Comparison of Livingstone®'s Estimates of Prevalence of Six Different Rare Blood Cancers with DARWIN EU

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BACKGROUND & AIMS

- Over 40,000 people in the UK are diagnosed annually with cancers of the blood according to Blood Cancer UK (1) and approximately 35% of submissions to the Committee for Orphan Medicinal Products (COMP) are for oncological conditions (2).
- Having accurate and trustworthy epidemiological data is essential for health service planning and disease designation.
- Livingstone® is an analytical platform that uses real-world data to generate reproducible epidemiological evidence (3).
- Using Livingstone®, we estimated the prevalence of six rare blood cancers and compared them to results for the UK from the Data Analysis and Real World Interrogation Network's (DARWIN EU) (4).

METHODS

- The Clinical Practice Research Database (CPRD) is a longitudinal, pseudonymised dataset from primary care practices in the UK that comprises two databases; CPRD GOLD and CPRD Aurum.
- Livingstone® and DARWIN EU used data from CPRD to study six rare blood cancers: acute lymphocytic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL), diffuse large B-Cell lymphoma (DLBCL), follicular lymphoma (FL) and multiple myeloma (MM).
- DARWIN EU estimated the prevalence of each cancer using CPRD GOLD whereas Livingstone® used a combination of CPRD GOLD and CPRD Aurum.
- In addition, Livingstone® generated a second analysis including CPRD practices linked to routine hospital data from the Hospital Episode Statistics (HES) database.
- The study population comprised all acceptable research quality patients. Any practices that migrated from GOLD, were removed to avoid any duplication of cases.
- Three rates were defined for each type of cancer based on different estimated durations of the cancer: lifetime prevalence, 5-year partial and 2-year partial prevalence.
- For the primary care analysis, prevalence estimates were compared for 2020. In addition, 5-year partial estimates were compared 2010-2020. For the second analysis including linked HES data, estimates were reported for 2019 due to data availability.
- Point prevalence was defined as the proportion of the population diagnosed with the condition prior to the midpoint of a given calendar year. The eligible CPRD population at each midyear formed the denominator.
- Estimates of prevalence were compared between Livingstone® and DARWIN EU using a rate ratio.
- For the yearly estimates using data from the 5-year duration, Lin's concordance correlation coefficient (CCC) was calculated between Livingstone® and DARWIN EU.
- This study received CPRD Research Data Governance approval (23_003134).

Prevalence concordance

- The concordance between annual prevalence values between DARWIN EU and primary care only ranged from –0.01 (95% CI: –0.01 – 0.00) to 0.54 (0.28 – 0.72).
- Whereas for primary care linked with HES, the concordance ranged from 0.00 (0.00–0.00) to 0.03 (0.00–0.06). (Table 2)
- All estimates from both Livingstone® analyses were greater than those reported by DARWIN EU (Figure 1).

Table 2: Condition specific concordance for 5-year prevalence from 2010–2020

Rare blood cancer	5-year Prevalence (2010–2020) Concordance (95% CI)	
	DARWIN EU vs Primary Care	DARWIN EU vs Primary Care linked with HES
Acute lymphocytic leukaemia (ALL)	0.11 (95% CI 0.02 – 0.19)	0.01 (95% CI 0.00 – 0.02)
Acute myeloid leukaemia (AML)	0.00 (95% CI 0.00 – 0.01)	0.00 (95% CI 0.00 – 0.00)
Chronic lymphocytic leukaemia (CLL)	–0.01 (95% CI –0.01 – 0.00)	0.00 (95% CI 0.00 – 0.00)
Diffuse Large B–Cell Lymphoma (DLBCL)	0.54 (95% CI 0.28 – 0.72)	0.03 (95% CI 0.00 – 0.06)
Follicular lymphoma (FL)	0.19 (95% CI 0.04 – 0.34)	0.01 (95% CI 0.00 – 0.03)
Multiple myeloma (MM)	0.03 (95% CI 0.00 – 0.06)	0.01 (95% CI 0.00 – 0.02)

