Diffust storcelligt B-cellslymfom - fokus på standardpatienten

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Var diagnosticeras och behandlas lymfom i Sverige?

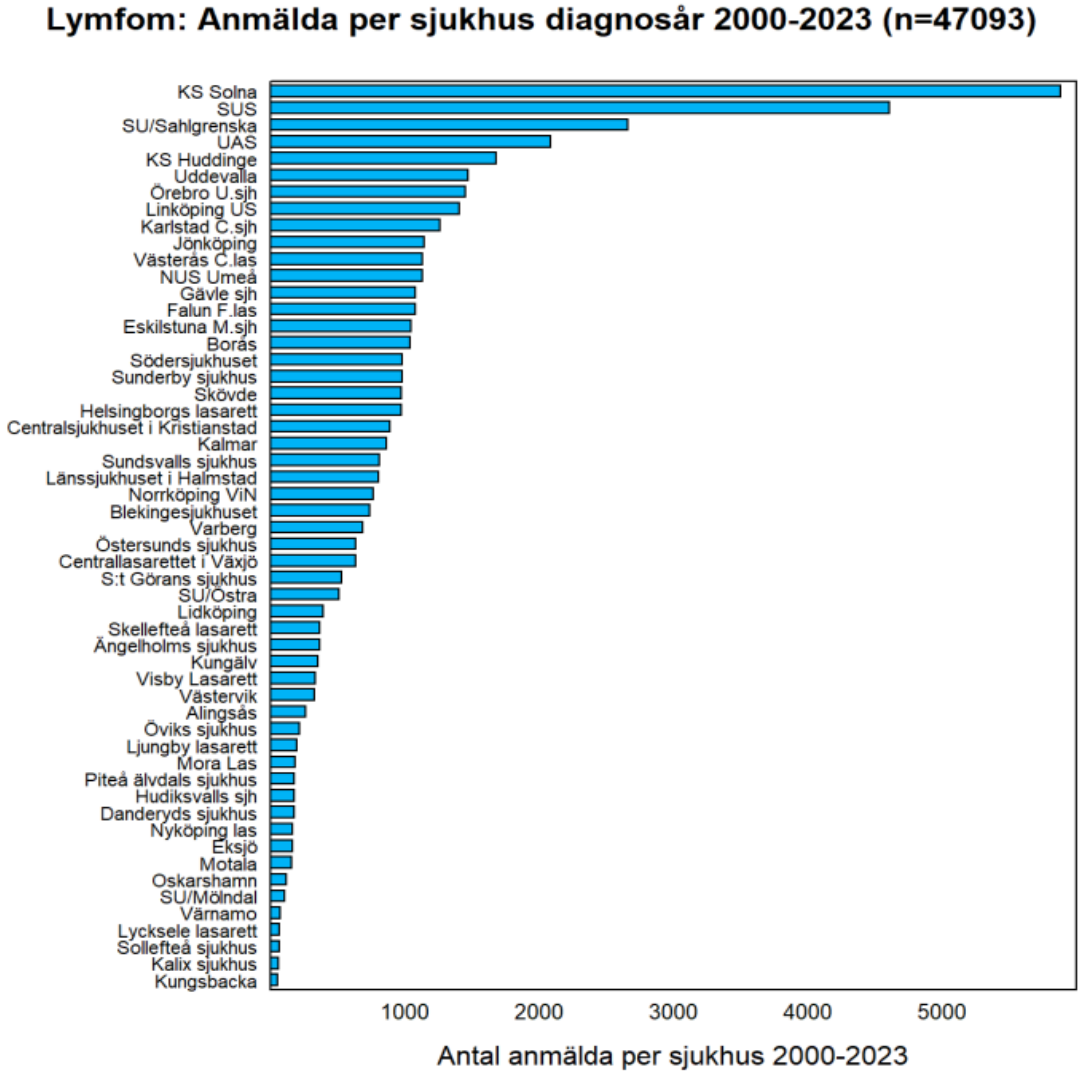
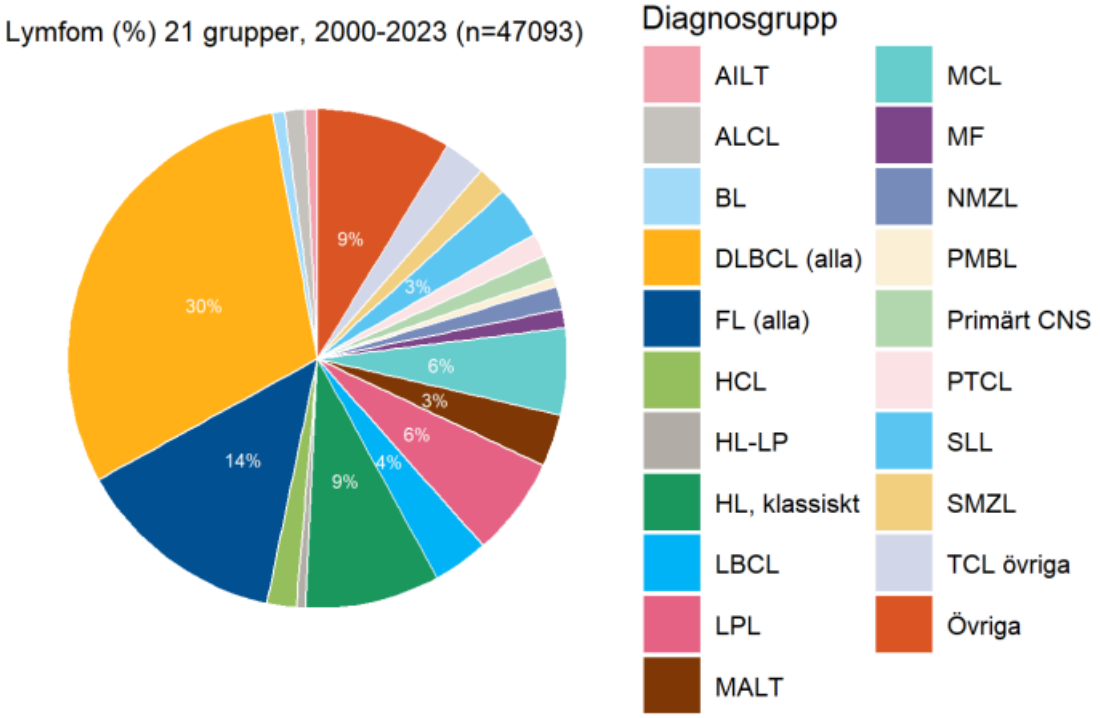


