

RIGHT TO BE FORGOTTEN IN THYROID CANCER: EVIDENCE TO INFORM WAITING PERIODS



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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ATA	American Thyroid Association
ATC	Anaplastic thyroid carcinoma
BCR	Belgian Cancer Registry
CNS	Conditional net survival
CT	Computed tomography
DHGTC	Differentiated high-grade thyroid carcinoma
DTC	Differentiated thyroid carcinoma
EMR	Excess mortality ratio
FNA	Fine-needle aspiration
FTC	Follicular thyroid carcinoma
ICD-O	International Classification of Diseases for Oncology
KCE	Belgian Health Care Knowledge Centre
MCM	Mixture cure model
NIFTP	Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
MTC	Medullary thyroid carcinoma
NMCM	Non-mixture cure model
NS	Net survival
OBT-BST	Opvolgingsbureau voor de Tarifiering Schuldsaldooverzekering – Bureau du Suivi de la tarification assurance solde restant dû
OCA	Oncocytic carcinoma of the thyroid
PDTC	Poorly differentiated thyroid carcinoma
PP	Pohar-Perme estimator
PTC	Papillary thyroid carcinoma
RAI	Radioactive iodine
RD	Royal Decree
RTBF	Right to be forgotten
SMR	Standardized mortality ratio
TC	Thyroid cancer
TNM	Tumour–node–metastasis
TTC	Time-to-Cure
UICC	Union for International Cancer Control
WBS	Whole-body scan
WDTC	Well-differentiated thyroid carcinoma
WHO	World Health Organisation



■ SCIENTIFIC REPORT

1 BACKGROUND

KEY POINTS

- **Long-term financial impacts of cancer:** Despite major advances in survival, a history of cancer can continue to create barriers to obtaining financial products - such as loans or credit-related insurance - long after treatment ends.
- **The Right to Be Forgotten (RTBF):** RTBF is a legal framework that restricts the use of cancer-related medical history in financial risk assessment once a specified relapse-free waiting period has passed after diagnosis or completion of treatment.
- **Rising importance across Europe:** The RTBF has become a prominent issue on EU-level policy agendas, and an increasing number of European countries have introduced national legislation to ensure equitable financial access for cancer survivors.
- **Belgium as an early mover:** Belgium was one of the first countries to implement RTBF legislation in 2019. Since then, it has progressively shortened the general waiting period for relapse-free cancer survivors - from 10 years initially to 5 years as of 2025. The law also permits shorter waiting periods for specific age groups or cancer types when medically and actuarially justified and supported by scientific evidence. The KCE is entrusted with periodically evaluating the RTBF reference grids.
- **Purpose of this study:** This study examines the survival of individuals diagnosed with thyroid cancer compared with the general Belgian population, with the goal of informing evidence-based recommendations for future updates to Belgium's RTBF reference grids.

1.1 Right to be forgotten for cancer survivors: uptake across Europe and worldwide

A cancer diagnosis can significantly affect an individual's life - not only physically, emotionally, and socially, but also financially. Cancer survivors frequently encounter stricter conditions when seeking financial services, and some are even denied products such as mortgages or loans. Across Europe, nearly 20 million people are living beyond their cancer diagnosis, yet many continue to face unjust financial disadvantages despite being long cured.[1]

Scientific progress in cancer treatment has improved survival outcomes, prompting new legislative responses. France pioneered the Right to be forgotten (RTBF) for cancer survivors in 2017.^{1, 2} As of March 2026, nine other European countries – Belgium, the Netherlands, Portugal, Romania, Spain, Cyprus, Italy, Slovenia and Malta – had adopted similar laws.³ This legislation ensures that after a defined “**waiting period**” following diagnosis or the end of treatment, and provided that the individual shows no signs of disease recurrence, survivors must be treated like individuals without a cancer history when applying for products such as mortgages and outstanding balance insurance. Several other EU countries that do not have RTBF legislation, e.g., Denmark, Ireland and Greece, have instead

¹ Article L1141-5 : https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000045272010

² Droit de résiliation à tout moment de l'assurance emprunteur et autres mesures de simplification (articles 1 à 8) : <https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000045268729>

³ [OVERVIEW OF LEGISLATION AT THE NATIONAL LEVEL - Ending Discrimination against Cancer Survivors](#)

introduced self-regulatory codes of conduct to improve access to financial services for cancer survivors (see Figure 1).

At the European level, important policy frameworks have emerged in the past years to address financial discrimination against cancer survivors. Under Europe's Beating Cancer Plan, the European Commission identified fair access to financial services as a priority and committed to developing an EU-wide approach to the RTBF.⁴ A major step towards harmonization came with the Consumer Credit Directive (2023), which prohibits insurers from using health data - including past cancer diagnoses - for credit insurance after a period set by Member States, capped at 15 years from the end of the medical treatment of the prospective policy holder.⁵ Member States must transpose the Consumer Credit Directive by 2025, with an additional year allowed for implementation.

While the RTBF principle is gaining traction across Europe, similar initiatives are emerging globally. For example, Chile and Monaco have already adopted laws based on the RTBF principle, Costa Rica has submitted a related bill.⁶

1.2 Evolution of the right to be forgotten in Belgium

Belgium took its first legislative step toward improving access to outstanding balance insurance for people with aggravated health risks with the Law of 21 January 2010, which amended the Law of 25 June 1992 on terrestrial insurance contracts to strengthen protections for such applicants (see Figure 1).⁷ This early reform was followed by a more comprehensive update through the Law of 4 April 2014 - often referred to as the Partyka Law - which further aimed to enhance the accessibility and affordability of outstanding balance insurance for individuals facing increased health risks.⁸ In addition, the Royal Decree (RD) of 10 April 2014 set out detailed rules governing certain outstanding balance insurance contracts to ensure the proper guarantee of mortgage loan repayment and to increase transparency and consumer protection.⁹

In 2018, the Insurance Commission - an independent advisory body for the insurance sector - evaluated the functioning of the outstanding balance insurance framework.¹⁰ Drawing on input from patient and consumer organizations, the Commission noted, among other issues (also see Supplement in [2]), that the central objective of the Partyka Law - namely, ensuring effective access to outstanding balance insurance for individuals with aggravated health risks - had not yet been sufficiently achieved. The Commission therefore placed more far-reaching measures on the agenda for discussion, taking inspiration from the French Right to Be Forgotten (RTBF) model.

⁴ <https://endingdiscrimination-cancersurvivors.eu/initiative-at-the-eu/>

⁵ Directive (EU) 2023/2225 of the European Parliament and of the Council of 18 October 2023 on credit agreements for consumers and repealing Directive 2008/48/EC, *OJ L*, 2023/2225, 30.10.2023

⁶ <https://endingdiscrimination-cancersurvivors.eu/initiatives-around-the-world/>

⁷ Wet van 21 januari 2010 tot wijziging van de wet van 25 juni 1992 op de landverzekeringsovereenkomst wat de schuldsaldoverzekeringen voor personen met een verhoogd gezondheidsrisico betreft, *B.S.* 3 oktober 2010. Loi du 21 janvier 2010 modifiant la loi du 25 juin 1992 sur le contrat d'assurance terrestre en ce qui concerne les assurances du solde restant dû pour les personnes présentant un risque de santé accru, *M.B.* 3 octobre 2010.

⁸ Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014. Loi du 4 avril 2014 relative aux assurances, *M.B.* 30 avril 2014.

⁹ Koninklijk besluit tot regeling van sommige verzekeringsovereenkomsten tot waarborg van de terugbetaling van het kapitaal van een hypothecair krediet, *B.S.* 10 juni 2014. Arrêté royal réglementant certains contrats d'assurance visant à garantir le remboursement du capital d'un crédit hypothécaire, *M.B.* 10 juin 2014.

¹⁰ DOC C2018/1



The RTBF was formally introduced in Belgium through the Law of 4 April 2019.¹¹ Since then, the RTBF framework has applied to outstanding balance insurance contracts taken out to guarantee repayment of a professional loan or of a loan related to the construction, transformation, or acquisition of the policyholder's sole and primary residence. The practical application of RTBF was further detailed by the RD of 26 May 2019.¹²

The initial general waiting period for cancer survivors to benefit from RTBF was set at **ten years** after the completion of treatment, as established by the Law of 4 April 2019. This period was subsequently reduced to **eight years** by the Law of October 30, 2022,¹³ and further shortened to **five years starting from 2025** (Law of 20 January 2025¹⁴). **Shorter waiting periods** may apply to specific cancer types or age groups; these are defined in legally binding **reference grids** established by RD. The RD of 26 of May 2019 issued the first reference grids, defining medical conditions and the corresponding waiting periods after which insurers may no longer take these conditions into account in their risk assessments. These reference grids were largely inspired by the waiting periods used in the French AERAS (Assurer et Emprunter avec un Risque Aggravé de Santé) Convention.¹⁵ To reflect medical progress and to extend the range of conditions covered, the RD of 7 June 2023 updated and expanded the reference list.¹⁶

1.3 KCE mission

The KCE is entrusted with periodically evaluating the RTBF reference grids, considering medical progress and scientific evidence. Based on a KCE proposal and following the opinion of the Price Monitoring Office for the Tariffication of outstanding balance insurance (see Text box 1), the King may adopt amendments to the reference grids in force through a RD, as foreseen in the legislative framework governing the RTBF reference grids. In line with the KCE recommendations on updated waiting periods for breast cancer, the reference grids were revised through the Royal Decree of 7 June 2023.

Candidate pathologies for a re-evaluation are selected based on well-substantiated proposals submitted to KCE by a broad range of stakeholders. To date, two research projects have been

¹¹ Wet van 4 april 2019 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen waarbij voor bepaalde persoonsverzekeringen een recht om vergeten te worden wordt ingevoerd, *B.S.* 18 april 2019. Loi du 4 avril 2019 modifiant la loi du 4 avril 2014 relative aux assurances et instaurant un droit à l'oubli pour certaines assurances de personnes, *M.B.* 18 avril 2019.