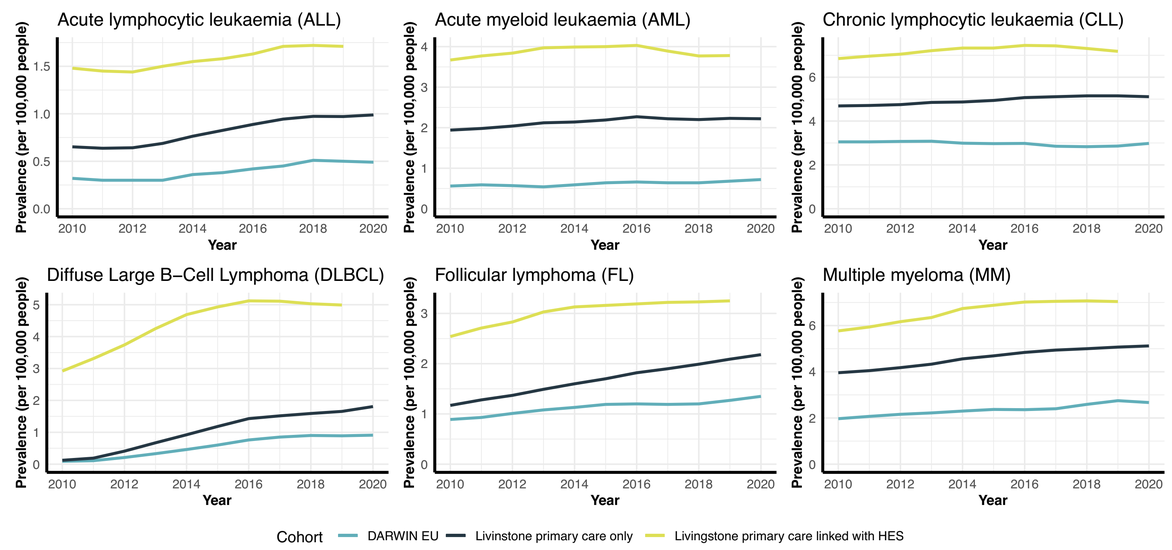

Figure 1: Estimated 5-year point prevalence of rare blood cancers from 2010–2020 for DARWIN EU and Livingstone®.

Table 1: Comparison of lifetime, 2-year partial and 5-year partial prevalence of rare blood cancers from DARWIN EU and Livingstone primary and secondary care.

Rare blood cancer	DARWIN (2020)		Livingstone – primary care only (2020)			Livingstone – primary care linked with HES (2019)		
	Count	Prevalence (95% CI)	Count	Prevalence (95% CI)	Rate ratio (95% CI)	Count	Prevalence (95% CI)	Rate ratio (95% CI)
Lifetime Prevalence (per 10,000 people)								
Acute lymphocytic leukaemia	313	1.04 (0.93-1.16)	3,582	2.13 (2.06-2.20)	2.04 (1.82-2.29)	4,165	3.06 (2.97-3.15)	2.93 (2.62-3.29)
Acute myeloid leukaemia	392	1.31 (1.18-1.44)	2,954	1.80 (1.74-1.87)	1.38 (1.24-1.53)	3,611	2.65 (2.56-2.74)	2.03 (1.83-2.25)
Chronic lymphocytic leukaemia	1,857	6.19 (5.91-6.48)	12,058	7.16 (7.03-7.29)	1.16 (1.10-1.21)	11,054	8.11 (7.96-8.26)	1.31 (1.25-1.38)
Diffuse Large B–Cell Lymphoma	407	1.36 (1.23-1.49)	3,105	1.71 (1.65-1.77)	1.26 (1.14-1.40)	6,997	5.13 (5.01-5.25)	3.78 (3.42-4.18)
Follicular lymphoma	782	2.61 (2.43-2.79)	5,186	3.08 (3.00-3.16)	1.18 (1.10-1.27)	6,356	4.66 (4.55-4.78)	1.79 (1.66-1.93)
Multiple myeloma	1,198	3.99 (3.77-4.22)	7,372	4.44 (4.34-4.54)	1.11 (1.05-1.18)	7,628	5.60 (5.48-5.73)	1.40 (1.32-1.49)
2-year partial prevalence (per 10,000 people)								
Acute lymphocytic leukaemia	63	0.21 (0.16-0.27)	809	0.48 (0.45-0.51)	2.28 (1.78-2.98)	1,355	1.00 (0.95-1.05)	4.75 (3.72-6.18)
Acute myeloid leukaemia	133	0.44 (0.37-0.52)	1,676	1.00 (0.95-1.05)	2.25 (1.90-2.70)	2,315	1.70 (1.63-1.77)	3.83 (3.23-4.58)
Chronic lymphocytic leukaemia	401	1.34 (1.21-1.47)	4,605	2.74 (2.66-2.82)	2.05 (1.85-2.27)	6,138	4.58 (4.47-4.70)	3.42 (3.10-3.80)
Diffuse Large B–Cell Lymphoma	123	0.41 (0.34-0.49)	1,424	0.85 (0.80-0.89)	2.07 (1.73-2.50)	3,063	2.25 (2.17-2.33)	5.48 (4.60-6.60)
Follicular lymphoma	190	0.63 (0.55-0.73)	1,902	1.13 (1.08-1.18)	1.78 (1.54-2.08)	2,599	1.19 (1.14-1.24)	1.88 (1.63-2.18)
Multiple myeloma	394	1.31 (1.19-1.45)	4,605	2.74 (2.66-2.82)	2.08 (1.88-2.31)	5,921	4.35 (4.24-4.46)	3.31 (2.99-3.67)
5-year partial prevalence (per 10,000 people)								
Acute lymphocytic leukaemia	148	0.49 (0.42-0.58)	1,662	0.99 (0.94-1.04)	2.00 (1.70-2.38)	2,334	1.71 (1.64-1.78)	3.46 (2.94-4.11)
Acute myeloid leukaemia	215	0.72 (0.62-0.82)	3,729	2.22 (2.15-2.29)	3.09 (2.70-3.56)	5,178	3.78 (3.68-3.88)	5.27 (4.61-6.05)
Chronic lymphocytic leukaemia	894	2.98 (2.79-3.18)	8,595	5.11 (5.00-5.22)	1.71 (1.60-1.84)	9,782	7.18 (7.04-7.32)	2.41 (2.25-2.58)
Diffuse Large B–Cell Lymphoma	272	0.91 (0.80-1.02)	3,042	1.81 (1.75-1.88)	1.99 (1.77-2.26)	6,799	4.99 (4.87-5.11)	5.50 (4.88-6.22)
Follicular lymphoma	405	1.35 (1.22-1.49)	3,671	2.18 (2.11-2.25)	1.61 (1.46-1.79)	4,433	3.25 (3.16-3.35)	2.41 (2.18-2.67)
Multiple myeloma	800	2.67 (2.49-2.86)	8,619	5.12 (5.01-5.23)	1.92 (1.79-2.07)	9,590	7.04 (6.90-7.18)	2.64 (2.46-2.84)