Bild från Svenska lymfomregistret årsrapport 2024
www.cancercentrum.se

Alla kliniker som behandlar lymfom registrerar patienter i svenska lymfom-registret på INCA (liktydigt med klinisk canceranmälan)

Lymfomsubtyper



Diffust storcelligt B-cellslymfom (DLBCL) enskilt vanligaste lymfom-subtypen - ca 30%

Klassiskt Hodgkin lymfom - ca 9%
Aggressiva T-cellslymfom (ALCL, AITL, PTCL nos) – ca 5%

WHO-klassifikationen (femte upplagan) (*Alaggio et al, Leukemia 2022*)

I den senaste WHO klassifikationen så använder man istället familjen/klassen “Large B-cell lymphoma (LBCL)”

90%

Samma tänk som DLBCL nos

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Large B-cell lymphomas	
Diffuse large B-cell lymphoma, NOS	(Same)
T-cell/histiocyte-rich large B-cell lymphoma	(Same)
Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with *MYC* and *BCL2* rearrangements	High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements
ALK-positive large B-cell lymphoma	(Same)
Large B-cell lymphoma with *IRF4* rearrangement	(Same)
High-grade B-cell lymphoma with 11q aberrations	Burkitt-like lymphoma with 11q aberration
Lymphomatoid granulomatosis	(Same)
EBV-positive diffuse large B-cell lymphoma	EBV-positive diffuse large B-cell lymphoma, NOS
Diffuse large B-cell lymphoma associated with chronic inflammation	(Same)
Fibrin-associated large B-cell lymphoma	*Not previously included* (Previously considered a subtype of diffuse large B-cell lymphoma associated with chronic inflammation)
Fluid overload-associated large B-cell lymphoma	*Not previously included*
Plasmablastic lymphoma	(Same)
Primary large B-cell lymphoma of immune-privileged sites	*Not previously included*, encompassing primary diffuse large B-cell lymphoma of the CNS in revised 4th edition (*plus primary large B-cell lymphoma of the vitreoretina and primary large B-cell lymphoma of the testis*)
Primary cutaneous diffuse large B-cell lymphoma, leg type	(Same)
Intravascular large B-cell lymphoma	(Same)
Primary mediastinal large B-cell lymphoma	(Same)
Mediastinal grey zone lymphoma	B-cell lymphoma, unclassifiable, with features intermediate between DLBCL and classic Hodgkin lymphoma
High-grade B-cell lymphoma, NOS	(Same)

WHO-klassifikationen från 2022

(*Alaggio et al, Leukemia*)

I den senaste WHO klassifikationen så använder man istället familjen/klassen “Large B-cell lymphoma (LBCL)”

Annat tänk

WHO Classification, 5th edition	WHO Classification, revised 4th edition
Large B-cell lymphomas	
Diffuse large B-cell lymphoma, NOS	(Same)
T-cell/histiocyte-rich large B-cell lymphoma	(Same)
Diffuse large B-cell lymphoma/ high grade B-cell lymphoma with *MYC* and *BCL2* rearrangements	High-grade B-cell lymphoma with *MYC* and *BCL2* and/or *BCL6* rearrangements
ALK-positive large B-cell lymphoma	(Same)
Large B-cell lymphoma with *IRF4* rearrangement	(Same)
High-grade B-cell lymphoma with 11q aberrations	Burkitt-like lymphoma with 11q aberration
Lymphomatoid granulomatosis	(Same)
EBV-positive diffuse large B-cell lymphoma	EBV-positive diffuse large B-cell lymphoma, NOS
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Etablerade prognosfaktorer

International Prognostic Index, IPI

1. stadium III/IV
2. förhöjt LD-värde
3. funktionsstatus (ECOG/WHO) 2–4
4. ålder > 60 år
5. > 1 extranodalt organ.

