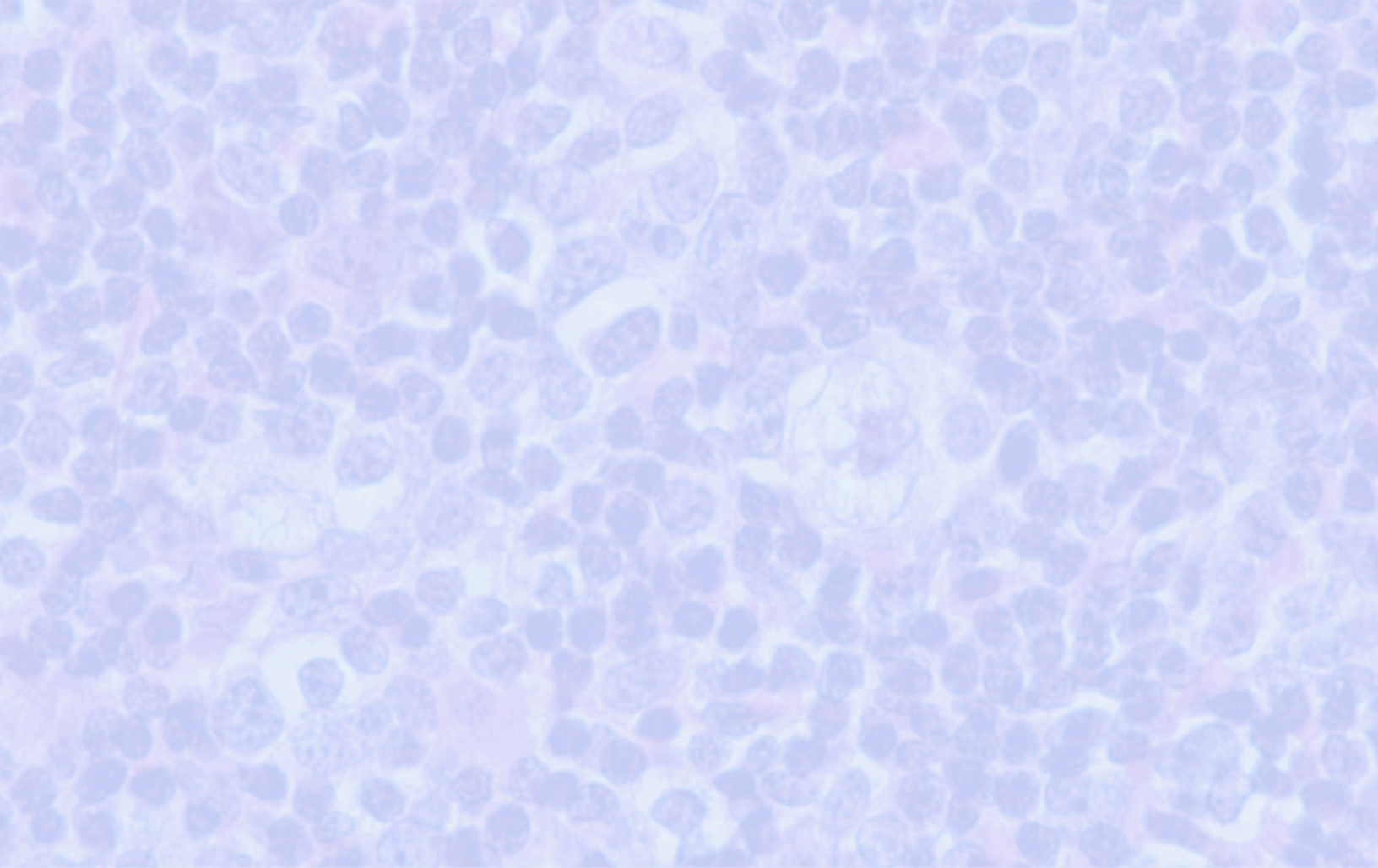




## Treatment options for patients with **fully removed** nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL): *Evidence Review Tables*

## Introduction

This document contains evidence review tables that informed a patient decision aid for people who have **nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL)** that has been fully removed and who have no other areas of the cancer in their body.