¹² Koninklijk besluit van 26 mei 2019 tot vaststelling van een referentierooster met betrekking tot het recht om vergeten te worden in het kader van bepaalde persoonsverzekeringen bedoeld in artikel 61/3 van de wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 14 juni 2019. Arrêté royal du 26 mai 2019 déterminant une grille de référence relative au droit à l'oubli en certaines assurances de personnes visée à l'article 61/3 de la loi du 4 avril 2014 relative aux assurances, *M.B.* 14 juin 2019

¹³ Wet van 30 oktober 2022 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen inzake het recht om vergeten te worden, *B.S.* 17 november 2022. Loi du 30 octobre 2022 modifiant la loi du 4 avril 2014 relative aux assurances en ce qui concerne le droit à l'oubli, *M.B.* 17 novembre 2022

¹⁴ Wet van 20 januari 2025 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, *B.S.* 30 mei 2025; Loi du 20 janvier 2025 modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli, *M.B.* 30 mai 2025

¹⁵ <https://www.aeras-infos.fr/sites/aeras/accueil/la-convention-aeras/le-cadre-de-la-convention-aeras/le-droit-a-loubli-et-la-grille-1/la-grille-de-reference-aeras-1.html>

¹⁶ Koninklijk besluit van 7 juni 2023 tot wijziging van het koninklijk besluit van 26 mei 2019 houdende de referentieroosters bedoeld in artikel 61/3 van de wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 17 juli 2023. Arrêté royal du 7 juin 2023 modifiant l'arrêté royal du 26 mai 2019 fixant les grilles de référence visées à l'article 61/3 de la loi du 4 avril 2014 relative aux assurances, *M.B.* 17 juillet 2023.

completed: one examining the application of the RTBF to breast cancer (2022)[2] and another focusing on type 1 diabetes (2024)[3].

1.4 Project objective

This project constitutes the third study within the KCE *Right to be forgotten* program, focusing specifically on thyroid cancer. The current exceptions to the general waiting period for individuals diagnosed with thyroid cancer are defined in the reference grids annexed to the RD of 7 June 2023. These reference grids establish the following waiting periods for individuals diagnosed with thyroid cancer – defined as time after completion of active treatment, during which no disease recurrence occurs:¹⁷

- Papillary or follicular thyroid cancer, Stage I, diagnosed before age 45: 3 years
- Papillary or follicular thyroid cancer, Stage I or II, diagnosed at age 45 or older: 3 years
- Papillary or follicular thyroid cancer, Stage III, diagnosed at age 45 or older: 5 years.

The objective is to assess the survival of individuals diagnosed with thyroid cancer compared with that of the general population in Belgium. Based on the most recent evidence, the project will formulate recommendations – particularly for the Price Monitoring Office and national legislators – regarding potential updates to the current reference grids.

Text box 1 – The Price Monitoring Office and the Compensation Fund

- The Partyka Law (2014) which aims to facilitate access to outstanding balance insurance for individuals with increased health risk, led to the creation of the **Price Monitoring Office for the Tariffication of Outstanding Balance Insurance** (Opvolgingsbureau voor de Tarifiering Schuldsaldooverzekering - Bureau du Suivi de la tarification assurance solde restant dû, **OBT-BST**) and the **Compensation Fund**.

The **OBT-BST**¹⁸ has been issued two main tasks.

- **First**, it investigates cases in which applications for outstanding balance insurance - linked to the purchase of a sole and primary residence - are refused on medical grounds or are subject to excessive premium surcharges. When a policyholder disagrees with the proposed premium, they notify the insurer, who must then submit the file to the reinsurer for reassessment. If coverage is refused or if the basic premium is increased by more than 75%, the prospective customer may submit the case to the OBT-BST for review. OBT-BST assesses whether the insurer's proposal is medically and actuarially justified. The insurer is obliged either to follow the OBT-BST's opinion or to withdraw from the contract.
- **Second**, the OBT-BST is responsible for approving the medical questions included in insurers' health questionnaires.
- The OBT-BST is composed of representatives from the insurance sector as well as patient and consumer organisations, and it is chaired by a magistrate. Requests for intervention are free of charge. The chair, the members, and any external experts consulted are entitled to remuneration. Operating costs are covered jointly by the Compensation Fund and the Insurance Ombudsman, which also provides logistical support.

¹⁷ [Referentierooster kankeraandoeningen | FOD Economie](#)

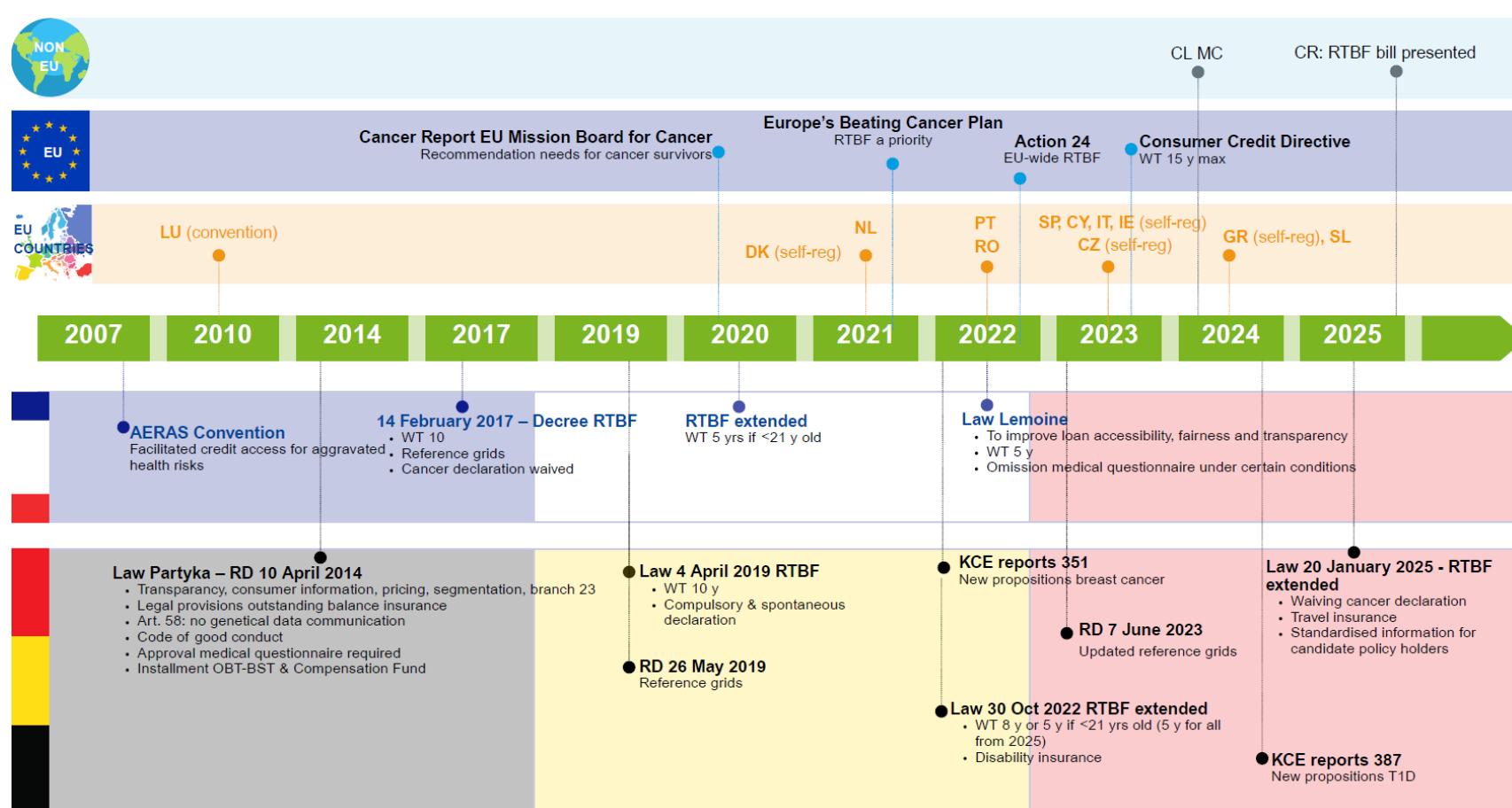
¹⁸ <https://www.opvolgingsbureau-bureaudusuivi.be/nl/>



- **The Compensation Fund** (Accesso vzw), jointly financed by insurers and credit institutions¹⁹, operates as a solidarity mechanism that distributes the cost of increased risks across all market actors. For outstanding balance insurance relating to the acquisition of a sole and primary home, it intervenes automatically when the basic premium is increased by more than 125% for medical reasons. In such cases, the Fund covers the portion above the 125% threshold up to a maximum of 925% of the basic premium, with any amount beyond 925% payable by the customer. This mechanism, operated by Accesso vzw, has been in place since 30 December 2014.

¹⁹<https://www.accesso.org/>

Figure 1 – The history of RTBF in Belgium within the international landscape—key milestones and provisions



Sources: KCE reports 351 and KCE reports 387, <https://endingdiscrimination-cancersurvivors.eu>, AERAS Convention (<https://www.aeras-info.fr/sites/areas/accueil.html>). For a description of the OBT-BST and Compensation Fund, see Textbox 1. ISO 3166 Country Codes are used: LU: Grand Duchess of Luxembourg, DK: Denmark, NL: the Netherlands, PT: Portugal, RO: Romania, SP: Spain, CY: Cyprus, IT: Italy, IE: Ireland, CZ: Czechia, GR: Greece, SL: Slovenia, CL: Chili, MC: Monaco, CR: Costa Rica. WT=waiting time, self-reg: self-regulatory practices/codes of conduct, T1D: type 1 diabetes, y: years, OBT-BST: Opvolgingsbureau-Bureau du Suivi, Price monitoring Office for outstanding balance insurance policies. This overview may not be exhaustive.



2 THYROID CANCER

KEY POINTS

- **Thyroid cancer is a relatively rare malignancy**, ranking fifteenth in incidence across Europe for both sexes combined. Incidence peaks in middle-aged adults and is about 2.5 times higher in women than in men.
- **Incidence increased markedly from the 1980s to the early 2010s**, largely due to enhanced detection of small, asymptomatic, and indolent tumours. Incidence rates have **plateaued in recent years**, coinciding with reclassification of certain indolent tumours as non-malignant and clinical guidelines aimed at reducing overdiagnosis and unnecessary treatment.
- **In Belgium**, about 1,000 new thyroid cancer cases are diagnosed annually. **Mortality is low, with a national 5-year net survival of 94%.**
- **Outcomes vary substantially by tumour type and by the extent of spread at diagnosis.** Most cases (~90%) are well-differentiated thyroid carcinomas, which generally have excellent survival. **Medullary thyroid carcinoma** accounts for ~4% of cases and shows good-to-intermediate prognosis, whereas **anaplastic thyroid carcinoma** represents 2-3% of cases and is associated with a **very poor prognosis**.

