member of Advisory Boards for Bayer. M Inês Neves, Christian Reich, and James Yang are employees of Real World Solutions, IQVIA, USA.