Health care teams may call this cancer “nodular lymphocyte-predominant B cell lymphoma” (NLPBL). **NLPHL and NLPBL are different names for the same type of cancer.**

## Evidence Review Summary Tables: General Notes

The tables listed in this document are meant to serve as a supplementary document to show the data used to inform the “Treatment options for patients with fully removed nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL): A Decision Aid.”

- Data sources listed below describing benefits, temporary side effects, and long term side effects contain what we believe to be the most relevant and current data available for the patients diagnosed with NLPHL that has been fully removed.
  - When possible, we included data from studies of patients who were diagnosed with stage IA NLPHL. In many cases, studies used different cancer stage groupings (such as “low stage,” stage I, etc.). Please see the full article(s) for additional information.
  - When data for patients with NLPHL was not available, we reviewed data from patients diagnosed with other types of slow-growing lymphomas, such as follicular and/or marginal zone lymphoma, or from patients with Hodgkin lymphoma or other non-Hodgkin lymphomas.
  - We focused our review on clinical trials and registry data published after 2010 with at least 50 patients receiving the reported treatment.
  - Some studies use alternative wording for monitoring such as “watch and wait” and “active surveillance.” As we note, several of these studies did not report whether or not the tumor(s) have been fully removed for those in the monitoring/watch and wait/active surveillance groups.
  - We included data from studies that used primarily involved-field radiation therapy, involved-site radiation therapy, and/or involved-node radiation therapy.
  - When NLPHL-specific data are available and/or these estimates are updated, we will update this document.
- Sources listed in **BLUE** indicate sources that we cited as evidence in the patient decision aid.
- If you have questions about the information in this document, please email [GLOW@urmc.rochester.edu](mailto:GLOW@urmc.rochester.edu).

## GRADE Ratings

The notes for each evidence review table indicate a rating of the certainty of the evidence using the GRADE system as follows:

- ++++ High certainty – further research is very unlikely to change the estimate.
- +++ Moderate certainty – further research may change the estimate.
- ++ Low certainty – further research is likely to change the estimate.
- + Very low certainty – further research is very likely to change the estimate.

## Abbreviations and Definitions

|              |                                                                    |                                                                                                                                                                                                                                          |
|--------------|--------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>DOI</b>   | Digital object identifier                                          | A string of letters and numbers assigned to a scientific publication that permanently links to the article; the DOI can be copied and pasted into any internet browser to find the publication.                                          |
| <b>FL</b>    | Follicular lymphoma                                                | A slow growing subtype of non-Hodgkin lymphoma.                                                                                                                                                                                          |
| <b>grade</b> | -                                                                  | Grade (lower-case) reflects the severity of a side effect according to <a href="#">Common Terminology Criteria for Adverse Events</a> (CTCAE) criteria.                                                                                  |
| <b>GRADE</b> | Grading of Recommendations, Assessment, Development, & Evaluations | A framework for showing summaries of evidence for clinical practice recommendations.                                                                                                                                                     |
| <b>HL</b>    | Hodgkin lymphoma                                                   | A cancer of the lymphatic system that contains Reed-Sternberg cells.                                                                                                                                                                     |
| <b>IFRT</b>  | Involved-field radiation therapy                                   | A radiation therapy technique where the radiation is aimed at the larger area of the lymph node(s) that had the lymphoma and surrounding tissue; IFRT uses a larger radiation field than ISRT and may expose nearby organs to radiation. |
| <b>INRT</b>  | Involved-node radiation therapy                                    | A radiation therapy technique where the radiation is aimed at only the lymph node(s) that had the lymphoma.                                                                                                                              |
| <b>ISRT</b>  | Involved-site radiation therapy                                    | A radiation therapy technique where the radiation is aimed at the lymph node(s) that had the lymphoma and at areas close to it ("sites").                                                                                                |
| -            | Meta-analysis                                                      | A meta-analysis is the statistical process of analyzing and combining results from several similar studies.                                                                                                                              |
| <b>MZL</b>   | Marginal zone lymphoma                                             | A slow growing subtype of non-Hodgkin lymphoma.                                                                                                                                                                                          |
| <b>NHL</b>   | Non-Hodgkin lymphoma                                               | A cancer of the lymphatic system that does not contain Reed-Sternberg cells.                                                                                                                                                             |
| -            | Non-inferiority trial                                              | A study that tests whether a new or experimental treatment is as effective as the current standard of care.                                                                                                                              |
| <b>NLPHL</b> | Nodular lymphocyte-predominant Hodgkin lymphoma                    | A subtype of Hodgkin lymphoma.                                                                                                                                                                                                           |
| <b>NRCT</b>  | Non-randomized clinical trial                                      | A clinical trial in which the participants are not assigned by chance to different treatment groups. Participants may choose which group they want to be in, or they may be assigned to the groups by the researchers.                   |
| -            | Observational study                                                | A type of study in which individuals are observed or certain outcomes are measured. No attempt is made to affect the outcome                                                                                                             |