2.1 Incidence

Thyroid cancer (TC) is the most common endocrine malignancy, yet it remains a relatively rare cancer overall, ranking fifteenth in incidence across Europe for both sexes combined.²⁰[4] Incidence peaks in middle-aged adults and is about 2.5 times higher in women than in men.²⁰

From the 1980s through the early 2010s, thyroid cancer incidence rose steadily in high- and middle-income countries, a trend largely attributed to increased detection of small, indolent tumours.[4-7] This rise coincided with the widespread use of diagnostic techniques such as neck ultrasonography and fine-needle aspiration (FNA), which substantially increased the detection of subclinical thyroid nodules and cancers.[8, 9] Over the past decade, however, incidence rates appear to have plateaued.[4, 5, 10-12] This stabilization is thought to reflect evolving clinical practice guidelines that discourage FNA of small, asymptomatic nodules and recommend surveillance for nodules with low-suspicion features and benign cytology.[7, 8, 13, 14] In addition, the fourth edition of the WHO Classification of Tumours (2017) reclassified certain indolent thyroid lesions, including non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP), thereby reducing their classification as malignant and contributing to lower reported thyroid cancer incidence.[15]

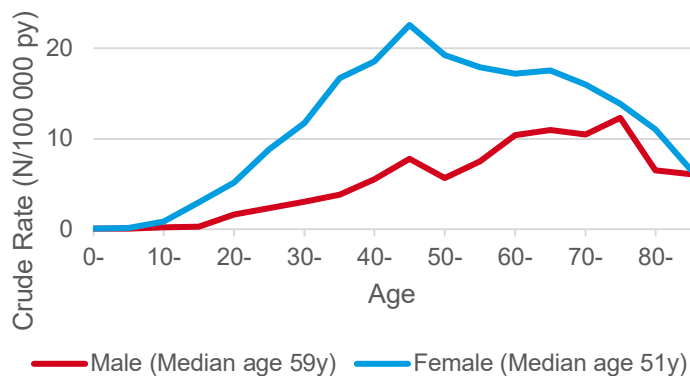
In Belgium, about 1,000 individuals have been diagnosed with thyroid cancer each year; most cases present at stage I (see Figure 2 and Figure 3).²¹ Mirroring international trends, thyroid cancer incidence in Belgium peaked around 2014 and has gradually declined since, particularly among women. A pronounced drop occurred in 2020, coinciding with the COVID-19 pandemic and the temporary reduction in non-urgent diagnostic activity (see Figure 4).²² Regional variation has been observed, with higher incidence rates in the southern part of the country (see Figure 5); this variation has been associated with regional differences in diagnostic imaging and thyroid surgery use, potentially reflecting increased detection of indolent thyroid carcinomas.[9, 16-18]

²⁰ [Cancer Today](#)

²¹ Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR): [2025_BE_CFS2023_THYROID_SEPT1_V3_0.pdf](#)

²² Kort rapport – Kanker in België, 2020 (English: “Short report – Cancer in Belgium, 2020”): [Brief](#)

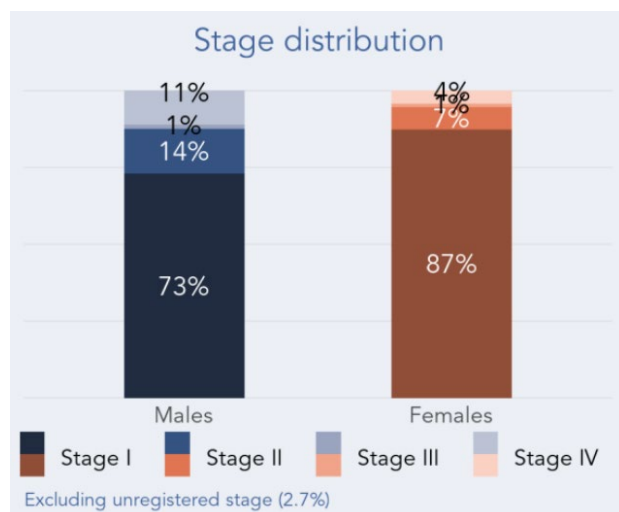
Figure 2 – Incidence rates of Thyroid Cancer in Belgium (2019-2023), by sex



Age-specific incidence rates: number per 100,000 person-years (py)

Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

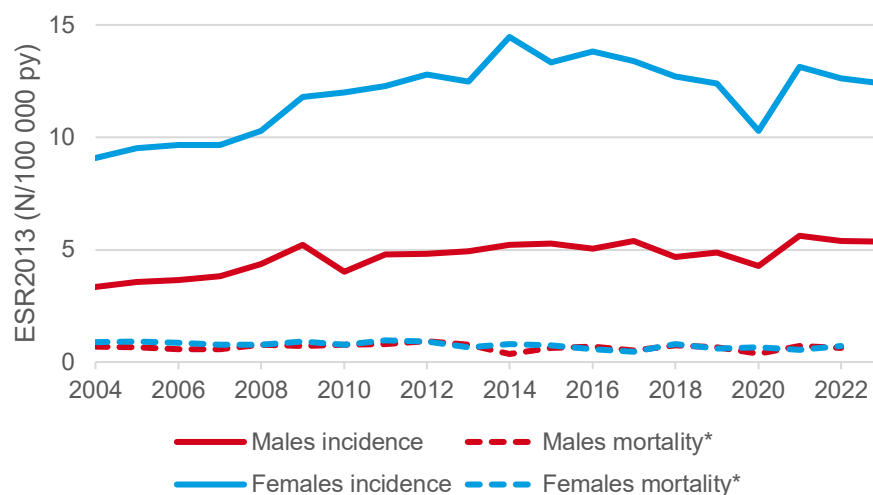
Figure 3 – Stage distribution at diagnosis Thyroid Cancer in Belgium (2023)



Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)



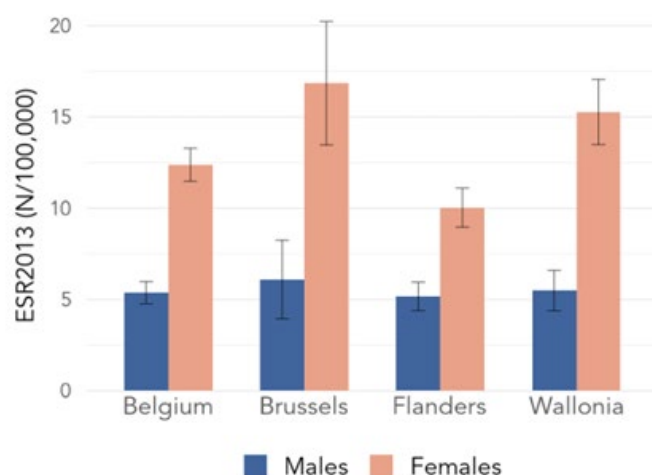
Figure 4 – Thyroid Cancer: trends in incidence and mortality in Belgium (2004-2022), by sex



Age-standardised incidence/ mortality according to the 2013 European Standard population (ESR2013).
Py=person-years

Source: Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

Figure 5 – Incidence rates of Thyroid Cancer in Belgium (2023), by region



Age-standardised incidence rates by region according to the 2013 European Standard Population (ESR2013)

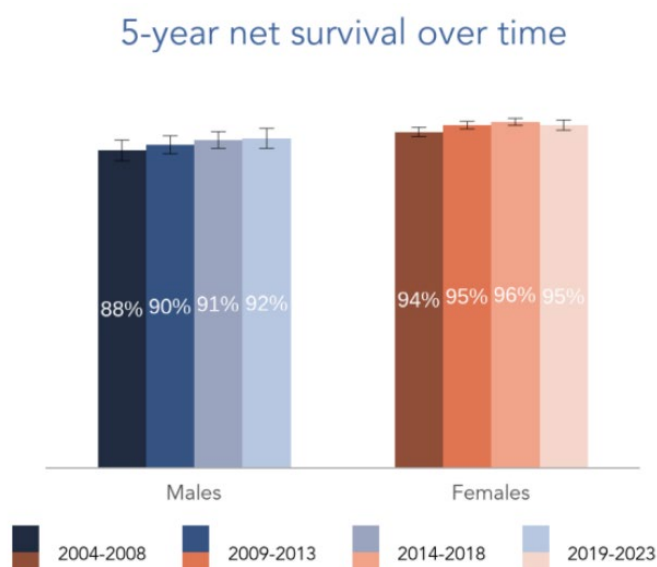
Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

2.2 Prognosis

2.2.1 Overall net survival

In contrast to the rising incidence observed over past decades, thyroid cancer mortality has decreased and remains consistently low worldwide, ranking approximately 24th among cancers.²³[19] The overall prognosis is favourable: in Belgium, the mortality is low, and the 5-year net survival²⁴ is approximately 94% (see Figure 4 and Figure 6), consistent with statistics from other countries.^{25 26 27 28 29 30 31} However, TC comprises heterogeneous histological subtypes with markedly different prognostic profiles. Survival outcomes depend on tumour biology, molecular characteristics, and disease extent at presentation.[20]

Figure 6 – Thyroid Cancer: 5-year net survival in Belgium (2004-2023), per 5-year incidence period, by sex



Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

²³ [32-thyroid-fact-sheet.pdf](#)

²⁴ Net survival is the probability of surviving cancer up to a given time since diagnosis, assuming that cancer is the only possible cause of death.

²⁵ <https://seer.cancer.gov/statistics-network/explorer/> (accessed on 8 May 2025)

²⁶ <https://ecis.jrc.ec.europa.eu/data-explorer/#/> (accessed on 8 May 2025)

²⁷ <https://www.iss.it/en/-/eurocare-5-study-results-database-1> (accessed on 8 May 2025)

²⁸ <https://www.e-cancer.fr/> et <https://www.santepubliquefrance.fr> (accessed on 8 May 2025)

²⁹ <https://nordcan.iarc.fr/en> (accessed on 13 May 2025)

³⁰ <https://nordcan.iarc.fr/en/dataviz> (accessed on 13 May 2025)

³¹ https://nkr-cijfers.iknl.nl/viewer/incidentie-per-jaar?language=en_GB&viewerId=d00ea024-7d10-4f33-98f1-b2c1dadaee6e (accessed on 13 May 2025)



2.2.2 Prognostic heterogeneity

2.2.2.1 TNM classification

The Union for International Cancer Control (UICC) tumour–node–metastasis (TNM) classification system stages thyroid carcinoma according to disease-specific mortality risk. The current 8th edition, implemented in 2018, applies distinct staging principles to three major categories of thyroid carcinoma: differentiated thyroid carcinomas, medullary thyroid carcinoma, and anaplastic thyroid carcinoma, each with its own TNM definitions (see Figure 7 and Figure 8).[21]

For differentiated thyroid carcinoma (DTC), TNM-8 applies a strongly age-dependent staging system. All patients younger than 55 years are classified as Stage I (no distant metastasis) or Stage II (distant metastasis present). In patients aged ≥ 55 years, stage grouping is determined by tumour size, gross extrathyroidal extension, and the presence of regional lymph-node involvement and/or distant metastasis.

For medullary thyroid carcinoma, TNM-8 applies an age-independent staging system based only on tumour size and extent, regional nodal disease, and distant metastasis. All anaplastic thyroid carcinomas are classified as Stage IV at diagnosis, regardless of tumour size, nodal status, or distant spread.

