

D:A:D Differences in Virological and Immunological Risk Factors for Non-Hodgkin and Hodgkin Lymphoma: The D:A:D Study

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BACKGROUND

- Non-Hodgkin (NHL) and Hodgkin lymphomas (HL) are common in HIV-positive (HIV +) people.
- Since the introduction of combination antiretroviral treatment (cART), a decline in NHL but not HL incidence has been observed.
- There is little evidence for whether factors affecting risk of NHL and HL are similar in HIV positive (HIV+) persons.

METHODS

- D:A:D participants were followed from the latest of study entry, first CD4 cell count, or 1/1/2004 until first NHL or HL diagnosis, last visit plus 6 months, death, or 1/2/2015.
- Crude incidence rates (IR) of NHL and HL were calculated.
- Adjusted incidence rate ratios (aIRR) were calculated using Poisson regression with generalised estimating equations. Both current and historical measures of HIV-viral load (VL) (current level, area under the curve [AUC] during follow-up) and CD4 (current and nadir level, AUC) were considered. Other risk factors investigated are listed in the footnote of **figure 3**.

RESULTS

41,420 persons were included contributing 335,644 person years of follow up (PYFU) (median of 9, interquartile range [IQR] 6,11 years per person).

Baseline characteristics

- Baseline characteristics are shown in **table 1**. At baseline, the median age was 40 years, 73% of the population was male and 50% were of white ethnicity. 44% were infected through MSM transmission. 51% were on cART, 62% had a CD4>350 cells/mm³ and 51% had a HIV-VL < 500 copies/mL.

Incidence of NHL:

- Overall,149 persons developed HL (incidence rate (IR) 0.44/1000 PYFU 5%CI:0.38,0.52) and 392 persons developed NHL (IR 1.17/1000 PYFU, 95%CI:1.06,1.29) (**figure 1**). In unadjusted analyses, HL incidence was stable (change/year: -3% (95%CI:-8%,3%), where as NHL declined by 13% (95%CI:16%,10%)/year from 2004-2015 (**figure 1**).

Adjusted Incidence rate ratios

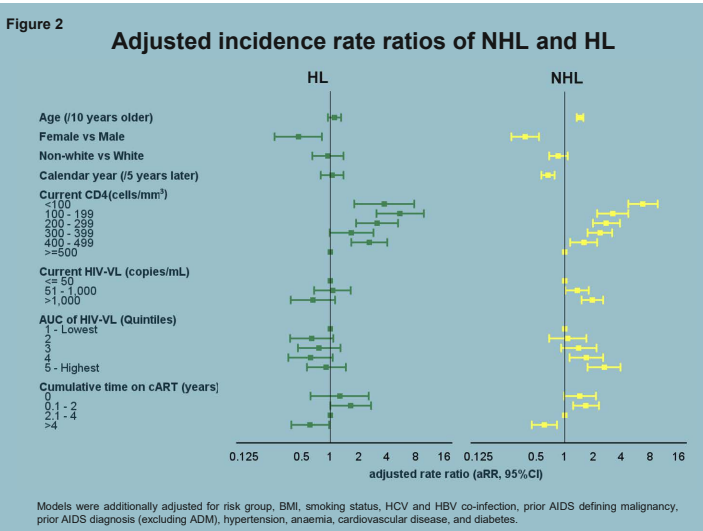
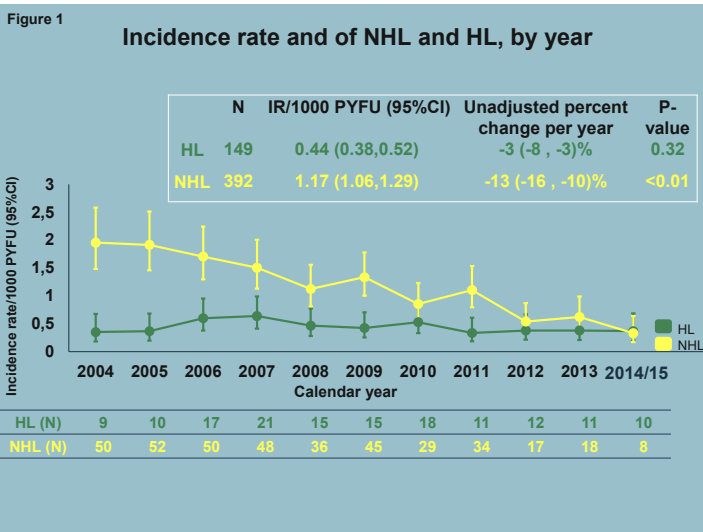
- After adjustment, the IR of NHL and HL was over 50% lower in females relative to males (**figure 2**).
- Older persons had higher IR of NHL only.
- Lower current-CD4 was the strongest predictor of higher NHL IR, however higher current VL and AUC of HIV-VL were also associated. Nadir and CD4 AUC were not associated with NHL after adjustment for current CD4 (data not shown, both P>0.05).
- HL IR was also associated with lower current CD4, but not with other markers of VL or CD4 in addition to current CD4. HL IR remained stable over time.

CONCLUSION

NHL incidence was associated with lower current CD4 and both current and historical exposure to viral replication, suggesting ongoing viral replication may play a part in NHL development in addition to current-immunodeficiency. Conversely, HL incidence was elevated in those with current-immunodeficiency, but current and historical exposure to uncontrolled HIV replication were not associated.

Table 1 Baseline characteristics						
Factor	Total		NHL		HL	
	N/median	%/IQR	N/median	%/IQR	N/median	%/IQR
Total	41420	100	392	100	149	100
Median age (years, IQR)	40	34 - 47	43	38 - 51	42	35 - 48
Median year of baseline (IQR)	2004	2004 - 2006	2004	2004 - 2006	2004	2004 - 2006
Male gender	30214	73	337	86	126	84.6
White ethnicity	20658	50	181	46	70	47
MSM transmission mode	18124	44	200	51	87	58
Prior AIDS (other than cancer)	8748	21	92	24	31	21
On cART	21310	51	160	41	69	46
CD4>350 cells/mm ³	25563	62	183	47	88	59
HIV-VL <500 copies/mL	21171	51	111	28	64	43

IQR: Interquartile range, baseline: latest of study entry or 1/1/2004



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Oral presentation: Tuesday

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