(for example, no treatment is given).

|            |                           |                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|------------|---------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>OS</b>  | Overall survival          | The length of time from either the date of diagnosis or the start of treatment for a disease, such as cancer, that patients diagnosed with the disease are still alive.                                                                                                                                                                                                                                                                               |
| <b>PFS</b> | Progression-free survival | The length of time during and after the treatment of a disease, such as cancer, that a patient lives with the disease but it does not get worse. In a clinical trial, measuring progression-free survival is one way to see how well a new treatment works.                                                                                                                                                                                           |
| <b>RA</b>  | Retrospective Analysis    | A retrospective analysis is performed using information on events that have taken place in the past. In most cases, the data have already been gathered and stored in a clinical trial database or registry. In a retrospective analysis, different patient populations can be compared for one or several outcomes.                                                                                                                                  |
| <b>RT</b>  | Radiation therapy         | The use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to kill cancer cells and shrink tumors.                                                                                                                                                                                                                                                                                                                |
| <b>RCT</b> | Randomized clinical trial | A scientific experiment in which patients are randomly assigned to different treatment groups in order to reduce bias when comparing different treatments. This study design is considered the most reliable way of comparing treatment outcomes.                                                                                                                                                                                                     |
| -          | Statistical significance  | A mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone. A p-value $\leq 0.05$ is a commonly used threshold for determining whether an observed difference is statistically significant. A p-value of $\leq 0.05$ suggests that there is a 5% probability or less that the observed differences were the result of chance. |
| -          | Systematic review         | A systematic review attempts to gather all available empirical research by using clearly defined, systematic methods to obtain answers to a specific question.                                                                                                                                                                                                                                                                                        |

## Benefits Table Notes

- GRADE rating (certainty of evidence): **++**
  - Low certainty – further research is likely to change the estimate.
  - We are extrapolating from historical data and studies with small sample sizes.
- Statistical significance is not available for the data included in this table.

| STUDY DESIGN           | AUTHOR, YEAR              | ARTICLE DOI                       | AGE (years) | CANCER & STAGE      | 5 YEAR PFS                        |                              | 5 YEAR OS                         |                              | COMMENTS                                                                                                                                                                                                                                                                                                                                         |
|------------------------|---------------------------|-----------------------------------|-------------|---------------------|-----------------------------------|------------------------------|-----------------------------------|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                        |                           |                                   |             |                     | MONITOR<br>% PATIENTS<br>AFFECTED | RT<br>% PATIENTS<br>AFFECTED | MONITOR<br>% PATIENTS<br>AFFECTED | RT<br>% PATIENTS<br>AFFECTED |                                                                                                                                                                                                                                                                                                                                                  |
| Retrospective analysis | Flerlage et al., 2026     | 10.1182/bloodadvances.2026.020012 | 3-89        | NLPHL, IA           | <b>66*</b>                        | <b>91*</b>                   | <b>97*</b>                        | <b>100*</b>                  | *6 year PFS and OS reported<br>There were <b>99 patients</b> aged 4-80 with complete resection and observation (monitoring). There were <b>53 patients</b> aged 11-89 with complete resection and RT. RT methods used include IFRT, INRT, and EFRT, with median dose of 30.6 Gy (range=25.5-40 Gy).                                              |
| NRCT                   | Shankar et al., 2026      | 10.1182/bloodadvances.2026.019765 | <18         | NLPHL, IA, IIA      | <b>80</b>                         | n/a                          | <b>100</b>                        | n/a                          | *87 patients in total with complete resection. 77 had stage IA and 10 had stage IIA. Of the 18 patients who had a relapse, 13 had stage IA at relapse, 2 had stage IIA, 1 had stage IIIA, and 1 had stage IVA.                                                                                                                                   |
| NRCT                   | Appel et al., 2016        | 10.1200/JCO.2015.65.3469          | <22         | NLPHL, IA           | <b>77*</b>                        | n/a                          | <b>100</b>                        | n/a                          | *EFS reported<br>There were <b>52 patients</b> with complete resection.                                                                                                                                                                                                                                                                          |
| Retrospective analysis | Eichenauer et al., 2015   | 10.1200/JCO.2014.60.4363          | 16-75       | NLPHL, IA           | n/a                               | <b>93*</b>                   | n/a                               | <b>99*</b>                   | *4 year PFS reported<br>There were <b>108 patients</b> who received IFRT. These include patients with incomplete resection.                                                                                                                                                                                                                      |
| Retrospective analysis | Chen et al., 2010         | 10.1200/JCO.2009.24.0945          | 3-77        | NLPHL, I, II        | n/a                               | <b>95</b>                    | n/a                               | <b>98</b>                    | Outcomes reported for patients with stage I or II (tumor resection status unknown) who had RT alone. This paper does not report the presence or absence of B symptoms, how many of the <b>93 patients</b> who received RT alone were diagnosed with stage I vs stage II NLPHL, nor the number of patients treated with "limited field RT" alone. |
| Retrospective analysis | Mauz-Körholz et al., 2007 | 10.1002/cncr.22762                | 4-17        | NLPHL, IA, IIA, IIA | <b>67*</b>                        | n/a                          | <b>100^</b>                       | n/a                          | *26 month (~2 year) PFS reported<br>^50 month (~4year) OS reported<br>There were <b>51 patients</b> with stage IA, IIA, or IIIA with complete resection.                                                                                                                                                                                         |

