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Trends in incidence, prevalence, and survival of primary liver cancer in the United Kingdom (2000-2021)

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JOURNAL ARTICLE

Trends in incidence, prevalence, and survival of primary liver cancer in the United Kingdom (2000–2021)

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Author Notes

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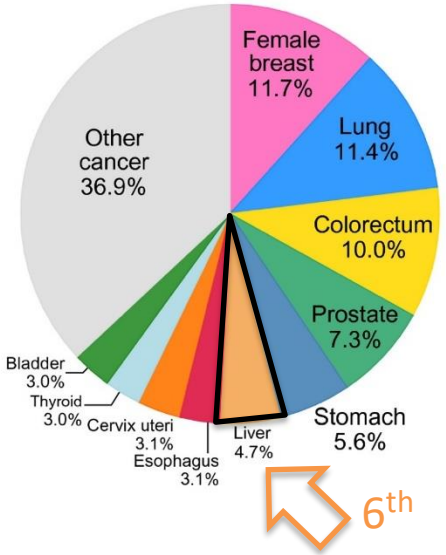
Background

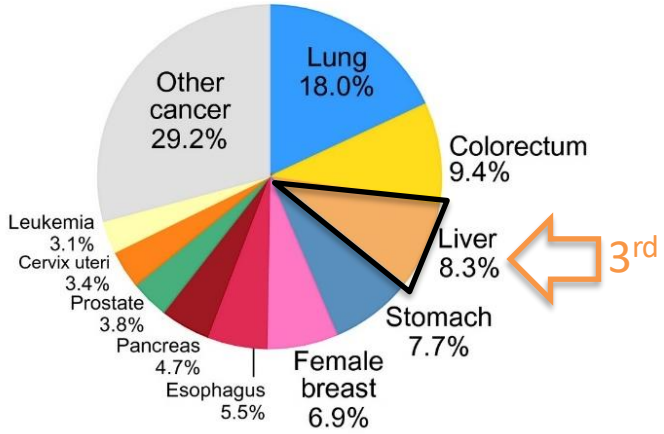
Primary liver cancer (PLC) remains a global health challenge

Hepatocellular carcinoma (HCC) accounts for ~90% of PLC cases

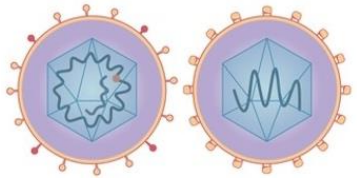
Incidence



Mortality



Main risk factors are shifting



HBV & HCV

Alcohol-related liver disease

Metabolic dysfunction-associated steatotic liver disease (MASLD)

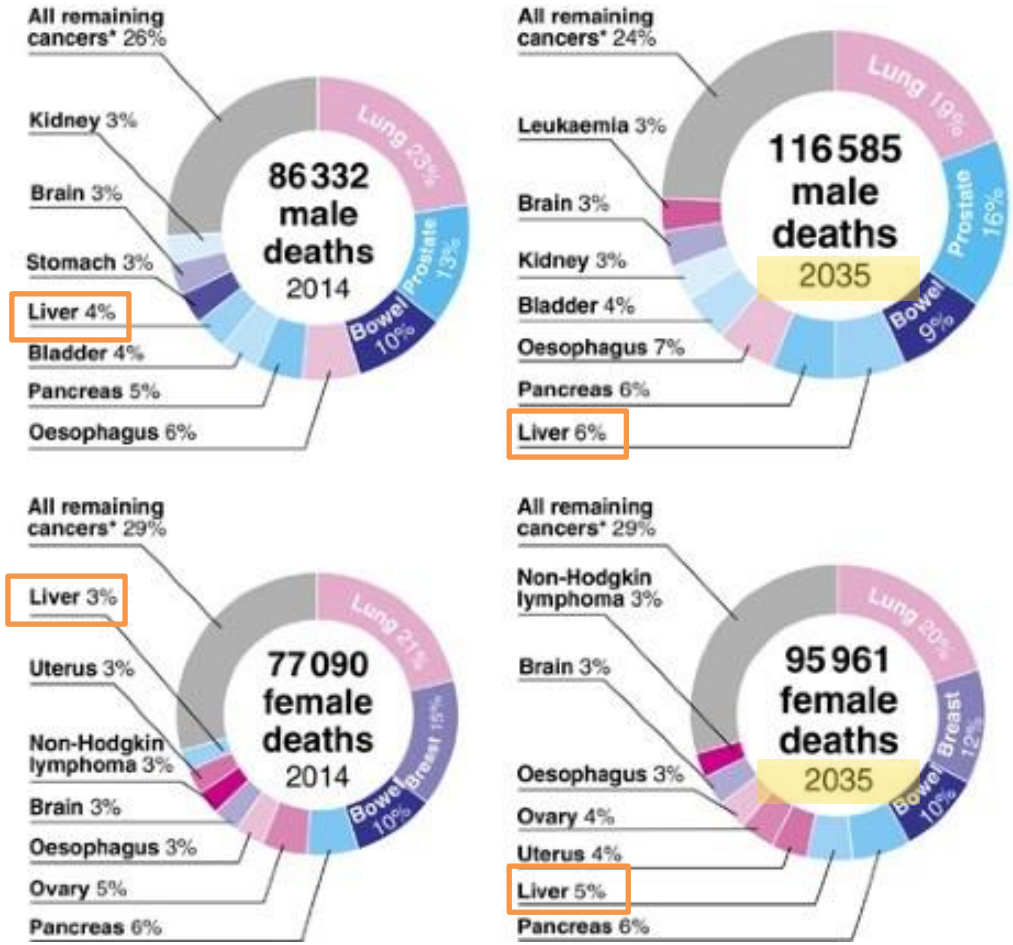
Sung H et al. GLOBOCAN. CA Cancer J Clin. 2021 // Llovet JM et al. Nat Rev Dis Primers. 2021
Smittenaar CR et al. Br J Cancer. 2016 // Lepage C et al. Eur J Cancer. 2015 // Kim D et al. Gastroenterology. 2016