Age-adjusted IPI, aaIPI

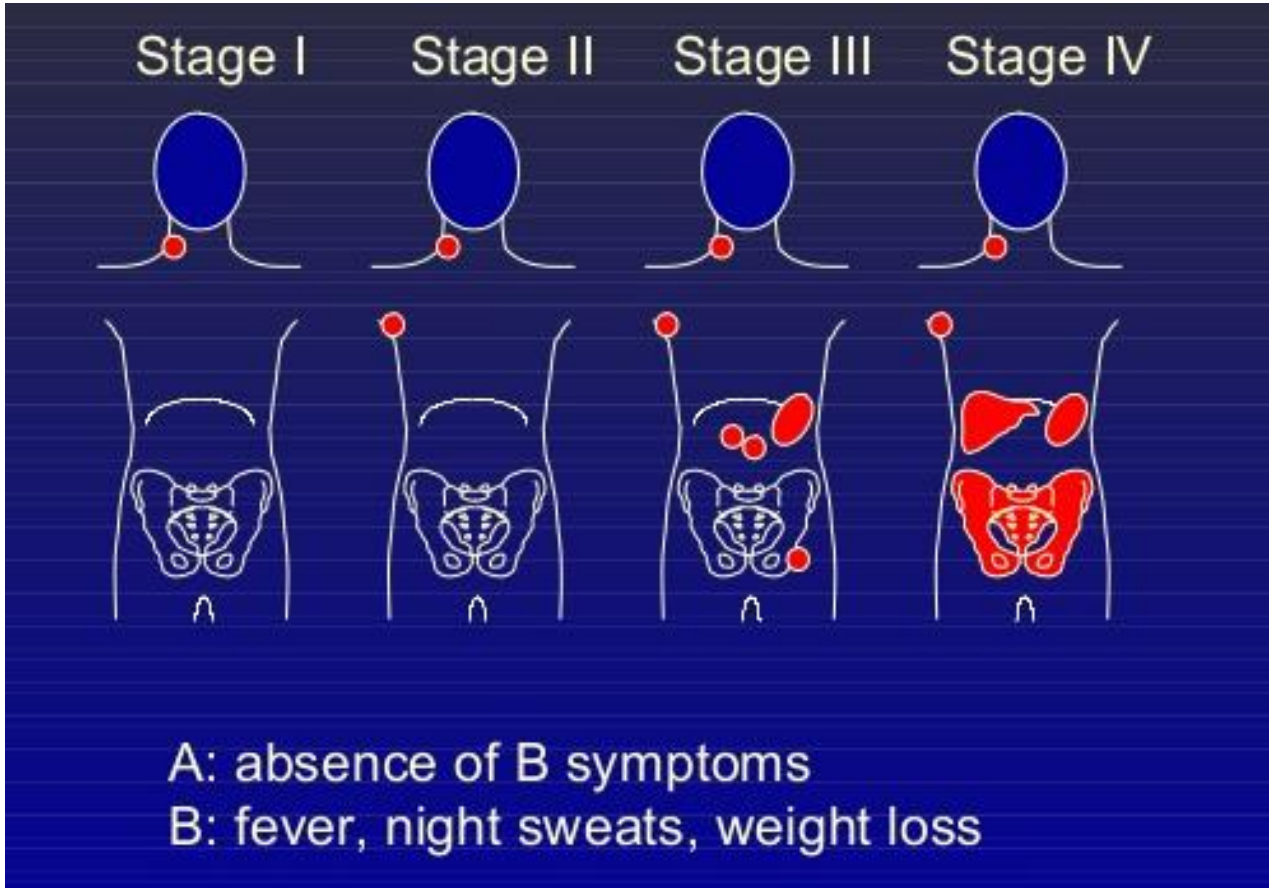
1. stadium III/IV
2. förhöjt LD-värde
3. funktionsstatus (ECOG/WHO) 2–4.

CNS-IPI

1. stadium III/IV
2. förhöjt LD-värde
3. funktionsstatus (ECOG/WHO) 2–4
4. ålder > 60 år
5. > 1 extranodalt organ
6. engagemang av njure/binjure.

Stadieindelning central för klinisk handläggning och behandlingsval

Enligt Ann Arbor



Lokal överväxt på extranodalt organ: E

Primärt extranodal (Pe) sjukdom (enligt Musshoff)

PeI – engagemang i ett extranodalt organ/vävnad

PeII – engagemang i ett extranodalt organ/vävnad med spridning till regionala lymfomkörtlar (PeII1) eller bortom detta men fortfarande samma sida om diafragma (PeII2)