## Temporary, Short-Term Side Effects Notes: Mental Health

- GRADE rating (certainty of evidence): ++
  - Low certainty – further research is likely to change the estimate.
  - We are extrapolating from slightly different patient populations and treatment methods and from studies with small sample sizes; current treatment methods may result in different reports of side effects.
- We are not aware of any data regarding mental health in patients with NPLHL diagnoses. As such, we have focused on mental health findings in patients with other slow-growing (indolent) lymphomas such as follicular lymphoma.

| STUDY DESIGN         | AUTHOR, YEAR           | ARTICLE DOI                   | AGE (years)                           | CANCER & STAGE                          | SIDE EFFECT                                               | MONITOR % PATIENTS AFFECTED | TREATMENT % PATIENTS AFFECTED | STATISTICAL SIGNIFICANCE | COMMENTS                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------|------------------------|-------------------------------|---------------------------------------|-----------------------------------------|-----------------------------------------------------------|-----------------------------|-------------------------------|--------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RCT*                 | Ardeshtna et al., 2014 | 10.1016/S1470-2045(14)70027-0 | 18+                                   | FL, advanced stage and without symptoms | Moderate/severe anxiety at 7 months                       | 15 <sup>^</sup>             | 10 <sup>^</sup>               | No p=0.72                | *This study uses data from a randomized clinical trial of 379 patients with asymptomatic, advanced stage, low tumor burden follicular lymphoma. There were <b>187 patients</b> assigned to "watch and wait" (monitoring; unknown if tumor removed) and <b>84 patients</b> assigned to rituximab induction (treatment).<br><sup>^</sup> Patients enrolled in the "watch and wait" (monitoring; unknown if tumor removed) arm or rituximab induction (treatment) arm of the trial. The study used the Hospital Anxiety and Depression Scale (HADS) Anxiety Subscale to measure anxiety. Borderline and case anxiety refer to anxiety that is considered more than "normal anxiety." Case anxiety refers to anxiety that is significant enough to require intervention by a mental health professional. These data are located in the supplementary appendix. |
|                      |                        |                               |                                       |                                         | Mild anxiety at 7 months                                  | 16 <sup>^</sup>             | 15 <sup>^</sup>               | Not reported             |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| RCT*                 | Ardeshtna, et al. 2014 | 10.1016/S1470-2045(14)70027-0 | 18+                                   | FL, advanced stage and without symptoms | Worry about disease becoming more aggressive              | 35 <sup>^</sup>             | 23 <sup>^</sup>               | No p=0.06                | *This study uses data from a randomized clinical trial of 379 patients with asymptomatic, advanced stage, low tumor burden follicular lymphoma. There were <b>187 patients</b> assigned to "watch and wait" (monitoring; unknown if tumor removed) and <b>84 patients</b> assigned to a rituximab induction (treatment) arm. <sup>^</sup> Percent of "watch and wait" (monitoring; unknown if tumor removed) patients or rituximab induction (treatment) patients who responded "Quite a bit/Very much." These data are located in the supplementary appendix.                                                                                                                                                                                                                                                                                             |
|                      |                        |                               |                                       |                                         | Worry about disease requiring treatment or more treatment | 32 <sup>^</sup>             | 18 <sup>^</sup>               | Yes p=0.03               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Observational study* | Oerlemans, et al. 2014 | doi.org/10.1111/ehj.12335     | All ages, mostly adults (mean age 59) | FL, any stage                           | Worry about future health                                 | 74 <sup>^</sup>             | 50 <sup>^</sup>               | No p=0.48                | *This study used data from a survey of 148 patients diagnosed with any stage of follicular lymphoma. This study included <b>19 patients</b> under active surveillance (monitoring; unknown if tumor removed), and <b>23 patients</b> treated with RT. A subanalysis of patients under wait and see (n = 19), who underwent one active treatment line (n = 94), and patients who had 2 or more active treatment lines (n = 33) showed no differences in HRQoL (data not shown).<br><sup>^</sup> Percent of patients with any stage of follicular lymphoma under active surveillance or treatment with RT. This study used the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) to measure quality of life.                                                                                  |