Background

PLC is projected to accelearte quickly in the UK

PLC incidence age standardised rates (ASRs) per 100 000 15–90+ year olds, for 1993 (observed), 2014 (observed) and 2035 (projected)

	1993 ASR	2014 ASR	2035 ASR	ASR % change 2014–2035
Males	6.36	16.21	23.23	43.27
Females	3.02	6.87	8.32	21.02



Prognosis remains poor:

1-year survival: **~40%** 5-year survival: **~10%**

Smittenaar CR et al. Br J Cancer. 2016 // Lepage C et al. Eur J Cancer. 2015
Cancer Research UK. Liver Cancer Statistics

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Aims of the study

To describe **temporal trends (2000–2021)** of PLC in the **UK** in terms of:

- → Incidence
- → Prevalence
- → Survival

To analyze differences by:

Age groups

Sex

Calendar period

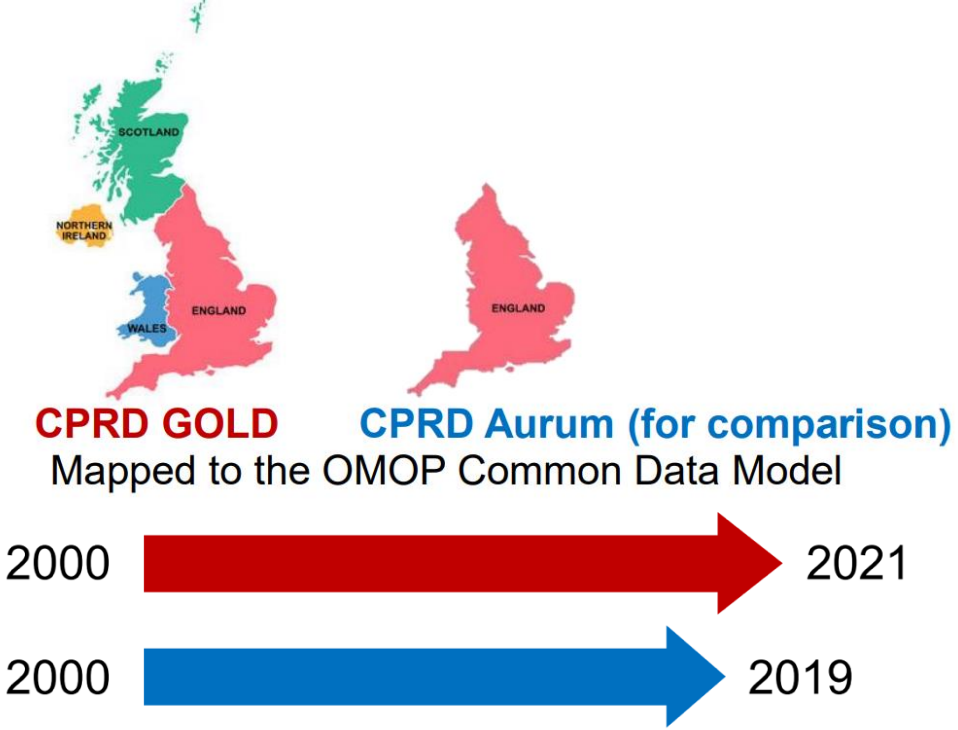
To provide **real-world evidence** using primary care databases

To inform **public health strategies and clinical decision-making**

Methodology

Population-based cohort study

Large, representative primary care databases. Source:



Aged 18+
At least 1 year of prior medical history
Primary liver cancer identified using **SNOMED CT codes**
Follow-up until exit from database, death, end of study
For survival: patients whose death and cancer diagnosis occurred on the same date were excluded

CPRD: Clinical Practice Research Datalink
OMOP: Observational Medical Outcomes Partnership
SNOMED-CT: Systematized Nomenclature of Medicine-Clinical Terms

Methodology

Main outcomes:

- **Incidence rates (IR)**: crude and age-standardized, per 100,000 person-years. Annual and overall.
- **Period prevalence (PP)**: crude annual period prevalence
- **Survival**: median survival and survival at 1-year, 5-year and 10-year

Stratified by:

Database

Age groups

Sex

Calendar period

OMOP-based computable phenotypes and analytical code are available on Github to enable reproducibility: https://github.com/oxfordpharmacoepi/EHDENCancerIncidencePrevalence

Analysis Methods:

- Crude and age-standardized incidence rates
- Kaplan–Meier survival analysis
- Median survival estimation
- Sensitivity analysis (including cholangiocarcinoma)
- Software: R

Results CPRD GOLD

11,388,117 eligible patients with at least 1 year of prior history

3999 patients with PLC

Results

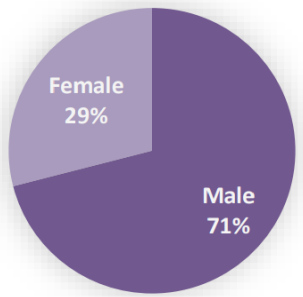
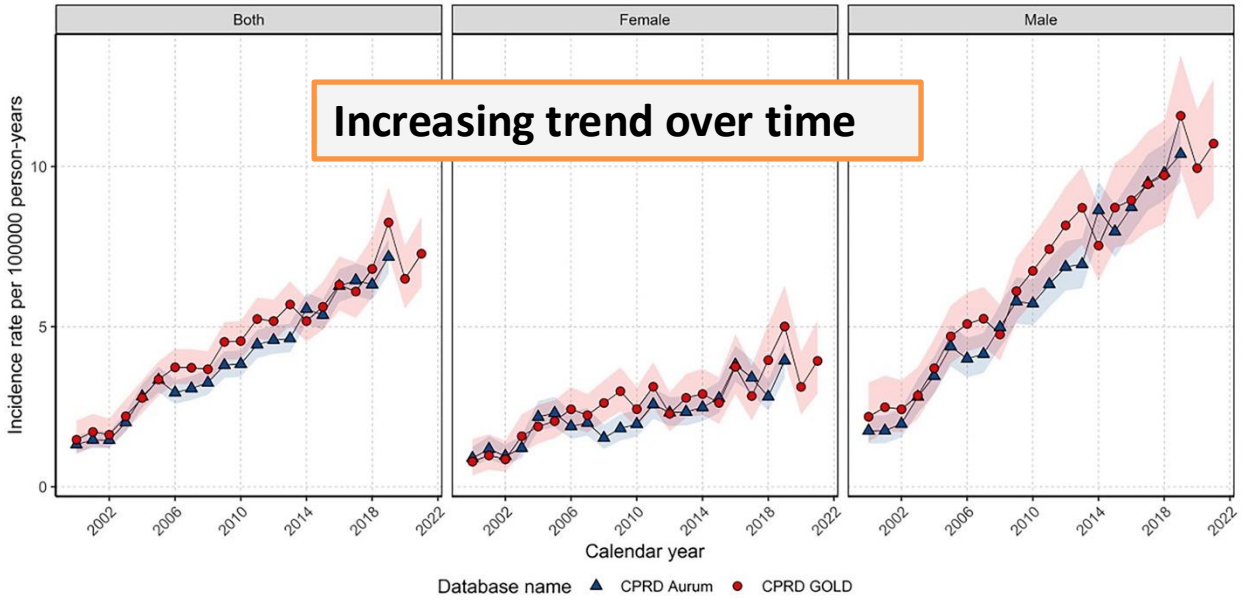


Table 1. Baseline characteristics of primary liver cancer patients at diagnosis stratified by sex from CPRD GOLD

Sex	Male	Female
Number of patients	2848	1151
Age in years, median (IQR)	70 (62–77)	73 (64–80)
Age groups in years, *N* (%)		
18–29	11 (0.4%)	<5
30–39	18 (0.6%)	9 (0.8%)
40–49	97 (3.4%)	41 (3.6%)
50–59	411 (14.4%)	149 (12.9%)
60–69	811 (28.5%)	260 (22.6%)
70–79	952 (33.4%)	385 (33.4%)
80–89	512 (18.0%)	271 (23.5%)
90+	36 (1.3%)	33 (2.9%)
Prior history in days, median (IQR)	3977 (2189–5642)	3943 (2110–5642)
Comorbid conditions (any time prior)		
Chronic liver disease, *N* (%)	663 (23.3%)	176 (15.3%)
Recorded risk factors for PLC, *N* (%)		
Alcoholic liver disease (ALD)	385 (13.5%)	52 (4.5%)
Hepatitis C	91 (3.2%)	25 (2.2%)
Hepatitis B	20 (0.7%)	<5
Non-alcoholic fatty liver disease (NAFLD)	80 (2.8%)	26 (2.3%)
Hemochromatosis	90 (3.2%)	9 (0.8%)
Autoimmune hepatitis	14 (0.5%)	37 (3.2%)
Other recorded risk factors, *N* (%)		
Hypertensive disorder	850 (29.8%)	349 (30.3%)
Diabetes	851 (29.9%)	215 (18.7%)
Hyperlipidaemia	209 (7.3%)	99 (8.6%)
Obesity	313 (11.0%)	102 (8.9%)
Smoking status (any time 5 years prior), *N* (%)		
Current/former smoker	806 (28.3%)	270 (23.0%)
Nonsmoker	954 (33.5%)	559 (48.6%)
Missing/no records	1088 (38.2%)	322 (28.0%)

Results

Figure 1. Crude annual incidence rates for PLC from 2000 to 2021 stratified by database and **sex**.