Figure 7 – Thyroid gland UICC TNM-8 staging system

Age at diagnosis	T category	N category	M category	Stage
<i>Differentiated thyroid cancer</i>				
<55 years	any T	any N	M0	I
	any T	any N	M1	II
≥ 55 years	T1	N0/NX	M0	I
	T1	N1	M0	II
	T2	N0/NX	M0	I
	T2	N1	M0	II
	T3a/T3b	any N	M0	II
	T4a	any N	M0	III
	T4b	any N	M0	IVA
	any T	any N	M1	IVB
<i>Medullary thyroid cancer</i>				
any	T1	N0	M0	I
	T2	N0	M0	II
	T3	N0	M0	II
	T1-3	N1a	M0	III
	T4a	any N	M0	IVA
	T1-3	N1b	M0	IVA
	T4b	any N	M0	IVB
	any T	any N	M1	IVC
<i>Anaplastic thyroid cancer</i>				
any	T1-T3a	N0/NX	M0	IVA
	T1-T3a	N1	M0	IVB
	T3b	any N	M0	IVB
	T4	any N	M0	IVB
	any T	any N	M1	IVC

Source: Unified UICC and AJCC (American Joint Committee on Cancer) Thyroid gland TNM-8 staging system: [Pathology Outlines - AJCC / TNM Staging](#)

Figure 8 – Thyroid gland TNM-8 staging system definitions

TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤ 2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤ 1 cm in greatest dimension limited to the thyroid
T1b	Tumor > 1 cm but ≤ 2 cm in greatest dimension limited to the thyroid
T2	Tumor > 2 cm but ≤ 4 cm in greatest dimension limited to the thyroid
T3*	Tumor > 4 cm limited to the thyroid or gross extrathyroidal extension invading only strap muscles
T3a*	Tumor > 4 cm limited to the thyroid
T3b*	Gross extrathyroidal extension invading only strap muscles (sternohyoid) from a tumor of any size
T4	Includes gross extrathyroidal extension into major neck structures
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing carotid artery or mediastinal vessels from a tumor of any size
NX	Regional lymph nodes cannot be assessed
N0	No evidence of regional lymph nodes metastasis
N0a*	One or more cytologic or histologically confirmed benign lymph node
N0b*	No radiologic or clinical evidence of locoregional lymph node metastasis
N1*	Metastasis to regional nodes
N1a*	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes; this can be unilateral or bilateral disease
N1b*	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes
M0	No distant metastasis
M1	Distant metastasis

*all categories may be subdivided as solitary tumor (s) and multifocal tumor (m) – the largest tumor determines the classification

Source: Unified UICC and AJCC Thyroid gland TNM-8 staging system: [Pathology Outlines - AJCC / TNM Staging](#)

Transitioning from TNM-6/7 to TNM-8 led to downstaging of up to one-third of patients, reflecting major conceptual revisions.[22-24] Key changes include:[8, 21]

- Increasing the age cut-off for DTC staging from 45 to 55 years.
- Removing microscopic extrathyroidal extension from the T3 definition.
- Eliminating N1 disease as an automatic criterion for Stage III.
- Introducing T3a (tumours >4 cm confined to the thyroid) and T3b (tumours with gross strap-muscle invasion).
- Reclassifying Level VII lymph nodes from N1b to N1a.
- Revising stage groupings in DTC for older adults with distant metastasis.

2.2.2.2 Histology-based prognosis

The differentiated thyroid carcinoma constitutes the groups with the most favourable prognosis overall. It encompasses several subtypes with distinct histological and biological characteristics:

- *Papillary thyroid carcinoma (PTC)* accounts for more than 80% of all thyroid cancers and is typically diagnosed at Stage I (see Figure 9).[13, 25] While certain rare variants (tall-cell, columnar-cell, hobnail) exhibit more aggressive behaviour, classical PTC carries an excellent prognosis, with 10-year overall survival of ~93%.[8, 26].
- *Follicular thyroid carcinoma (FTC)* represents ~4% of cases and generally has a very good outcome, with 10-year overall survival of ~87%.[27]
- *Oncocytic carcinoma (OCA)*, previously classified as a subtype of FTC, accounts for ~2% of thyroid cancers. It exhibits greater aggressiveness, with an estimated 10-year survival of



~82%.[27, 28] In BCR statistics, OCA has historically been pooled with FTC due to its low incidence and coding conventions (see Figure 10).

- *Poorly differentiated thyroid carcinoma (PDTC)* comprises invasive, high-grade follicular-cell–derived tumours characterized by solid, trabecular, and insular growth patterns. PDTC is rare and has a markedly worse prognosis than other DTC, with 10-year overall survival ~50%.[20, 29, 30] Population-based cancer registries, including BCR, do not report PDTC separately, reflecting historical ICD-O coding, diagnostic variability, very low incidence, and the need for epidemiological stability.

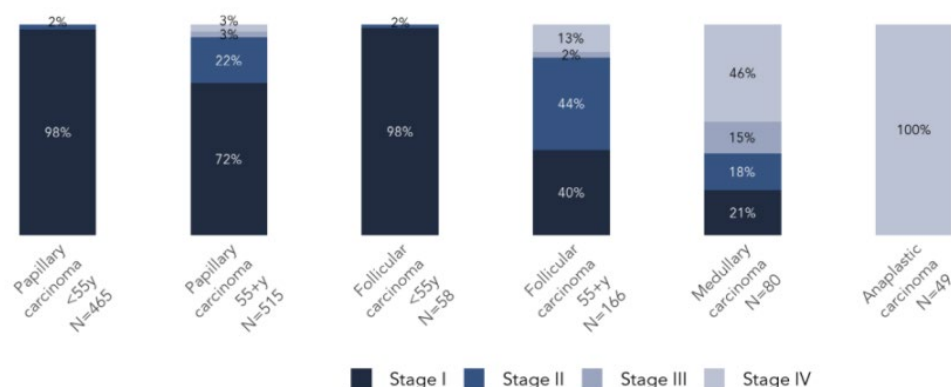
PTC, FTC and OCA collectively constitute the **well-differentiated thyroid carcinomas (WDTC)**.³² Despite some prognostic variation across histological subtypes, WDTC overall carry an excellent prognosis, with surgery being curative for most patients.[13, 25] Across WDTC, the strongest predictor of disease-specific survival is the presence of distant metastasis at diagnosis.[8] Importantly, the vast majority of WDTC patients (~97%) present without evidence of distant metastasis.[31]

The 5th edition WHO classification (2022) further refined the taxonomy of DTC (see section 2.2.2.4).

Anaplastic thyroid carcinoma (ATC), also termed undifferentiated carcinoma, is rare (~2-3% of all thyroid carcinoma cases) but highly aggressive and is considered one of the most lethal human solid tumours. Median survival following diagnosis is approximately 4 months.[13, 20]

Figure 9 – Thyroid Cancer: stage distribution at diagnosis in Belgium (2019-2023), by sex and histology

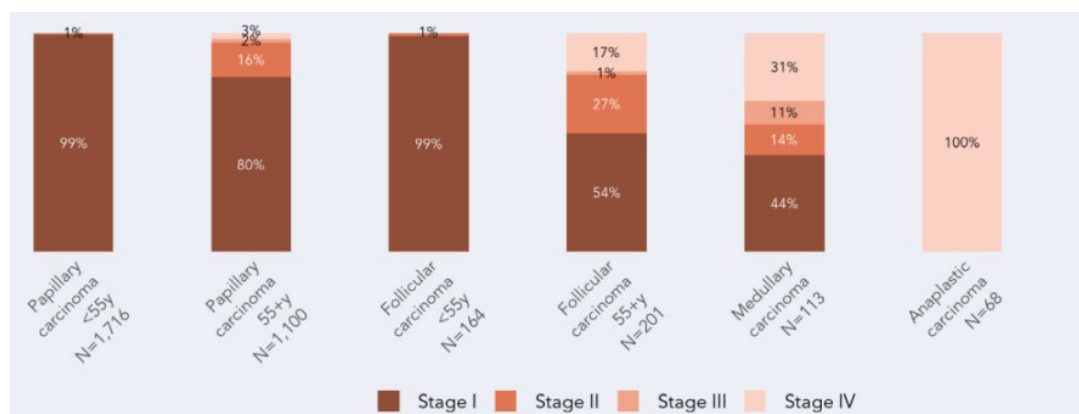
Males



³²

A type of thyroid cancer in which the cancer cells resemble normal thyroid cells when viewed under a microscope (source: [Definition of differentiated thyroid cancer - NCI Dictionary of Cancer Terms - NCI](#))

Females



Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

Figure 10 – Thyroid Cancer: 5-year net survival by histology (2019-2023)

5-year net survival by type, 2019-2023, % (95% CI)				
	Males		Females	
Total	91.8%	(89.0%; 94.6%)	95.5%	(94.1%; 96.8%)
Type				
Papillary carcinoma	98.0%	(95.3%; 100.8%)	98.4%	(97.2%; 99.7%)
Follicular carcinoma	94.4%	(87.9%; 101.4%)	94.4%	(88.8%; 100.4%)
Medullary carcinoma	81.8%	(68.5%; 97.8%)	94.4%	(84.3%; 105.8%)
Anaplastic carcinoma	26.1%	(15.7%; 43.4%)	5.4%	(1.9%; 15.9%)

Source: Cancer Fact Sheets 2023, Belgian Cancer Registry (BCR)

Medullary thyroid carcinoma (MTC) comprises ~4% of thyroid cancer cases and derives from parafollicular C-cells, making it biologically distinct from follicular-cell–derived tumours (DTC and ATC). The 10-year net survival in MTC is ~78%. [14, 32, 33]

2.2.2.3 Other prognostic factors

Next to TNM stage, several additional factors influence outcomes:

- **Tumour related factors:** Radioactive iodine (RAI) non-avidity, high mitotic and necrotic activity, solid/ trabecular/ insular growth patterns are associated with poorer clinical outcomes. [14, 34] In MTC, sporadic type, characterized by somatic gene mutations, confers a worse prognosis than hereditary disease. [35]
- **Biochemical factors:** Rising serum thyroglobulin levels in DTC and increasing calcitonin levels in MTC, especially when accompanied by a short doubling time, suggest a worse prognosis. [14]
- **Molecular and genetic factors:** Mutations such as BRAF V600E and TERT promoter alterations are associated with more aggressive tumour behaviour and worse prognosis. [14]
- **Diagnosis – and treatment related factors:** Timely diagnosis and adherence to evidence-based treatment protocol, as well as response to therapy have been associated with better prognosis [14].