## Side Effects Notes: Radiation Therapy

- GRADE rating (certainty of evidence: **++**
  - Low certainty – further research is likely to change the estimate.
  - We are extrapolating from slightly different patient populations and historical data; current treatment methods may result in different reports of side effects.
- The side effects of radiation therapy depend on the radiation dose and on the area of the body that is treated.
- 20-30 Gy is the standard dose for definitive radiation therapy for NLPHL. This table summarizes the risk of side effects when a dose of around 20-30 Gy is given to parts of the body that are most commonly affected by NLPHL.
- Side effects of radiation should be the same, regardless of whether the cancer was fully removed and regardless of the type of cancer that was treated. Therefore, this table includes results when radiation was given for cancers other than NLPHL and without fully removed disease. The risk of side effects should be the same when radiation is given for completely removed NLPHL.
- Statistical significance is not available for the data included in this table.

| STUDY DESIGN | AUTHOR, YEAR        | ARTICLE DOI                   | AGE (years) | CANCER & STAGE                       | RT METHOD & DOSE           | SIDE EFFECT                        | % PATIENTS AFFECTED | COMMENTS                                                                                                                                                                                                                                                                                  |
|--------------|---------------------|-------------------------------|-------------|--------------------------------------|----------------------------|------------------------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| RCT*         | Hoskin et al., 2014 | 10.1016/S1470-2045(14)70036-1 | >18         | FL and MZL, any stage                | Local RT, 24 Gy            | Fatigue <sup>^</sup>               | 0.7*                | *This was a randomized non-inferiority trial. <b>260 patients</b> were assigned to receive 24 Gy RT.<br><sup>^</sup> Grades (side effect severity) 3-4 reported [From our experience, older adults tend to experience more fatigue than pediatric, adolescent, and young adult patients.] |
| RCT*         | Hoskin et al., 2021 | 10.1016/S1470-2045(20)30686-0 | >18         | FL and MZL, any stage                | IFRT, 4 Gy or 24 Gy        | Fatigue, 12 week, grades 1-2       | 2.4                 | *This was a randomised phase 3 non-inferiority trial. <b>299</b> patients were assigned to receive 24 Gy IFRT. Results noted here are for patients who received 24 Gy only.                                                                                                               |
|              |                     |                               |             |                                      |                            | Fatigue, 6 month, grades 1-2       | 1.1                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Fatigue, 1 year, grades 1-2        | 0.4                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Alopecia, 12 week, grades 1-2      | 6.6                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Alopecia, 6 month, grades 1-2      | 2.6                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Alopecia, 1 year, grades 1-2       | 3.6                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Skin changes, 12 week, grades 1-2  | 1.4                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Nausea, 12 week, grades 1-2        | 1.7                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Fibrosis, 12 week, grades 1-2      | 1.7                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Fibrosis, 6 month, grades 1-2      | 0.7                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Hypothyroidism, 1 year, grades 1-2 | 0.4                 |                                                                                                                                                                                                                                                                                           |
| RCT*         | Lowry et al., 2011  | 10.1016/j.radonc.2011.05.013  | 18-92       | Indolent NHL, <sup>^</sup> any stage | Method not reported, 24 Gy | Skin changes, all grades           | 1-34.8              | *This study was a randomized phase 3 clinical trial.<br><sup>^</sup> Indolent NHLs included were primarily FL and MZL. <b>180 patients</b> aged 29-85 with indolent NHL received 24 Gy treatment.                                                                                         |
|              |                     |                               |             |                                      |                            | Skin changes, grade 2-3            | 0-8                 |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Hair thinning or loss, all grades  | 16                  |                                                                                                                                                                                                                                                                                           |
|              |                     |                               |             |                                      |                            | Hair thinning or loss, grade 2-3   | 3                   |                                                                                                                                                                                                                                                                                           |

