

# GLOBAL INCIDENCE, PREVALENCE, AND SURVIVAL IN RELAPSED/REFRACTORY (R/R) ADULT ACUTE LYMPHOBLASTIC LEUKEMIA (aALL): A SYSTEMATIC LITERATURE REVIEW AND DESK RESEARCH

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## BACKGROUND

- Acute lymphoblastic leukemia (ALL) is a heterogeneous group of lymphoid disorders resulting from the clonal proliferation of immature lymphocytes of B-cell or T-cell lineage in the blood, bone marrow, and other organs.<sup>1</sup>
- Roughly half of the adult patients relapse after receiving first-line treatment, and effective treatment options are needed for relapsed/refractory (R/R) B-precursor adult ALL (aALL).<sup>2</sup>
- Detailed epidemiologic data can help stakeholders understand variability in incidence, prevalence, and severity of (R/R) B-precursor ALL across countries.

## RESEARCH OBJECTIVES

- This study summarizes the most recent data on the epidemiology of patients with B-cell R/R aALL globally, with a particular focus on the US, Canada, and EUS.

## METHODS

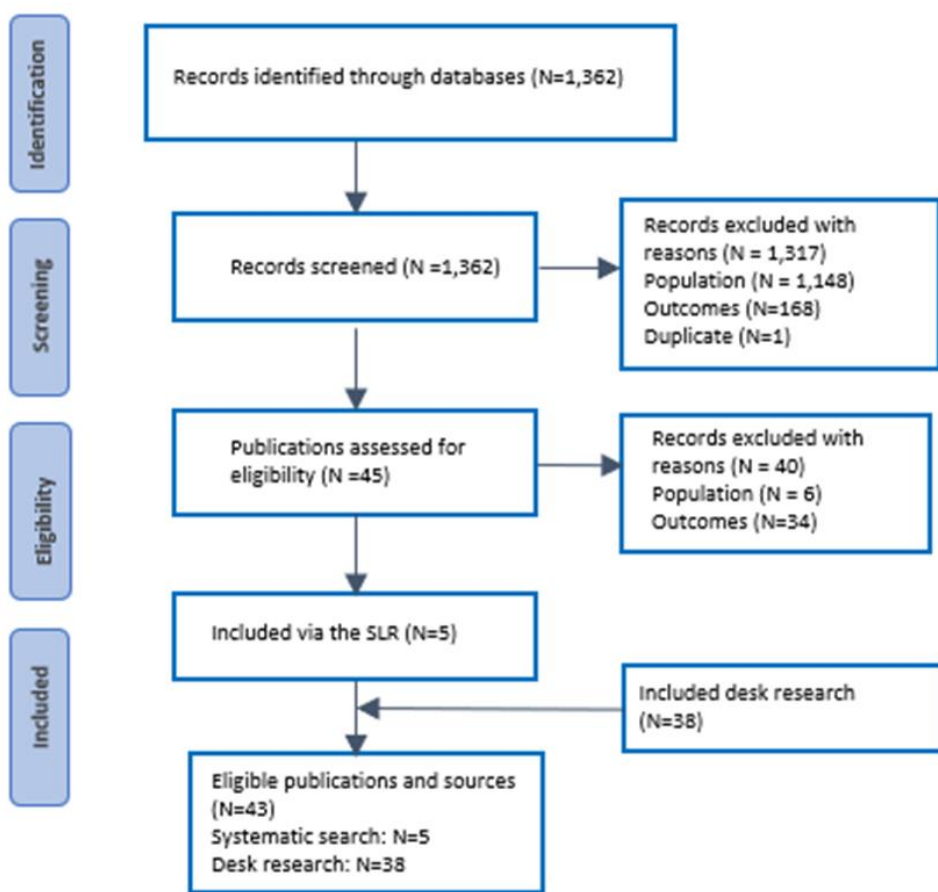
- A structured literature review and desk research were carried out to identify recent country-specific epidemiological evidence for R/R B-precursor aALL. Inclusion and exclusion criteria were:
  - Reporting the outcomes of incidence, prevalence, morbidity, or mortality for R/R B-precursor aALL
  - Trials, databases analysis, cohort studies, cross-sectional studies, case-control studies
  - Peer-reviewed articles, evidence from credible websites
- ProQuest, Embase and Medline searches were run simultaneously using combinations of R/R B-precursor ALL and epidemiologic terms, and desk research was conducted using the Google search engine and Health technology assessment (HTA) websites.