- **Sex:** Male sex has been associated with higher prevalence of advanced stage, however, multivariable analyses have not confirmed sex as an independent prognostic factor for disease-specific survival in follicular-derived thyroid carcinoma.[36] Because of this lack of independent prognostic value, sex is not included in the American Thyroid Association (ATA) risk of recurrence prediction modelling.[8]
- **Nodal disease burden:** The prognostic significance of regional lymph node metastasis in PTC remains incompletely defined. While some studies suggest that high-volume nodal disease may be associated with increased recurrence and potentially higher mortality risk, others report little to no effect on survival.[8, 37-39] In MTC, the number of metastatic lymph nodes involved is well established as a prognostic factor and is consistently associated with worse patient outcomes.[40, 41]
- **Distant metastasis in DTC:** Among patients with DTC and distant metastases, the lungs represent the most common site of involvement.[8] Importantly, a distinction must be made between clinically evident distant metastases detectable by conventional anatomic imaging modalities such as computed tomography (CT), and small-volume (“micrometastatic”) distant disease, typically defined as metastatic deposits <10 mm in diameter.[34] Such micrometastatic disease is frequently CT-occult and is most often identified by functional imaging, particularly radioiodine whole-body scanning (WBS), commonly performed after RAI therapy.[8, 34, 42-44] While macroscopic (≥ 10 mm) distant metastases, particularly when RAI-refractory, are consistently associated with inferior disease-specific survival,[45, 46] patients with pulmonary micrometastatic disease demonstrate high rates of response to RAI therapy, frequently achieving complete structural and biochemical remission, translating into excellent long-term prognosis.[34, 47, 48]
- **Age at diagnosis:** The TNM-8 classification applies different staging for DTC patients younger than 55 years versus those aged 55 years or older, based on validation studies supporting the 55-year age cutoff.[31]. However, the prognostic role of age for certain disease-related outcomes remains debated, as a more recent large cohort study found no association between age and treatment-free survival in DTC.[8, 49]. Conversely, although age is not incorporated into the current UICC staging system, it has been shown to have prognostic significance in medullary TC.[32]

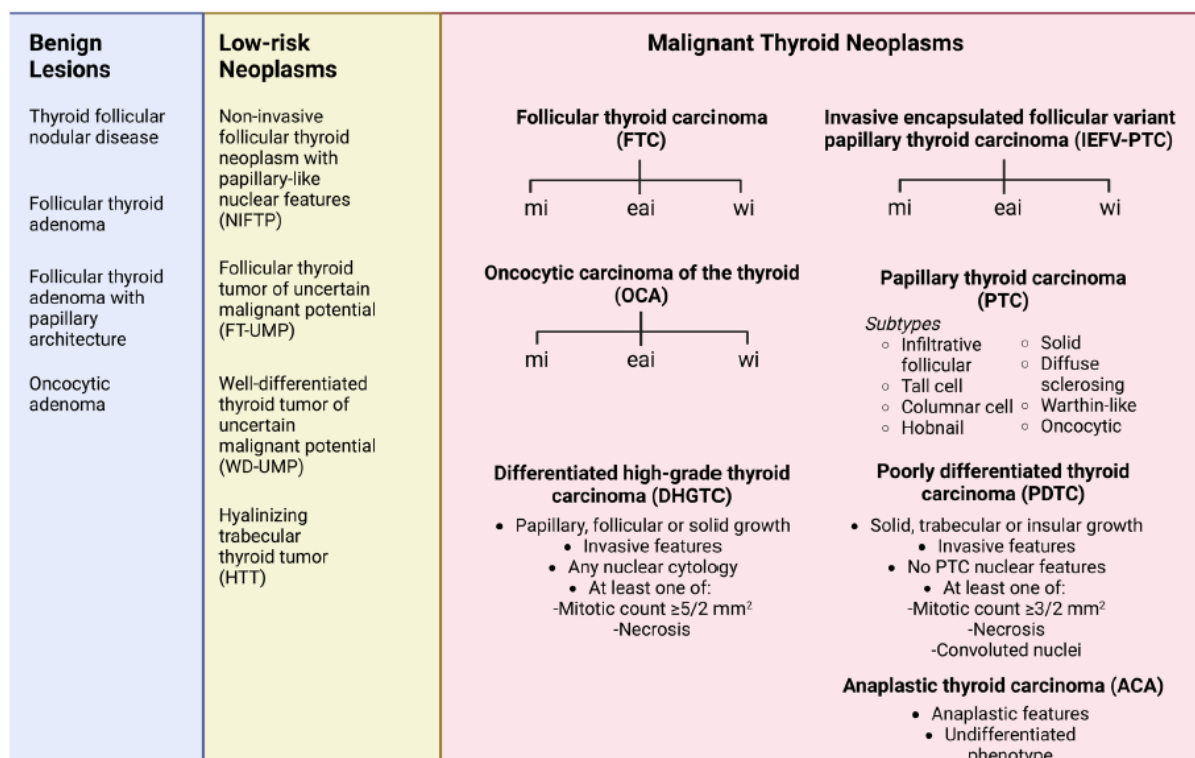
2.2.2.4 2022 WHO diagnostic and prognostic classification of thyroid neoplasms

The 2022 WHO Classification of Endocrine Tumours introduced a refined diagnostic framework that integrates cell of origin, cytopathologic and histopathologic characteristics, molecular alterations, and biological behaviour.[20] Follicular-cell-derived neoplasms are now systematically organized into three categories: benign neoplasms, low-risk neoplasms, and malignant neoplasms; and several new malignant tumour groups have been distinguished (see Figure 11).

The key updates relevant to malignant thyroid carcinoma in the 2022 WHO classification include the following:[20, 29]

- **Invasive encapsulated follicular variant papillary TC (IEFV-PTC)** is now separated from classical PTC due to its RAS-like molecular profile, which is biologically closer to FTC than to BRAF-mutated PTC. IEFV-PTC represents about 6% of TC and has survival prognosis comparable with classic PTC.[20]
- **Differentiated high-grade thyroid carcinoma (DHGTC)** is introduced as a new diagnostic category. It includes PTC, FTC and OCA with high-grade features, characterized by increased mitotic activity (cell division within the tumour), tumour necrosis (cell death within the tumour), and more aggressive clinical behaviour than WDTC. DHGTC is biologically and clinically related to PDTC. Together, PDTC and DHGTC represent up to 5% of thyroid carcinomas and typically occur in adults >50 years, often with large tumours and frequent nodal metastases.[20, 29]

Figure 11 – Main diagnostic groups of the 2022 WHO classification



Overview of the main diagnostic groups of the 2022 WHO classification of thyroid tumors. Not included here are mixed medullary and follicular cell-derived carcinomas, salivary gland-type carcinomas of the thyroid, thyroid tumors of uncertain histogenesis, intrathyroid thymic tumors and embryonal thyroid neoplasms. MI, minimally invasive; EAI, encapsulated angioinvasive; WI, widely invasive. Created using BioRender.com.

Source: Juhlin et al. 2023 [29]

- **Squamous cell carcinoma** of the thyroid is now re-classified as a subtype of anaplastic thyroid carcinoma, reflecting its shared biology and uniformly poor prognosis.
- **Oncocytic carcinoma**, formerly referred to as Hürthle cell carcinoma, is reaffirmed as a distinct histotype, characterized by >75% oncocytic cells.

The 2022 WHO update also introduces a **prognostic grading system** for follicular-cell-derived carcinomas, based on differentiation and proliferative grading, i.e. high mitotic activity and tumour necrosis (see Figure 12).[20] Well-differentiated carcinomas (PTC, FTC, OCA) retain characteristic follicular or papillary structures and low mitotic activity, resulting in excellent survival. High-grade follicular-cell-derived tumours (DHGTC, PDTC) demonstrate increased mitoses and tumour necrosis, corresponding to an intermediate prognosis. Complete loss of differentiation, as seen in anaplastic carcinoma, is associated with the poorest outcomes.

An overview of the histological types and variants of thyroid carcinoma, including estimated prevalence and 10-year overall survival, is provided in Appendix 1.



Figure 12 – Prognostically relevant classification of follicular-cell-derived carcinomas of the thyroid (WHO classification update, 2022)

Histotype	Differentiation (growth pattern)	Grade (mitotic activity, tumor necrosis)	Prognosis
PTC	Good (papillae, follicles)	Low	Excellent
FTC			
OCA			
DHGTC (papillary, follicular, oncocytic)		High	Intermediate
PDTC	Poor (solid/trabecular/insular growth)		
ACA	Absent (undifferentiated growth)		Dismal

PTC - papillary thyroid carcinoma; FTC - follicular thyroid carcinoma; OCA - oncocytic carcinoma, DHGTC - differentiated high grade thyroid carcinoma; PDTC - poorly differentiated thyroid carcinoma; ACA - anaplastic carcinoma.

Tumors with mixed histologic features should be typed according to the component with highest grade and least differentiation

Source: Baloch et al. 2022[20]

3 METHODOLOGICAL EXPLORATION

KEY POINTS

- **Waiting periods for accessing the Right to Be Forgotten (RTBF) for cancer survivors vary markedly across Europe.** These differences reflect not only the limited availability of robust scientific evidence to support harmonized timelines, but also national variation in legislative pathways.
- **Time-to-cure (TTC) analysis is a robust and appropriate method** for defining RTBF waiting periods and has already informed reference grids in several countries.
 - Cure models derive TTC using **net survival**, accounting for background mortality in the general population and assuming cure once the net survival function stabilizes into a plateau.
 - Statistical cure corresponds to the time point at which net survival approaches 100%, indicating that **residual excess mortality has become negligible**. It is defined at the group level and is not equivalent to clinical cure, which is defined by the absence of detectable disease at the individual level.
 - There is no universally accepted definition of “negligible” excess mortality; the previous KCE report adopted a stringent threshold, requiring **the annual conditional net survival (CNS) to exceed 99%**.
 - Both **mixture and non-mixture cure models are methodologically valid**; the choice depends on model fit and analytic aims. Flexible parametric non-mixture models are able to accommodate complex net survival trajectories.
- In actuarial practice, the Standardized Mortality Ratio (SMR) and its derivative, the Excess Mortality Ratio ($EMR = SMR - 1$) are commonly used to determine premium surcharges for applicants with elevated risk. Although not grounded in published evidence or formal regulation, **the Belgian Price Monitoring Committee considers $EMR \leq 25\%$ as negligible excess mortality**.
- This study uses flexible parametric non-mixture cure models to determine time-to-cure (TTC) in thyroid cancer and **cross-validates these TTC estimates with SMR-based excess-mortality measures** commonly used in actuarial practice, ensuring results that are both epidemiologically robust and actuarially interpretable.
- The data from the **Belgian Cancer Registry (BCR)**, which has captured **over 99% of cancer diagnoses in Belgium since 2004**, enable up to 21.3 years of follow-up. Based on the variables available in the BCR and consistent with the TNM staging system, the thyroid cancer cohort is stratified into the main clinical categories - differentiated, medullary and anaplastic thyroid carcinoma. Age and the presence of clinically confirmed distant metastasis at diagnosis are incorporated as additional prognostic factors.