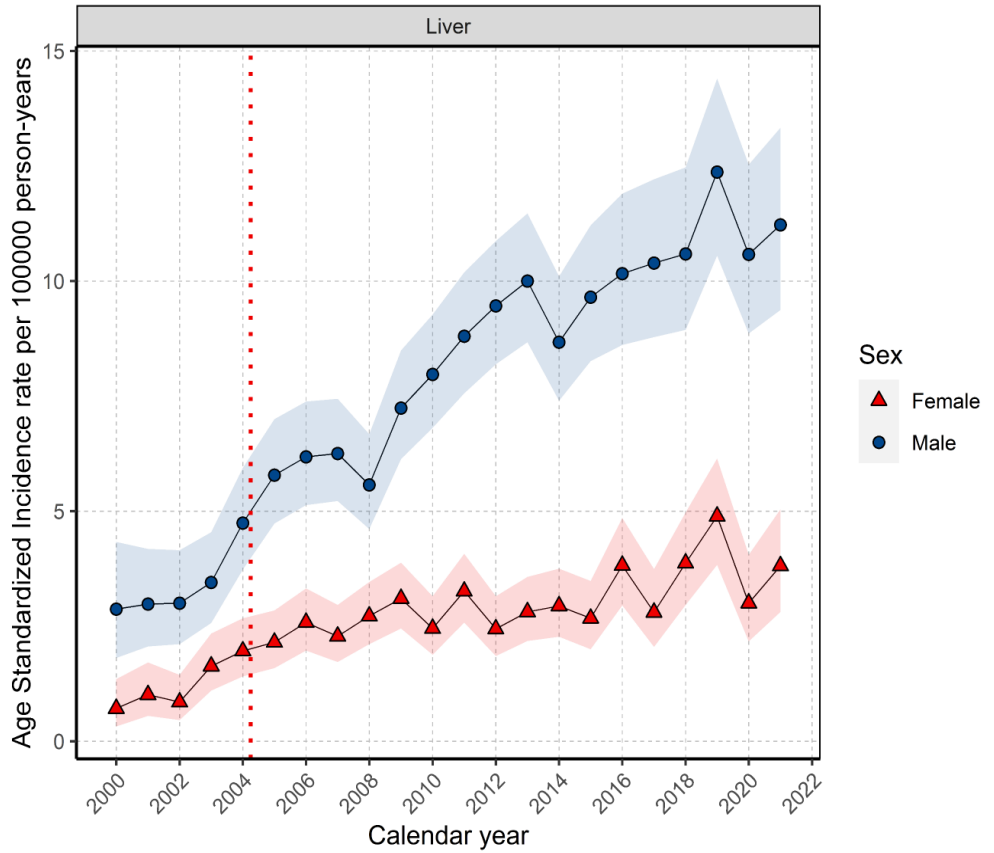
Increasing trend over time

Overall PLC IR: 4.56 (95% CI 4.42–4.70) per 100,000 person-years

2.58 (95% CI 2.44– 2.74) per 100,000 person-years

6.6 (95% CI 6.36–6.85) per 100,000 person-years

S4: Age standardised Incidence by the European Standard Population for incidence rates for CPRD GOLD for PLC stratified by **sex** (red dotted line denotes introduction of Quality and Outcomes Framework (QOF) in 2004)



Full results are available in a user-friendly interactive web application: https://dpa-pde-oxford.shinyapps.io/LiverCancerIncPrevSurvShiny/