## RESULTS

### SEARCH RESULTS

- The SLR and desk research identified 43 eligible publications and sources for inclusion (Figure 1)
- Data were identified for Australia, Canada, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Spain, Sweden, United Kingdom (UK) and the United States (US) (Table 1)

FIGURE 1. PRISMA FLOW



### INCIDENCE

- Incidence rates for R/R B-precursor ALL were only identified for the US, and EUS (France, Germany, Italy, Spain, and the UK).
- Where specific incidence data for R/R ALL B-precursor ALL was not available, it was calculated by dividing the major types of ALL according to immunophenotype and Philadelphia chromosome status. Literature-based approximations of these disease characteristics were applied to published incidence estimates in an approach devised by Katz et al, 2015<sup>4</sup> (Figure 2).
- Published incidence rates for R/R B-precursor ALL ranged from 0.12 to 0.25 per 100,000 in the UK<sup>3,4</sup>, and for all other countries incidence rates ranged from 0.12-0.20.<sup>4</sup> (Table 1).

## CONCLUSIONS

- Although limited data were found, incidence for R/R aALL seems comparable across countries.
- Prevalence and survival of R/R aALL vary substantially between countries. The drivers behind differences in observed prevalence between countries need to be further examined.
- Current treatments are associated with poor survival and better treatment options are needed to improve outcomes.

## REFERENCES

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- Outcome of 609 adults after relapse of acute lymphoblastic leukemia (ALL); an MRC UKALL12/ECOG 2993 study by Fielding et al. *Blood*. 2007 Feb 1;109(3):944-50. doi: 10.1182/blood-2006-05-018192
- Outcome of relapsed adult lymphoblastic leukemia depends on response to salvage chemotherapy, prognostic factors, and performance of stem cell transplantation by Gökbuğut et al. *Blood*. 2012 Sep 6;120(10):2032-41. doi: 10.1182/blood-2011-12-399287.

## RESULTS Cont.

### PREVALENCE

- Recent studies (2016-2017) that reported prevalence rates for ALL regardless of treatment line or age were identified for all countries. However, there were no published estimates for the R/R B-precursor ALL.
- The overall prevalence rate for ALL ranged from 5.6 in the US males and females to 31 per 100,000 in Finnish males.<sup>5,6</sup> Prevalence varied substantially across countries. Germany, the UK and the US had relatively low reported prevalence of ALL.
- Most data were retrieved from the Global Health Data Exchange (GHDx)<sup>5</sup> database. From these data, it is unclear why prevalence varies substantially across countries. Potentially, varying prevalence might be attributable to differences in treatment landscape and healthcare system within these countries.