3.1 Variation in waiting periods to open right to be forgotten across Europe

Relative survival analysis based on population-wide cancer registry data are routinely performed in cancer epidemiology[50-55], yet methods tailored specifically to the RTBF context remain scarce. Beyond France³³ and Belgium³⁴, reference grids with reduced waiting periods have also been incorporated into RTBF frameworks in Luxembourg³⁵, Italy³⁶, and the Netherlands^{37, 38}. In the earliest editions of these frameworks, both Luxembourg and Belgium largely re-used the French reference grid. In contrast, Italy and the Netherlands have introduced markedly different waiting periods for cancer survivors, including individuals with a history of thyroid cancer (see Table 1).

Table 1 – Reduced waiting periods for thyroid carcinoma across national RTBF legislations

Country	Population scope	Waiting period (years from end of treatment)
France (2022)* Belgium (2025)*	Papillary or follicular thyroid cancer, Stage I, diagnosed before age 45	3
	Papillary or follicular thyroid cancer, Stage I or II, diagnosed at age 45 or older	3
	Papillary or follicular thyroid cancer, Stage III, diagnosed at age 45 or older	5
Italy (2024)	Thyroid cancer: women diagnosed at age < 55 years; men diagnosed at age < 45 years; excluding anaplastic tumours for both sexes	1
Netherlands (2025)	Hürthle cell, follicular, papillary, incl. mixed subtypes, thyroid cancer Stage: T1N0M0; T2N0M0; T3N0M0	3
	Hürthle cell, follicular, papillary, incl. mixed subtypes, thyroid cancer in men and women diagnosed at age <55 years Stage: T1N1M0; T2N1M0; T3N1M0	6
	Medullary: T1N0M0	6

**In France and Belgium, the general RTBF waiting period was reduced to 5 years in 2022 and 2025, respectively. As a result, the previously defined 6-year waiting period for papillary or follicular thyroid cancer, Stage III, age ≥ 45, is now effectively capped at 5 years.*

Dedicated scientific studies supporting evidence-based RTBF grids have so far been published only in Belgium.[2, 3] Nevertheless, several research groups recommend using *time-to-cure* analyses

³³ <https://www.aeras-infos.fr/sites/aeras/accueil/la-convention-aeras/le-cadre-de-la-convention-aeras/le-droit-a-loubli-et-la-grille-1/la-grille-de-reference-aeras-1.html>

³⁴ Updated reference grids RD 7 June 2022, https://www.ejustice.just.fgov.be/mopdf/2023/07/17_1.pdf#Page10

³⁵ <https://www.aca.lu/wp-content/uploads/2022/06/CONVENTION-DROIT-A-LOUBLI-.pdf>

³⁶ <https://www.gazzettaufficiale.it/eli/id/2024/04/24/24A02057/SG>

³⁷ <https://www.kanker.nl/gevolgen-van-kanker/verzekeringen-en-kanker/algemeen/schone-lei-regeling-voor-ex-kankerpatienten>

³⁸ ['Schone lei-regeling' uitgebreid: ex-kankerpatiënten kunnen zich makkelijker verzekeren - NTVO](#)

based on population-based registry data to inform waiting periods,[2, 56-60] and such analyses have already been used to support RTBF legislation in Italy, France³⁹ and Belgium.[2] The substantial inconsistencies across European countries likely reflect differences in national legislative processes and in the relative weight given to scientific evidence versus stakeholder consensus, notably insurers and patient organizations.

3.2 The concept of statistical cure

Time-to-cure analysis relies on the concept of statistical cure, which applies only at the population level and does not necessarily imply medical cure for individual patients.[61] A group of cancer survivors is considered statistically cured when they experience the same mortality as matched individuals from the general population.[62] For most cancers, all-cause mortality peaks shortly after diagnosis, then decreases and eventually plateaus at the level of the general population's mortality.[63]

Time-to-cure (TTC) is defined as the point in time at which the all-cause mortality rate of cancer survivors returns to the level expected in the general population.[50, 59, 60, 64, 65]

TTC is obtained with the so-called *cure models*, by using the concept of **net survival (NS)**, which represents the probability of survival if cancer were the only possible cause of death.[66] Using national mortality statistics, NS quantifies the excess hazard attributable to cancer after matching patients to the general population by age, sex, and year of diagnosis.[67] Statistical cure is achieved when excess mortality approaches zero and the all-cause hazard converges to that of the general population.[67]

TTC is closely linked to **conditional net survival (CNS)**, the probability of surviving an additional number of years (k), given that patients already survived a certain number of years (t):

$$\text{CNS}(t,k) = \text{NS}(t+k)/\text{NS}(t).$$

CNS reflects how risk of death evolves over time.

TTC can be defined by the CNS threshold at which excess mortality is deemed negligible. As of today, a shared or simple definition of cancer cure is still lacking.[68] Some groups define TTC as “the time post-diagnosis at which 5-year CNS exceeds 95%”,[50, 57, 58, 68-71] while others as “time to attain cure probability ≥ 0.95 ”.[59] The KCE breast cancer report defined statistical cure as time point at the 1-year CNS lies above 99% (including the upper bound of its 95% confidence interval), in combination with an excess mortality rate <50 per 1000 person-years.[2] Actuarial experts have criticized the 0.99 1-year CNS cut-off as arbitrary, arguing that it may still imply significantly elevated death probabilities relative to the general population.[60, 72]

3.3 Time-to-cure methods

Due to lack of international consensus, a rapid review of TTC methods was conducted (see Appendix 2). Across seventeen studies published in the past fifteen years, two primary model classes emerge: *mixture* and *non-mixture cure models*. Both are fitted to net survival outcomes derived from the Pohar-Perme estimator,[73] and both require specifying a cure threshold.

³⁹ Personal communication with G. Dal Maso and V. Jooste, the principal investigators of the time-to-cure analysis in Italy and France, respectively.



3.3.1 Mixture cure models

In mixture cure models (MCM), a population is treated as a mixture of two groups: cured individuals, whose mortality matches that of the general population, and uncured individuals, who remain at excess risk of death due to cancer.[50, 56-58, 61, 70, 74-76] MCM estimate the survival function $S(t)$ is a weighted sum of the survival function of the cured fraction ($S_0(t)$) and that of the uncured patients $S_1(t)$:

$$S(t) = \pi S_0(t) + (1 - \pi) S_1(t),$$

where π is the cured proportion.[61, 67]

The EUROCARE studies define TTC as the time from diagnosis needed to reach a 5-year CNS>95%, i.e. a cumulative net survival probability >95% over the 5-year interval $[t, t+5]$ conditional on surviving up to time t , assuming that the residual 5% excess mortality is clinically negligible.[58]

3.3.2 Non-mixture cure models

Non-mixture cure models (NMCM) do not explicitly split the population into cured and uncured groups, assuming a single survival distribution for the entire population.[59, 65, 77-79] The model estimates an asymptote for the survival function at the cure proportion, i.e. predicts a point where the survival function levels off, indicating the proportion of patients who are considered cured. This parametric NMCM was subsequently extended to the net survival framework by incorporating expected mortality rates from the general population. Overall survival can be expressed as the product of the expected survival and disease-related (relative) survival:

$$S(t) = S_*(t) \pi^{(1 - S_{z(t)})},$$

where $S_*(t)$ is the expected survival function, π is the cure fraction, and $S_{z(t)}$ is a standard parametric survival function, for example a Weibull or lognormal distribution.[64, 67]

Flexible parametric cure model use cubic splines to model the underlying hazard function without imposing a predefined parametric distribution.[64] A cubic spline is a flexible parametric function to model complex, non-linear relationships between variables. It involves dividing the data into several sequential intervals and fitting a cubic polynomial (a polynomial of degree three) to each interval.[80] These polynomials are joined smoothly at points called “knots”. [81] The number of knots is determined by the user. By adjusting the number and placement of knots, cubic splines can adapt to various data patterns.[81]

In the most published NMCMs, time to cure was defined as “the minimum time since cancer diagnosis to reach a cure probability ≥ 0.95 ”, with the cure probability at a given time calculated as the ratio between the cure proportion and the net survival.

3.3.3 Practical application of cure models

A comparative evaluation of MCM, flexible parametric NMCM, and flexible mixture cure models (FMCM) has shown that MCMs are often too restrictive for accurately capturing survival dynamics.[82, 83] Flexible parametric NMCMs or FMCMs are recommended as more suitable alternatives, although FMCMs may produce wide confidence intervals in some settings.[83]

In practice, model selection generally depends on data structure and intended interpretation.[84] MCMs allow differential covariate effects on cure probability vs survival of the uncured (useful for therapy effects), while NMCMs model the cohort as a whole.[84]

When survival is either notably high or low, flexible parametric models are recommended, with a graphical assessment of goodness of fit.[85] These models appear to offer greater adaptability in shaping the parametric distribution and greater sensitivity to small excess risk.[85]

The accuracy of estimates is based on the size of the study population and the length of patient follow-up. Robust estimations require large samples and a long follow-up period - at least 15 years - to identify a clear plateau.[85] Estimates based on extrapolated rather than observed data may be biased, with results sensitive to extrapolation methods.[72, 82]

TTC estimates also vary depending on the chosen CNS threshold,[59, 82, 84] and recent research has attempted to circumvent arbitrary survival cut-offs by estimating the time to null excess mortality hazard[65] or by adapting actuarial correction factors used for premium calculations in the general population.[72] There is therefore no universally accepted standard for estimating waiting periods in the RTBF context, leaving room for further methodological development.

3.4 Actuarial methods

The types of mortgages and the principles of mortgage insurance are addressed in the insurance-technical section of the KCE report on the right to be forgotten in type 1 diabetes.[3] The life insurance premium in the context of an outstanding balance insurance is computed as the sum, over all years until maturity, of the outstanding amount to be reimbursed in case the policyholder dies during a certain year k , discounted with the guaranteed rate. It represents the net present value of the future cash-flows, weighted by the survival probability: [3, 60, 72]

$$P_x = \sum_{k=0}^{n-1} SRD_k \cdot {}_k p_x \cdot q_{x+k} \cdot \frac{1}{(1+i)^{k+1/2}}$$

where

- P_x : Unique premium for the outstanding balance product
- x : Age at the underwriting date
- n : Length of the mortgage (and thus of the insurance contract)
- SRD_k : Outstanding amount at time k
- q_{x+k} : Annual mortality probability at age $x+k$
- i : Guaranteed interest rate

The survival and mortality probabilities, which vary with age, are estimated from standard life tables and applied over the duration of the mortgage. Insurers may use different versions of the life tables to estimate the annual probability of mortality/ survival in the general population:[3, 60]

- Annually published life tables of Statbel⁴⁰ (the Belgian statistical office);
- Regulatory “XK” life tables, derived from Statbel’s national mortality statistics and calibrated using a methodology defined in Annex 1 of the Royal Decree of 14 November 2003 governing life insurance activities;
- Experience market life tables constructed by the National Bank of Belgium (NBB) and reflecting the mortality observed within portfolios of companies controlled by NBB.