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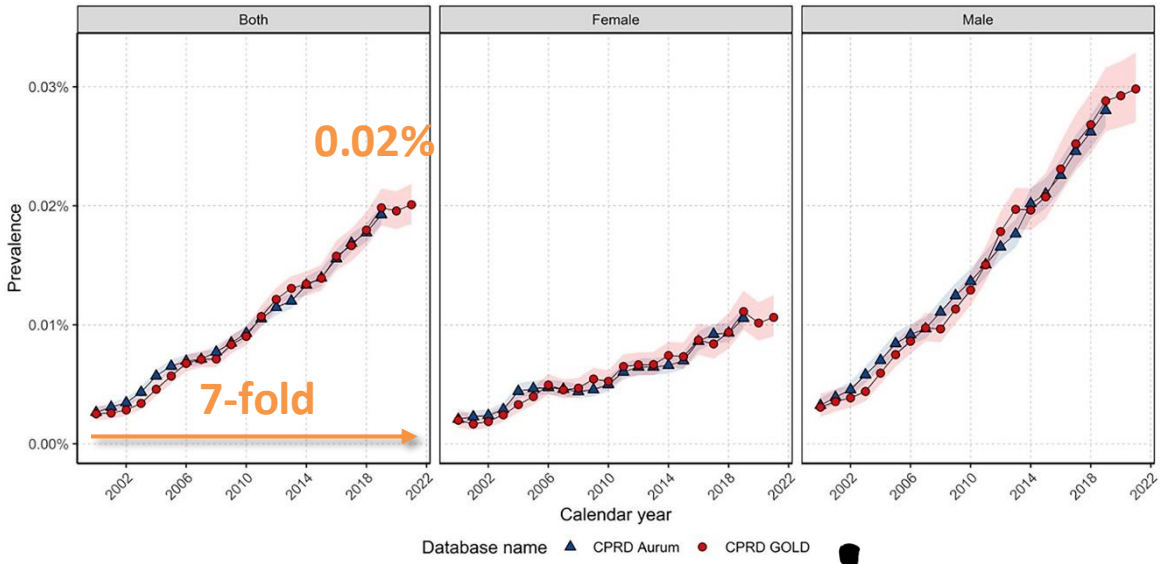
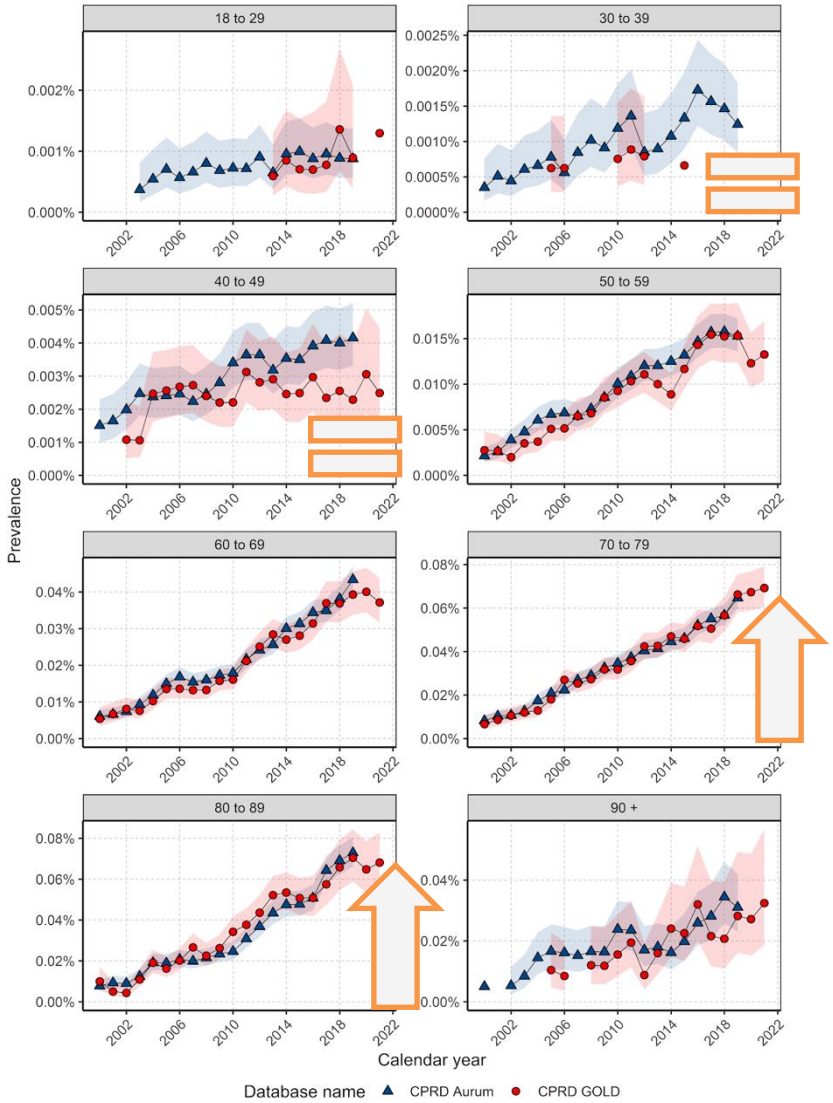
Results

Figure 2. Crude annual prevalence from 2000 to 2021 for whole population and stratified by **sex**.



2.7-fold higher PP in males than females

S10: **Annualised prevalence** for PLC from 2000 to 2021 stratified by database and **age group**.