### MORTALITY

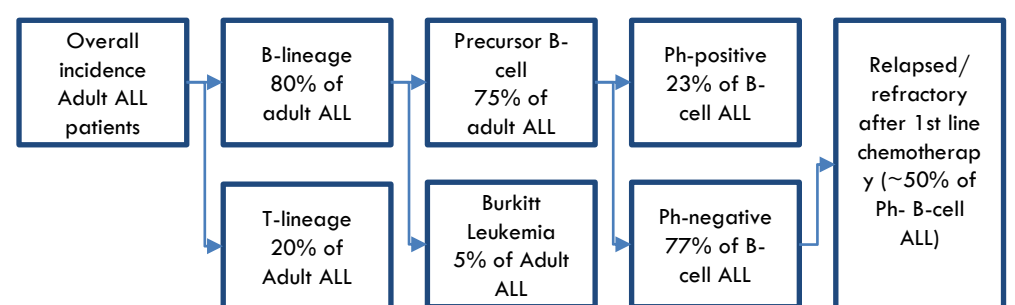
- Recent studies that reported mortality rates for ALL regardless of treatment line or age were identified. However, no studies reported mortality for R/R B-precursor ALL.
- Overall mortality rates for ALL patients ranged from 0.2 in female patients in Sweden<sup>5</sup> to 0.85 per 100,000 in males and females in Australia.<sup>5</sup>
- Country-specific survival was identified for adult ALL patients after first relapse or receipt of first salvage therapy: US 1-yr survival was 13-19%<sup>7</sup>; UK 5-yr. and 1-yr. survival were 8% and 22%<sup>8</sup>; and Germany 3-yr survival was 24%<sup>9</sup>.
- Most data were retrieved from the GHDx database.<sup>5</sup>

TABLE 1: COUNTRY-SPECIFIC INCIDENCE, PREVALENCE, MORTALITY

Country	Incidence rate ranges	Prevalence rate	Mortality rate	Survival rate R/R ALL	Overall Incidence of aALL patients	R/R after 1 <sup>st</sup> line chemo
Australia	ALL: 0.93-1.6	ALL: 20.2	ALL: 0.4-0.85	—	140-150**	40-43**
Canada	ALL: 0.46-1.4	ALL: 15.7	ALL: 0.39	—	173-526***	50-152***
Denmark	ALL: 0.57-1.7	ALL: 22-27 (male)	ALL: 0.2-0.53	—	25-30**	7-9**
Finland	ALL: 0.72-2.3	ALL: 21.3-31 (male)	ALL: 0.3-0.58	—	40-127***	11-37***
France	R/R ALL: 0.17 ALL: 0.47-0.77	ALL: 15.6	ALL: 0.4	—	410-450**	120-130*
Germany	R/R ALL: 0.19 ALL: 0.54-0.75	ALL: 9.1	ALL: 0.46	3-yr survival: 24%	550-600*	160-175*
Italy	R/R ALL: 0.20 ALL: 0.73-0.74	ALL: 23.36	ALL: 0.61	—	410-460*	120-135*
Netherlands	ALL: 0.26-0.45	ALL: 15.98	ALL: 0.40	—	45-78***	13-22***
Norway	ALL: 0.45-2.0	ALL: 12.71-27 (male)	ALL: 0.39	—	24-105***	7-30***
Spain	R/R ALL: 0.17 ALL: 0.54-0.71	ALL: 22.63	ALL: 0.45	—	270-300*	80-85*
Sweden	ALL: 0.46-1.8	ALL: 14.32-24	ALL: 0.2 (female) - 0.38	—	47-184***	14-53***
United Kingdom	R/R ALL: 0.12-0.25 ALL: 0.49-0.5	ALL: 5.6-17.04	ALL: 0.4-0.41	1-year survival: 22%, 5-yr survival: 8%	280-310*	80-90*
United States	R/R ALL: 0.19 ALL: 0.55-1.9	ALL: 6.3	ALL: 0.43-0.53	1-yr survival 13-19%	2150-2370*	620-685*

Rates per 100,000. \* Calculated in Katz 2015,<sup>4</sup> \*\* Overall incidence of adult ALL from Katz 2015 and calculated, \*\*\* Calculated and does not differentiate between adults and children

FIGURE 2. SUBTYPES OF ALL AND THEIR DISTRIBUTION AMONG ADULT PATIENTS



## LIMITATIONS

- Given that ALL is rare, incidence estimates from the regions require cautious interpretation as they are based on small numbers of patients and are susceptible to random variation.
- The lack of data for R/R ALL lead to reliance on calculations based from overall incidence rates and literature-based approximations of subtypes of ALL. Where possible age-standardised incidence rates were used, and literature-based approximations were for the adult population. Hence, these calculations should be interpreted with caution.