The NBB life tables exhibit the lowest mortality rates compared to Statbel and XK life tables, due to the higher socio-economic profile of the insured population.[60]

For individuals with elevated health risks—such as those with a history of cancer—insurers often rely on scientific population studies to quantify mortality risk over time relative to the general population. A



common metric used in this context is the Standardized Mortality Ratio (SMR), which represents the ratio of observed deaths in the study population to the expected number of deaths in a demographically matched general population (adjusted for age, sex, and calendar year). To estimate the premium surcharge, insurers use the Excess Mortality Ratio (EMR), calculated as $EMR = SMR - 1$.⁴¹ There is no universally fixed threshold for what constitutes a "negligible" EMR in insurance underwriting. However, in practice, $EMR \leq 25\%$, corresponding with $SMR \leq 1.25$ is considered negligible by the insurers, meaning no additional premium is applied.⁴²

3.5 Strengths and limitations of the cancer registry data for thyroid cancer

This study uses data from the Belgian cancer registry (BCR),⁴³ established on 28 June 2005 to ensure the systematic and continuous collection of cancer data in Belgium. Its mission is to collect, validate, and analyse nationwide cancer information in a uniform and high-quality manner.⁴⁴

Hospitals and pathology laboratories are legally required to report a minimum dataset to the BCR, including unique patient identifier, incidence date, basis of diagnosis, WHO performance score, tumour topography and morphology, behaviour, laterality, grade of differentiation, stage (clinical, pathological and combined TNM). The BCR captures more than 99% of all cancer diagnoses in Belgium and provides up to 21.3 years of follow-up, making it a robust source for population-based incidence and survival analyses. Nevertheless, several clinically relevant prognostic variables are not routinely registered (see Table 2).

Table 2 – Prognostic factors in thyroid cancer and their availability in BCR

Prognostic factor at diagnosis*	Routinely captured?
Age	yes
Tumour histology	yes
TNM stage	yes
Tumour grade	no
Tumour differentiation	no
Vascular invasion	no
Extrathyroidal extension (ETE)	no
Multifocality	no
Mitotic/necrotic activity	no
Molecular and genetic markers	no
Biochemical markers	no
Treatment received	no
Response to treatment	no
Tumour progression	no
Patient comorbidities	no

*See Chapter Thyroid cancer

⁴¹ Based on the IA-BE (Institute of Actuaries in Belgium) training and Reacfin survey (see KCE report on T1DM), the excess mortality rates are provided by the re-insurers.

⁴² Source: OBT-BST communication; IA-BE training

⁴³ <https://kankerregister.org/en/mission>

⁴⁴ The organisation of cancer registration in Belgium is detailed in the law of 13 December 2006.

Stratification of the cohort by histology presents certain limitations. The currently used 3rd edition of the WHO's International Classification of Diseases for Oncology (ICD-O-3), issued in 2000, does not assign unique morphology codes to several aggressive thyroid cancer subtypes — such as hobnail and diffuse sclerosing variants of PTC. Furthermore, due to absence of specific codes for PDTC and DHGTC, and because tumour grade and differentiation are inconsistently captured, the prognostic categorization introduced in 2022 WHO classification cannot be applied. The forthcoming fourth edition (ICD-O-4) is expected to address these gaps by clarifying morphology codes for rare and aggressive variants and aligning with the 5th edition of the WHO Classification of Endocrine Tumours.⁴⁵

A TNM-stage-based segmentation also presents challenges because the TNM system has undergone major revisions over time. Across the 6th, 7th, and 8th editions (2004–2023), several definitions and stage groupings were modified, affecting comparability and prognostic interpretation (see Section 2.2.2.1). As a result of these changes, a tumour categorized as T3 in 2005 may be classified as T1 or T2 in 2020, solely due to evolving criteria.

An additional limitation inherent to cancer registry data is the reliance on patient status at diagnosis, which represents a static assessment and does not account for changes in risk and prognosis over time. In DTC, post-treatment re-assessment - particularly response to RAI therapy - may result in downstaging, or identification (and subsequent eradication) of RAI-avid micrometastatic disease (also see 2.2.2.3).

Given these limitations, the prognostic framework used in this analysis is based on the factors captured in the BCR that remained stable over the follow-up period, namely TNM-defined clinical subgroups - differentiated thyroid carcinoma (WDTC, PDTC, and DHGTC combined), medullary thyroid carcinoma, and anaplastic thyroid carcinoma. Age and the presence of clinically confirmed distant metastasis at diagnosis, defined as metastases detected by clinical symptoms and/or conventional imaging, were incorporated as additional prognostic factors.

⁴⁵[IACR - International Classification of Diseases for Oncology \(ICD-O\)](#)



4 ETHICAL AND LEGAL ISSUES

KEY POINTS

Fair segmentation in insurance: a balance between individualistic and group-based equality

- Fair segmentation in private insurance means balancing **individualistic equality** - ensuring universal access and non-discrimination - with **group-based equality**, where segmentation aligns premiums with the risk individuals bring to the pool.
- In recent decades, the individualistic approach to equality has influenced insurance law, prompting specific regulations on segmentation criteria like gender, age, genetics and other factors. Insurers now face restrictions on using certain traits, which can lead to subsidizing solidarity between groups, potentially raising premiums or limiting underwriting flexibility.

Regulated Segmentation Criteria:

- **Genetic information**
 - In Belgium, prospective policyholders must disclose manifested genetic conditions, but not non-manifested (predictive) genetic information.
- **Gender**
 - Insurers are not allowed to apply different premiums and benefits to insured based on gender.
- **Age**

Insurers may differentiate based on age, provided the distinction is objectively justified by a legitimate aim and the means of achieving that aim are appropriate and necessary.

The right to be forgotten legislation

- The right to be forgotten legislation has introduced significant elements of solidarity in the private insurance industry - such as **uniform, limited waiting periods, right to withhold cancer history after a certain period, and caps on excess premiums**.
- However, there is **no absolute right to obtain outstanding balance insurance** for citizens with significantly elevated health risk.

4.1 Introduction

As outlined in Project objective, this study will assess whether and for which patient groups with a history of thyroid cancer a waiting period deviating from the 'standard' 5-years period is appropriate. To this end, the survival and mortality among individuals with thyroid cancer will be compared with those of the general population. Time to statistical cure will be estimated in the full cohort as well as in clinically distinct subgroups.

Traditionally, it has been widely accepted that private insurers are legitimately allowed to classify and differentiate between applicants according to specific risk factors such as health-based factors (except for certain genetic information, cfr. 4.5.2). An important question, however, is **the extent** to which segmentation can be applied in the field of private insurance. On what grounds is it acceptable to differentiate between individuals who would like to insure themselves voluntarily, especially when it concerns traits that individuals cannot control, such as health-based factors? The justification whether a certain type of differentiation is fair or unfair leads to the consideration of **solidarity in private insurances**: which risk factors or groups deserve solidarity? Over the past decades, solidarity in private insurance has increasingly been incorporated through non-discrimination legislation based on

gender or genetic profile and via the right to be forgotten legislation for persons with a cancer history or with a chronic disease.

In the scope of this report, new challenges regarding fair segmentation and **the extent of solidarity** arise. For example, determining net survival for each TNM group may lead to risk individualization. Combining TNM groups, on the other hand, can result in a shorter waiting period for the worse risks and/or a longer waiting period for the better risks. A shorter waiting period for the worse risks implies that – based on the right to be forgotten – they can benefit earlier from more beneficial premiums, i.e. those charged to the candidate insured without a cancer history. Solidarity from the better risks (i.e., the insured with no cancer history and the insured with a more favourable TNM) towards the worse risks may thus take place.

In order to understand the reasons behind the choice of one option over another in this report and the dynamics this creates, it is necessary to gain insight into certain principles in insurances and how these principles have been challenged over time. In this context, it is important to grasp the rationale of the existing solidarity measures that have been introduced through anti-discrimination laws and in the right to be forgotten legislation in the past decades.

4.2 Methods

Targeted literature review was performed to identify the relevant legal and non-legal literature (e.g., handbooks and papers published in journals on legal and social sciences, policy reports, working papers, position papers from various stakeholders). The legal methodology entails systematic collection and analysis of the national and European law applicable to the subject, parliamentary discussions leading to their adoption, case-law and policy documents.

To collect relevant literature, various databases and search tools were used, including Jura, Stradalex, ScienceDirect, Google Scholar, Medline (Ovid), Embase and Scopus. Relatively simple search strings were applied combining keywords such as solidarity (e.g., chance and subsidizing solidarity), ‘private insurance’, ‘risk classification’, ‘segmentation’, and types of discrimination (e.g., genetic-, sex/gender). After identifying and analyzing key sources, the so-called “snowball method” was used, reviewing the references of those sources to uncover additional essential references. To collect the legislation and case-law, the official legislation and case-law databases such as Eurlex, Curia, Belgian Official journal were consulted.

4.3 Basic principles in insurances: actuarial fairness, segmentation and solidarity

Actuarial fairness is the guiding principle of the insurance industry. It refers to **the idea that all members of an insurance pool should contribute premiums that reflect the level of risk they represent within that pool.**[86, 87] The aim is to ensure equal insurance conditions for similar risks, based on statistical analysis. In practice, insurers aim at preserving **equality between** groups rather than individuals, relying on averages – such as the “average woman” or “the average man”, to guide risk assessment and pricing.[87-90]

Segmentation is a key mechanism to achieve actuarial fairness. **As defined** by Depril and Dhaene, it is *“a technique used by the insurer to differentiate the premium and possibly the cover according to some specific characteristics of the risk to be insured (i.e. the segmentation criteria), with the aim of achieving a better match between the expected cost of the claim and the burden that a given person places on the community of policyholders and the premium that this person has to pay for the cover offered”*.[91]

During the underwriting process, the insurer assesses whether the risk of the prospective policyholder aligns with the assumptions underlying its tariff structure and the associated premium differentiation. If the identified risk does not correspond to any of the predefined risk groups underlying the ordinary tariff framework, the insurer may impose additional conditions, apply a special tariff, or reject the insurance application.



There are **different types of segmentation in insurance**.^[87] Prior to the introduction of the right to be forgotten, **segmentation** practices in outstanding balance insurance for persons treated for cancer or chronic diseases often led to differentiated **tariffs, waiting periods, or even refusal of the insurance contract**. **With the implementation of the right to be forgotten in the Belgian legislation, standardized waiting periods** have been established. This allows individuals (or groups) with a cancer history to access outstanding balance insurance under the same conditions as those without such a history.