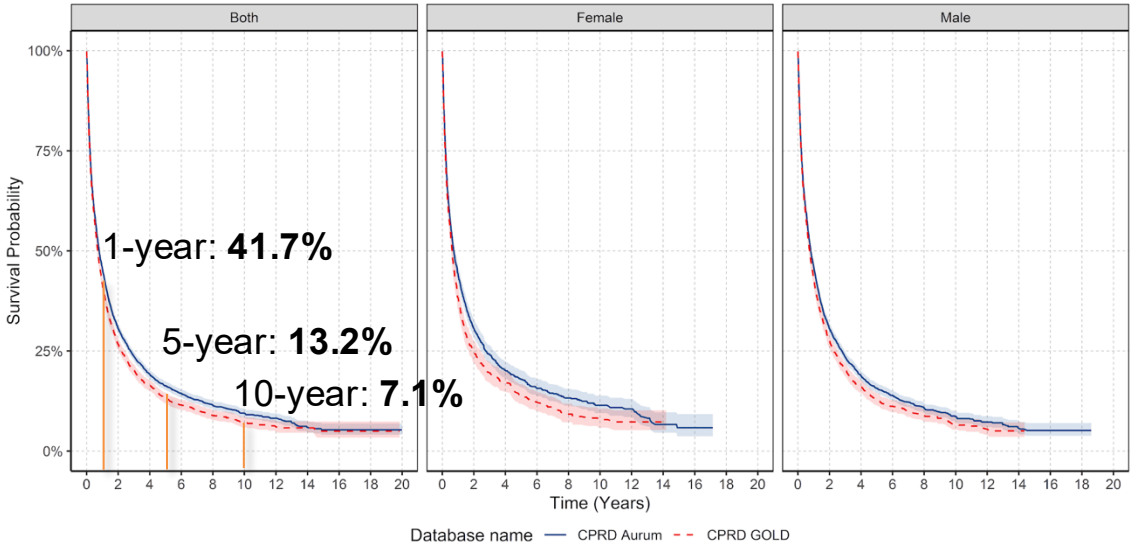
Results

Table 2. Survival rates of PLC from 2000 to 2019 for CPRD Aurum and 2000–2021 for GOLD stratified by database and age group

Age group	Survival (%)		
	One-year	Five-year	10-year
Aurum			
18–29	62.9 (47.6–83.0)	46 (30.3–69.9)	–
30–39	65.7 (55.7–77.3)	51.9 (41–65.7)	46.7 (34.1-63.9)
40–49	60.3 (54.9–66.3)	35.8 (30–42.7)	25.5 (19.5–33.3)
50–59	53.3 (50.3–56.5)	22.4 (19.6–25.7)	17.1 (14.1–20.7)
60–69	50.7 (48.4–53.1)	19.1 (17.0–21.4)	10.3 (8.3–12.8)
70–79	42.4 (40.3–44.5)	12.4 (10.8–14.2)	5.3 (3.9–7.2)
80–89	33.9 (31.2–36.8)	6.9 (5.21–9.11)	1.9 (0.7–5.2)
90+	21.6 (15.6–30)	1.6 (0.26–10.2)	–
GOLD			
18–29	31.8 (14.2–70.8)	–	–
30–39	62.5 (45.7–85.5)	44.2 (26.7–73.3)	–
40–49	54.9 (47.1–64.1)	29.1 (21.5–39.3)	26.5 (19.1–36.8)
50–59	48.4 (44.3–52.9)	20.3 (16.8–24.7)	12.5 (9.0–17.4)
60–69	47.8 (44.9–51.0)	16.0 (13.6–18.9)	9.2 (6.9–12.4)
70–79	37.7 (35.1–40.5)	10.1 (8.3–12.3)	3.6 (2.3–5.7)
80–89	28.1 (25.0–31.6)	5.0 (3.3–7.6)	0.7 (0.1–4.3)
90+	30.3 (20.6–44.6)	3.1 (0.5–19.6)	–