RESULTS

Lifetime Prevalence

- All lifetime prevalence estimates by Livingstone® were significantly higher than those produced by DARWIN EU in both primary care only and primary care linked with HES analyses (all p<0.0001; Table 1).
- For the comparison of primary care sources, estimates for ALL showed the highest prevalence rate ratio of 2.04 (95% CI: 1.82–2.29).
- The largest difference in primary care linked with HES was for DLBCL with a rate ratio of 3.78 (3.42–4.18).

Two-year partial prevalence

- All two-year values in primary care and primary care linked with HES were significantly greater than that of DARWIN EU (all p<0.0001; Table 1).
- The greatest difference in prevalence was for ALL with a rate ratio of 2.28 cases per 10,000 people (1.78–2.98) between DARWIN EU and Livingstone® primary care.
- For Livingstone® primary care linked with HES, DLBCL showed the highest rate ratio between DARWIN EU and Livingstone®, with a rate ratio of 5.48 cases per 10,000 people (4.60–6.60).

Five-year partial prevalence

- All five-year rate ratios from the comparison between Livingstone® and DARWIN EU estimates were significantly greater (all p <0.0001; Table 1).
- The largest increase between prevalence rates in DARWIN EU versus Livingstone® primary care only was for AML with a rate ratio of 3.09 cases per 10,000 people (2.70–3.56).
- For the comparison between DARWIN EU and Livingstone® primary care linked with HES, DLBCL was found to have the highest rate ratio of 5.50 (4.88–6.22).

This study is based in part on data from the Clinical Practice Research Datalink obtained under licence from the UK Medicines and Healthcare products Regulatory Agency. The data is provided by patients and collected by the NHS as part of their care and support. HES data (Copyright © 2023), re-used with the permission of The Health & Social Care Information Centre. All rights reserved. All authors are employed by Human Data Sciences. Human Data Sciences funded this study and developed the Livingstone® platform.

CONCLUSION

- Estimates of lifetime prevalence, 2-year partial prevalence, and 5-year partial prevalence from Livingstone® were consistently higher than those reported for the UK by the DARWIN EU study.
- All rate ratios were statistically significant, implying higher case ascertainment in Livingstone® for both primary care and when linked with HES.
- Differences in the comparison of data sources solely from primary care may have been due to population differences between practices in Aurum and GOLD.
- Our secondary analyses showed greater differences when linked records from hospital sources were included in the analysis, emphasising the importance of using linked secondary care data when estimating the epidemiology of diseases and conditions that are likely to be diagnosed and/or managed in hospital.
- As part of the orphan designation, the accepted prevalence threshold is 5 cases per 10,000 people. In this study, the higher lifetime prevalence observed in Livingstone® would recatergorise two cancers (DLBCL and MM) away from orphan status.
- The difference in findings using differing data source highlights the need for analytical standardisation, and an imperative to use all available linked data sources to avoid potential biases in case ascertainment.

REFERENCES

1. Blood Cancer UK. Understanding blood cancer. Available from: https://bloodcancer.org.uk/understanding–blood–cancer/
2. Polsinelli B, Tsigkos S, Naumann–Winter F, Mariz S, Sepodes B. Evolving prevalence of haematological malignancies in orphan designation procedures in the European Union. Orphanet Journal of Rare Diseases 2017;12:17. doi:10.1186/s13023–017–0567–7
3. Heywood BR, Morgan CL, Berni TR, Summers DR, Jones BI, et al. (2023) Real–world evidence from the first online healthcare analytics platform—Livingstone. Validation of its descriptive epidemiology module. PLOS Digital Health 2(7): e0000310. https://doi.org/10.1371/journal.pdig.0000310
4. Burn E, Català M. Prevalence of rare blood cancers in Europe. DARWIN EU. Available from: https://www.encepp.eu/encepp/openAttachment/studyResult/104210

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Presented at International Society for Pharmacoeconomics and Outcomes Research (ISPOR)-EU 2023, Copenhagen, Denmark