Lokal överväxt på extranodalt organ: E

OBS! viss extranodal sjukdom klassas direkt som Ann Arbor stadium IV

- **Engagemang i benmärg, CNS, lever, pleura eller lunga**

- **Diffust spritt engagemang i ett extranodalt organ**

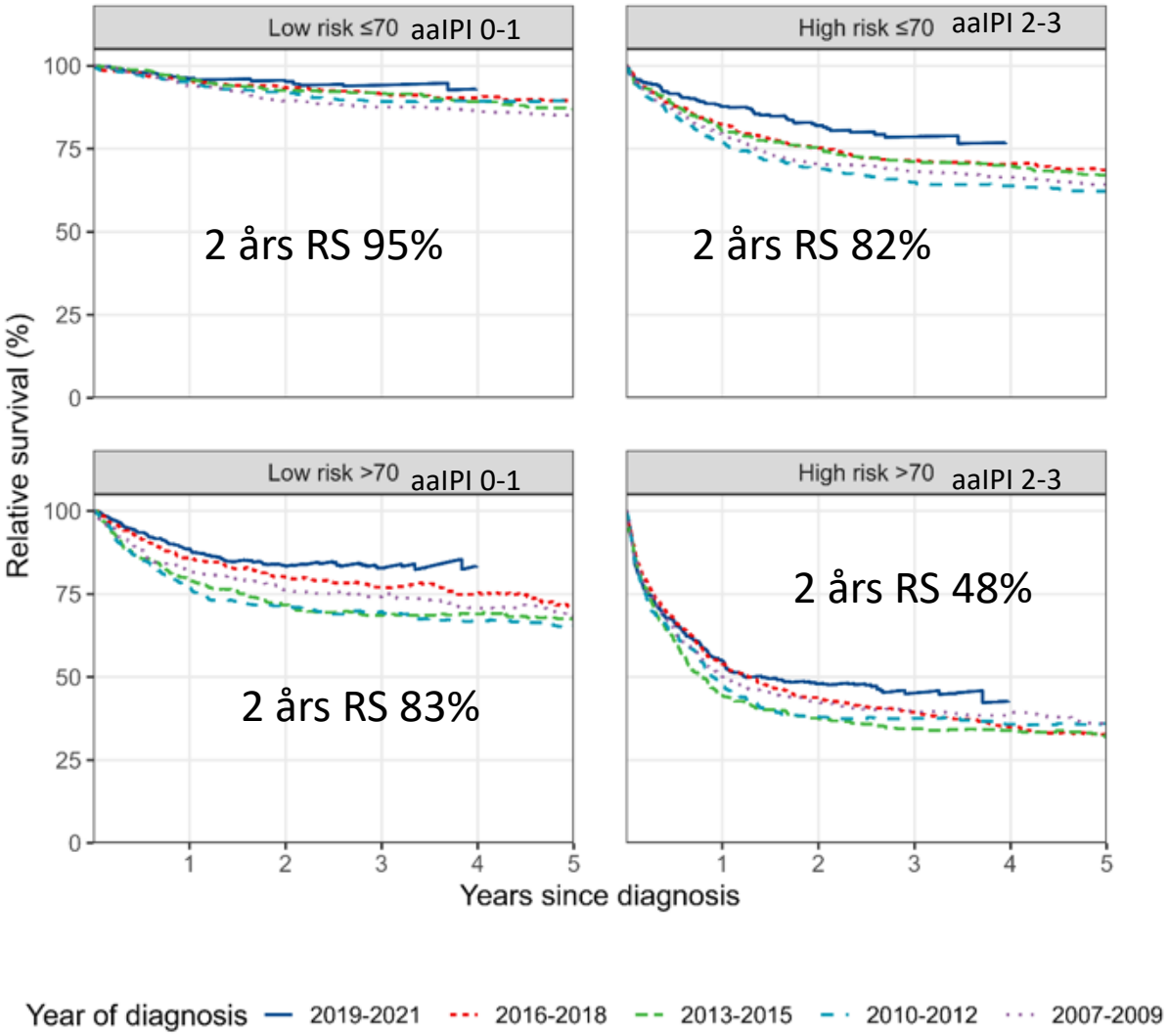
Armitage JO. Staging non-Hodgkin lymphoma. CA Cancer J Clin. 2005;55(6):368-76.

DLBCL, not otherwise specified (nos) – hur ser det ut i Sverige?

	Overall	2007-2009	2010-2012	2013-2015	2016-2018	2019-2021
SWEDEN, total	8833	1649	1709	1851	1917	1707
Age median IQR	72 (63, 80)	70 (61, 79)	71 (62, 80)	71 (63, 80)	72 (63, 80)	74 (64, 81)
Sex						
Female	3831 (43.4)	742 (45)	747 (43.7)	803 (43.4)	837 (43.7)	702 (41.1)
Male	5002 (56.6)	907 (55)	962 (56.3)	1048 (56.6)	1080 (56.3)	1005 (58.9)

Harrysson et al, BJH, 2025

DLBCL, not otherwise specified (nos) – hur ser det ut i Sverige?