Median survival was 0.70 (95% CI 0.65–0.74) years

S12: Kaplan-Meier survival curve of PLC stratified by **database and sex**

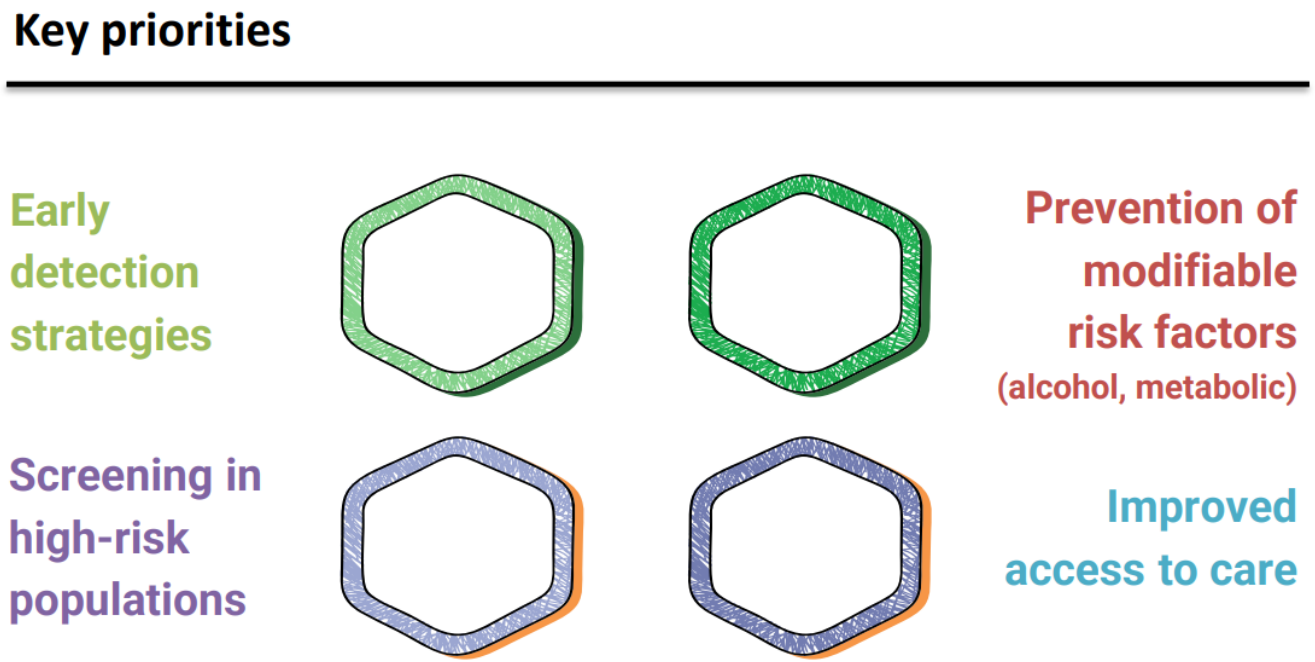


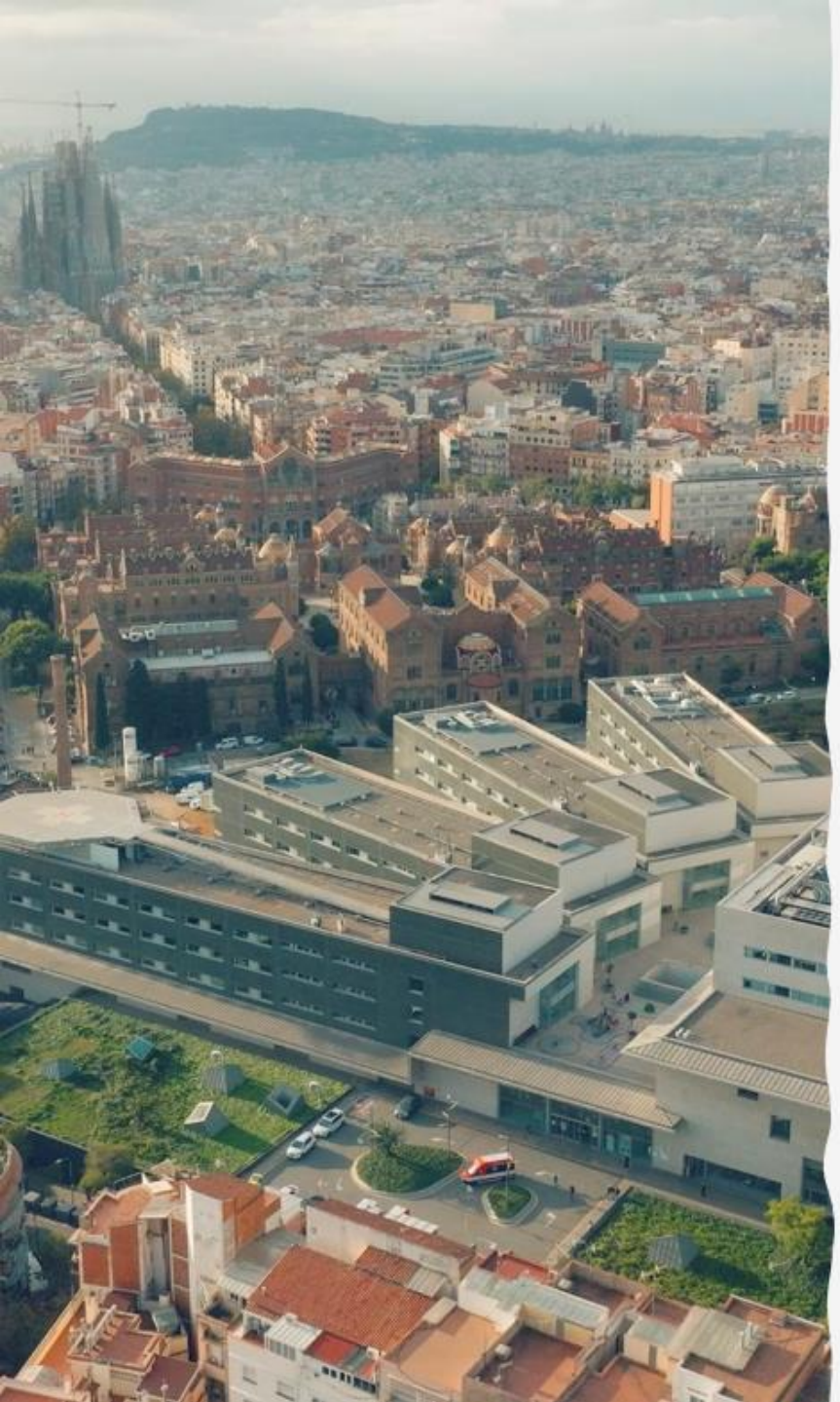
S18: Survival (%) after one and five years after PLC diagnosis stratified by **sex** and **calendar year** for CPRD GOLD.