| STUDY DESIGN                       | AUTHOR, YEAR          | ARTICLE DOI                  | AGE (years)      | CANCER & STAGE       | RT METHOD & DOSE                                     | SIDE EFFECT                                    | % PATIENTS AFFECTED | COMMENTS                                                                                                                                                                                   |
|------------------------------------|-----------------------|------------------------------|------------------|----------------------|------------------------------------------------------|------------------------------------------------|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                    |                       |                              |                  |                      |                                                      | Sore throat/ discomfort swallowing, all grades | 23                  |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Sore throat/discomfort swallowing, grade 2-3   | 8                   |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Nausea, all grades                             | 11                  |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Nausea, grade 2-3                              | 4                   |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Internal scar tissue (fibrosis), all grades    | 17                  |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Internal scar tissue (fibrosis), grade 2-3     | 2                   |                                                                                                                                                                                            |
| Systematic review & meta-analysis* | Milano et al., 2024   | 10.1016/j.ijrobp.2021.02.001 | <21 at diagnosis | Mostly HL, any stage | Method not reported, 10-30 Gy                        | Clinical hypothyroidism                        | 7^                  | *This article summarizes 8 studies available for dose-response analysis.<br>^Based on 20 Gy dose                                                                                           |
|                                    |                       |                              |                  |                      |                                                      | Subclinical hypothyroidism                     | 25^                 |                                                                                                                                                                                            |
| RA                                 | Cellap et al., 2011   | 10.1016/j.ijrobp.2010.09.054 | 14-70            | HL, any stage        | IFRT, median 32 Gy (range 30–36 Gy)                  | Hypothyroidism, lab evidence, 32 months        | 41.5                | This study included <b>61 patients</b> receiving treatment between 2001 and 2009.                                                                                                          |
|                                    |                       |                              |                  |                      |                                                      | Hypothyroidism, est. incidence, 24 months      | 43.5                |                                                                                                                                                                                            |
|                                    |                       |                              |                  |                      |                                                      | Hypothyroidism, est. incidence, 60 months      | 49.1                |                                                                                                                                                                                            |
| RA                                 | Conway et al., 2016   | 10.1016/j.ijrobp.2016.10.004 | <50 at diagnosis | HL, any stage        | ISRT, IFRT, or INRT, median 35 Gy (range 15.8-52 Gy) | Secondary breast cancer                        | 2.7                 | This study followed <b>185 patients</b> treated for HL from 1961 -2009. Patients receiving SFRT (ISRT, IFRT, or INRT) were followed for approx. 2-51 years. Median follow-up was 14 years. |
| RA                                 | Wolden et al., 1998   | 10.1200/JCO.1998.16.2.536    | <21 at treatment | HL, any stage        | Variable method, median 38 Gy (range 7.5-59.7 Gy)*   | Second cancers                                 | 8                   | *This study followed <b>697 patients</b> treated for HL with RT alone, chemotherapy and RT, and chemotherapy alone. Patients were followed for 1-31.6 years after treatment.               |
| Literature review*                 | van Dorp et al., 2011 | 10.1093/humup d/dmr038       | 2-20*            | HL, any stage        | Variable                                             | Impact on growth of bones and muscles          | See article         | *This article summarizes 7 studies with a total of <b>481 patients</b> who were treated for HL at ages 2-20.                                                                               |

**This information is not intended to replace the advice of a health care practitioner.**

### **Content editors**

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### **Author Disclosures**

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### **About this decision aid**

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### **For more information**

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