Relativ överlevnad (RS):

<u>Överlevnad bland patienterna</u>
Överlevnad i befolkningen

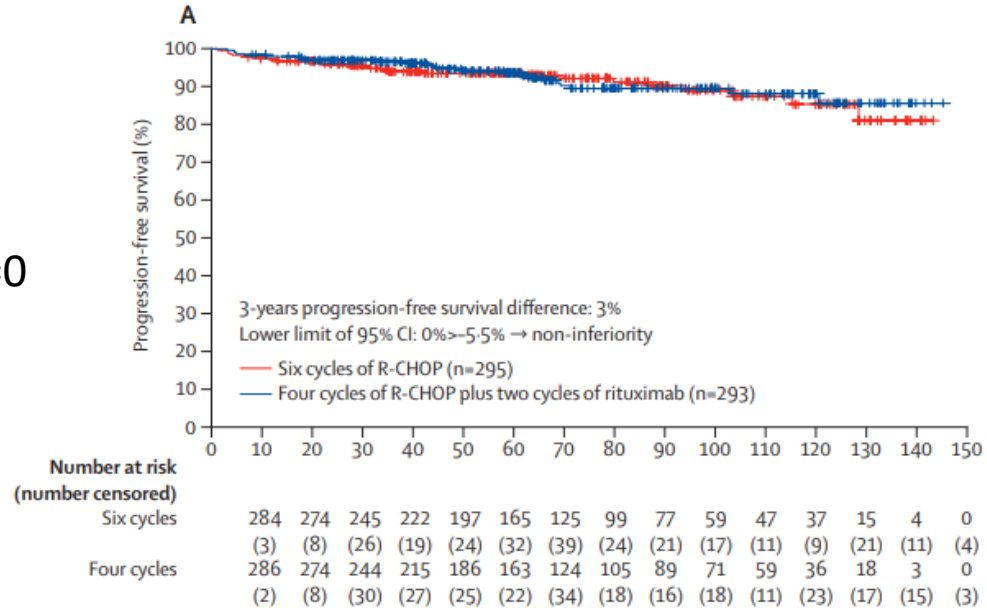
Harrysson et al, BJH, 2025

Flyer-studien: R-CHOPx6 vs R-CHOPx4 + Rx2

(Poeschel et al, Lancet 2019)

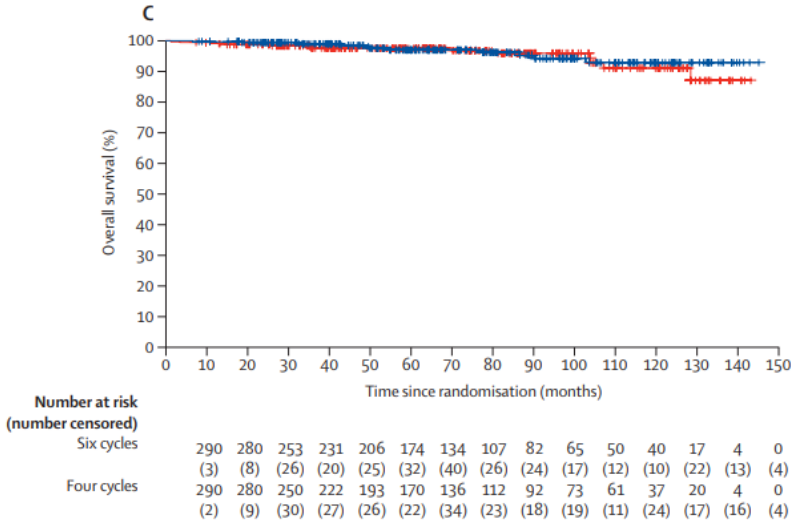
Inklusionskriterier:
18-60 år
DLBCL stadium I-II
Normalt LD
Performance 0-1
Ej bulky (<7.5 cm)

} aaIPI =0



Slutsatser:
Lika bra resultat i armarna
men färre biverkningar med kortare behandling

Viktigt att undvika överbehandling om vi kan!