Calendar Year	Time (years)	% Survival (95% CI)	Sex
2000 to 2004	1	35.57 (30.47 - 41.51)	Both
2005 to 2009		35.34 (32.32 - 38.65)	
2010 to 2014		43.26 (40.53 - 46.17)	
2015 to 2019		46.74 (43.75 - 49.92)	
2020 to 2021		42.66 (36.85 - 49.38)	
2000 to 2004		40.57 (31.69 - 51.93)	Female
2005 to 2009		31.81 (26.78 - 37.78)	
2010 to 2014		43.34 (38.19 - 49.18)	
2015 to 2019		39.65 (34.19 - 45.98)	
2020 to 2021		34.57 (24.26 - 49.25)	
2000 to 2004		33.18 (27.24 - 40.41)	Male
2005 to 2009		36.99 (33.32 - 41.05)	
2010 to 2014		43.23 (40.07 - 46.64)	
2015 to 2019		49.33 (45.85 - 53.08)	
2020 to 2021		45.52 (38.82 - 53.38)	

Conclusions

- PLC burden in the UK has **substantially increased** over the past two decades
- Shift from virus-related to **non-viral liver disease**
- **Incidence and prevalence rising** across all groups
- **Survival remains poor** despite slight improvements (50% of patients with PLC are not alive after 1 year)





Thank you for your attention

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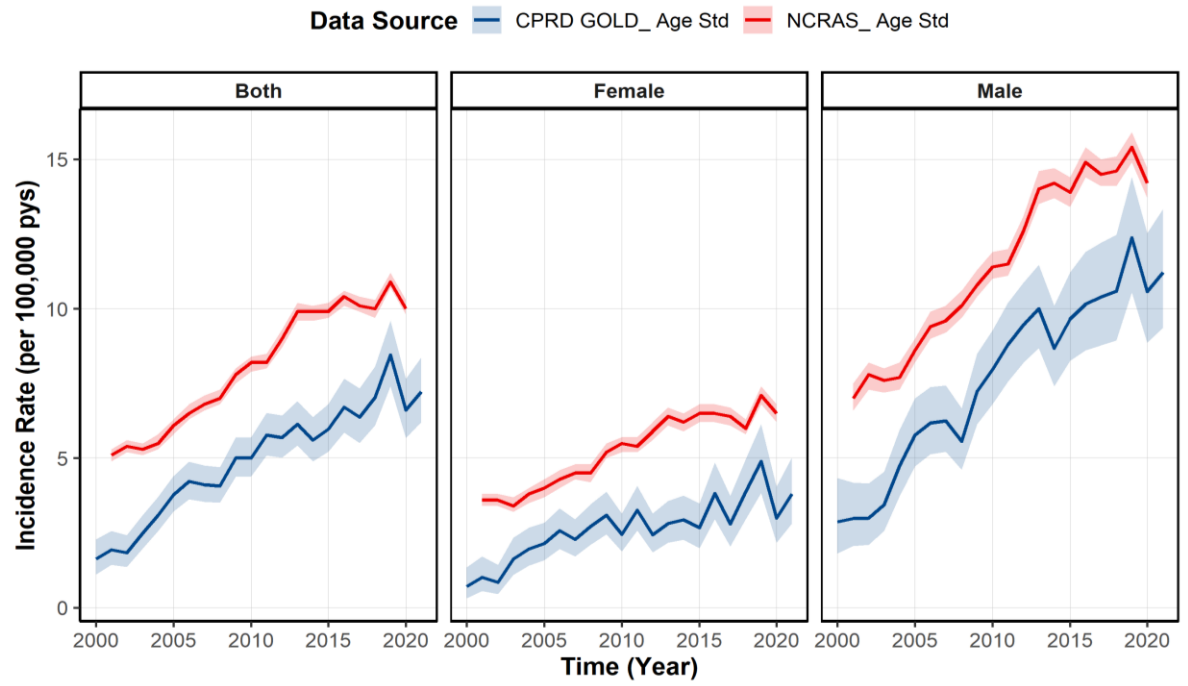
S6: Comparison of **age standardised incidence rates** (European Standard Population 2013) for CPRD GOLD and National Cancer Registration and Analysis Service (NCRAS) for PLC



Comparison with national cancer registry age-standardized IRs from England showed similar trends but lower age-standardized rates in this work (more population included in the national cancer registry)

IRs are presented as crude rates to reflect the actual burden of disease.
However age-standardized rates were calculated to avoid the factor that population is aging.