Värt att notera:
- extranodal sjukdom inkluderades men bland testislymfom fick 3 av 11 återfall (27%)
- ingen hänsyn togs till ytterl biomarkörer

Rekommenderad behandling testis-lymfom tidigt stadium

Ökad risk för CNS recidiv vid extranodalt engagemang i testis, njure/binjure, ovarier

Ge full behandling (6 kurer R-CHOP eller R-CHOEP)

Ge CNS profylax:
- it mtx
- systemiskt (högdos MTX/Ara-C efter R-CHOP (CRY-protokollet) eller efter R-CHOP 1 och 2 och Ara-C på slutet (CHIC-protokollet)

Strålbehandling mot kontralaterala testikeln till 30 Gy

Låg evidens för nytta med CNS profylax men fortfarande motiverat vid specifikt extranodalt engagemang så som testis, njure, binjure

Största studien hittills med 2418 patienter med DLBCL med CNS-IPI 4-6 visar ingen tydlig nytta av högdos MTX (dock ej randomiserad)

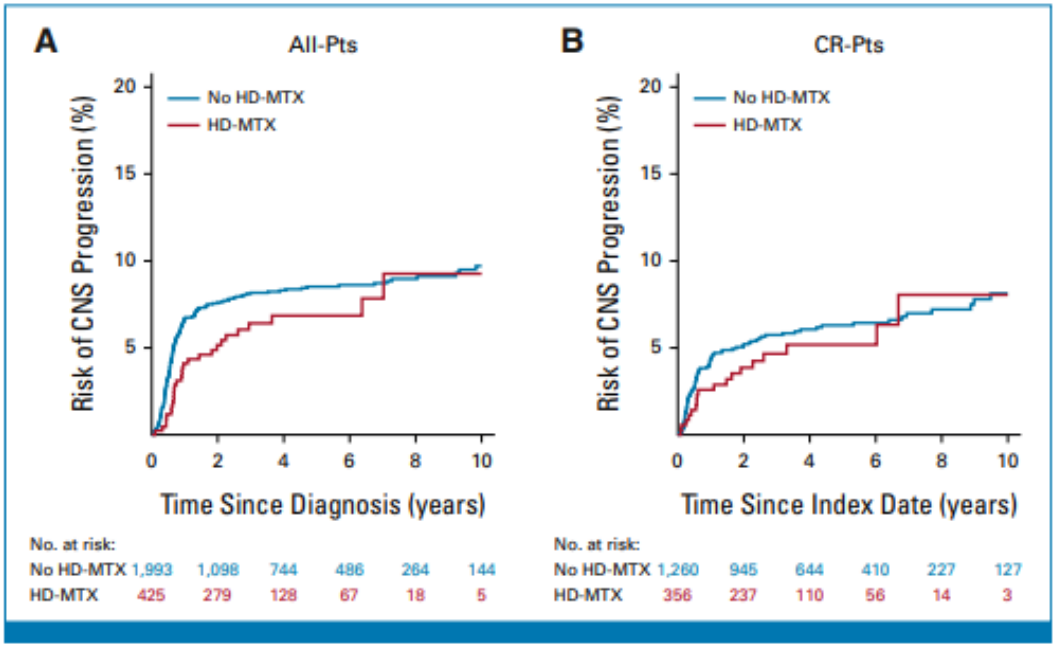


FIG 2. Crude cumulative risk of CNS progression in patients receiving first-line immunochemotherapy with or without systemic methotrexate (HD-MTX). (A) All-pts. (B) Patients in complete response at the end of first-line systemic therapy (CR-pts). All-Pts, all patients; CR-pts, patients in complete response at completion of chemoimmunotherapy; HD-MTX, high-dose methotrexate.

Lewis et al, JCO 2023