The **objective of segmentation** is to organise the groups in such a way that the total premiums collected are sufficient to cover the claims arising within each group.^[92] In principle, insurers aim to establish **solidarity** among individuals with (estimated) equal risks, who may or may not experience a claim. This type of insurance solidarity, called “**chance solidarity**”, refers to the basic logic of insurance as a risk sharing mechanism between the fortunate and the unfortunate. The solidarity here is based purely on chance or coincidence.^[87]

However, if the insurer charges the same premium to everyone, or if the segmentation is poorly constructed, the total premiums may fall short of covering the claims within a group. Therefore, an additional layer of solidarity emerges, classified as “**subsidising (risk) solidarity**”. This occurs when certain risk factors are unknown, non-quantifiable, or deliberately excluded from consideration.^[91, 93] As a result, individuals with lower risk may end up subsidizing those with higher risk.

Deliberate subsidising solidarity is a process where known risk factors are deliberately disregarded, resulting in some policyholders paying a disproportionately high premium to benefit others. Usually this involves a transfer of resources from lower-risk individuals to those with higher risks. An extreme form of deliberate subsidising solidarity can be found in risk-neutral contributions, which are the norm in statutory social insurance systems. In such systems, the whole population is treated as a single, unified risk pool, and each member is entitled to equal-rated solidarity, regardless of individual risk.^[93] The underlying idea is that for insurance schemes deemed essential – such as statutory health insurance – risks are shared across the whole population, and no one is penalized for having poorer health, not even those who maintain an unhealthy lifestyle. For example, smokers do not pay higher contributions to mandatory health insurance than non-smokers, even though they face a higher risk of developing lung cancer. In some social insurance schemes, subsidising **income solidarity may also come into play**. This refers to the equalization of pool members’ financial contribution or benefits based on their economic profiles.^[86, 94]

The right to be forgotten legislation also reflects a form of deliberate subsidizing risk solidarity, as it involves disregarding **the potentially less favourable relative survival** of cancer patients after a waiting period of 5 years (cfr. 4.6.1). Moreover, an additional layer of solidarity has been introduced through the imposition of a **cap on the excess premium** that can be charged to policyholders with an increased risk (cfr. 4.6.3).

4.4 The challenge of “fair” segmentation

The question of what ‘fair’ segmentation is and to what extent it can be applied in private insurance, is closely linked to the concept of **equality**. There is an **inherent tension between an individualistic human rights approach to equality and the “group-based” logic traditionally used in insurance**. A fair insurance system must navigate this tension and strike a balance between these two perspectives.

4.4.1 Human rights approach - equality between individuals

In a human rights context, **equality between individuals** means that all people are entitled to the same rights and freedoms **without discrimination**. They should be treated with **equal dignity and respect and have universal access to essential services**. From this perspective, segmentation based on personal characteristics – such as age, gender, health status, or genetic predisposition – can

be perceived as unfair or even discriminatory, especially when it results in exclusion from services or unaffordable premiums.[95, 96]

This approach to fairness and non-discrimination in insurance is firmly grounded in **international human rights law**, such as the **Universal Declaration of Human Rights**⁴⁶ and the **International Covenant on Civil and Political Rights**⁴⁷, both of which emphasize the right to equality and protection from discrimination.

At the **European Union level**, principles of equality and non-discrimination are embedded in key constitutional instruments. Article 21 of the Charter of Fundamental Rights of the European Union⁴⁸ prohibits discrimination on grounds such as gender, race, genetic features, age, and disability. Complementing this, Article 19 Treaty on the Functioning of the European Union⁴⁹ provides the legal basis for the EU to adopt legislation to combat discrimination, enabling regulatory action across various domains, including private-sector practices such as insurance underwriting.

These EU-level protections operate alongside the European Convention on Human Rights (ECHR)⁵⁰, particularly article 14 and Protocol No. 12. While Article 14 prohibits discrimination in the enjoyment of Convention rights, Protocol No. 12⁵¹ establishes a broader, autonomous ban on discrimination. Together, these instruments form a multilayered framework that constrains the use of personal characteristics in risk segmentation.

Although the human rights contained in the Charter, the Treaty, and the ECHR do not generally have direct horizontal effect - meaning these rights do not, on their own, create standalone claims directly against private insurers - they nevertheless influence private law relationships indirectly. They do so primarily through EU secondary legislation and national implementation measures. In this context, the EU Gender Directive⁵² and the General Data Protection Regulation⁵³ play central roles by restricting how insurers may collect, use, and process sensitive personal data. National legal systems across the EU have incorporated these principles into domestic law⁵⁴, in some cases going further - for instance, by prohibiting the use of genetic information in insurance underwriting. [97, 98]

Moreover, national courts are under a duty to interpret domestic law consistently with EU fundamental rights and, where necessary, to disapply national provisions that violate EU general principles or

⁴⁶ Art. 7 Universal Declaration of Human Rights, [OHCHR | Universal Declaration of Human Rights - English](#)

⁴⁷ Art. 26 International Covenant on Civil and Political Rights, [Ch_IV_04.pdf](#)

⁴⁸ Art. 21 Charter of Fundamental Rights of the European Union, *OJ C 326*, 26.10.2012, [EUR-Lex - 12012P/TXT - EN - EUR-Lex](#)

⁴⁹ Art. 19 Treaty on the Functioning of the European Union, *OJ C 115*, 9.5.2008, p. 1–388, [EUR-Lex - C2008/115/01 - EN - EUR-Lex](#)

⁵⁰ European Convention on Human Rights, ETS N° 005, Rome, 4 November 1950

⁵¹ Protocol No. 12 to the Convention for the Protection of Human Rights and Fundamental Freedoms, ETS , n° 177, Rome, 4.November 2000

⁵² Council Directive 2004/113/EC of 13 December 2004 implementing the principle of equal treatment between men and women in the access to and supply of goods and services, *OJ L 373*, 21.12.2004, p. 37–43, 2004/113/EC-[Directive - 2004/113 - EN - EUR-Lex](#)

⁵³ Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation), *OJ L 119*, 4.5.2016, p. 1–88, GDPR- [Regulation - 2016/679 - EN - gdpr - EUR-Lex](#)

⁵⁴ For Belgium Art. 10 and 11 of the Belgian Constitution form the foundation for **equality and non-discrimination**, reinforcing the legal basis for challenging discriminatory practices—including in areas like insurance, employment, and public services.



Charter rights when acting within the scope of EU law. Through this interpretative duty and the obligation to give primacy to EU law, fundamental rights shape how private-law rules - such as those governing contracts, and insurance practices - are applied in disputes between individuals.

4.4.2 *Insurance approach - equality between groups*

The human rights interpretation of equality between **individuals** stands in contrast to traditional insurance practices, which prioritize **group-based risk classification** and actuarial fairness over individual equity. Upholding equality between **groups** can result in de facto inequality between individuals.[95, 96] Insurance companies have traditionally used segmentation criteria such as **age, gender, and health status** to group individuals and determine premiums. This practice is rooted in the principle of **actuarial fairness** (cfr. 4.3) and is supported by **industrial** and **market-based reasoning**. [93]

From an industrial perspective, segmentation is essential for maintaining financial stability. It enables insurers to use actuarial data to predict risk accurately, avoid adverse selection, and preserve solvency. It is often argued that a policy holder may be reluctant to contribute to the risk coverage of those with higher estimated risk, especially if it results in increased premiums for themselves. If a premium is set higher than what is justified by an individual's (assumed) risk, that person may choose to leave the insurance pool. This phenomenon is known as **subsidy aversion**. [91, 95] This, in turn, results in insurance pools containing a disproportionate share of high-risk individuals, which increases the expected losses within the pool. As premiums rise to compensate for these higher risks, lower-risk individuals are further discouraged from participating - a dynamic known as **adverse selection**. This not only undermines the stability of the insurance pool but also creates a competitive disadvantage for insurance companies. Segmentation also plays a role in counteracting **moral hazard** – the tendency for individuals to take less care in avoiding insured risk because they are protected from the financial consequences. However, if higher risk individuals are required to pay a higher premium, they are incentivised to take the necessary care to prevent the insured event from occurring. [95]

One might assume that insurers always strive for the most accurate and individualized risk classification possible, aiming to minimize subsidizing solidarity. However, in practice, insurers may exhibit aversion to excessive individualisation and do not always pursue extensive segmentation. This is because segmentation goes with costs – such as data collection, analysis, and administrative complexity. If the cost of the segmentation outweighs the financial benefit it brings, further segmentation becomes economically unattractive for the insurer. For prospective policyholders, the cost of segmentation may be reflected in a higher premium, which may make insurance unaffordable. Moreover, when segmentation results in very small groups, it reduces the potential for risk diversification, ultimately leading to uninsurability. [87]

From a market perspective, segmentation aligns with principles such as freedom of contract, where both the insurer and the client are free to enter into an agreement based on mutually accepted terms, including pricing. It also reflects the principle of symmetry of information, where both parties have access to relevant data -such as health status or age- enabling them to make informed decisions. Furthermore, segmentation supports healthy competition by allowing insurers to offer tailored products and pricing strategies that better match individual or group risk profiles.

While these justifications are valid within the insurance industry, they must be carefully balanced against broader concerns related to fairness and equal treatment. Segmentation practices raise important ethical and legal questions especially when they result in exclusion or high additional premiums. As societies increasingly emphasize equality and access, the challenge lies in reconciling industry-driven segmentation with broader social values and commitments to non-discrimination. [93]

4.5 The cases of gender discrimination and genetic discrimination

The cases of banning gender and genetic discrimination have challenged traditional insurance logics regarding the necessity and justification of risk classification. These cases highlight the ethical tension between actuarial fairness and social equity, questioning the assumption that all risk-based distinctions are inherently legitimate. When insurers rely on characteristics such as gender or genetic predisposition - traits that individuals cannot control - there is a risk of reinforcing existing inequalities and excluding vulnerable populations from adequate insurance coverage. As a result, legal and societal debates have emerged around how fairness should be defined in the context of insurance, and whether certain forms of risk classification should be restricted or prohibited.

4.5.1 Ban on gender-based discrimination

In the context of promoting gender equality in the provision of financial services, the European Union adopted a specific legal instrument to address discriminatory practices in insurance. The EU “Gender Directive”⁵⁵ bans direct and indirect discrimination⁵⁶ based on gender in access to and provision of goods and services, including insurance, from 21 December 2007 on. Hence, the use of gender as a factor in the calculation of premiums and benefits may not result in differences between individuals⁵⁷. However, art. 5(2) of the directive allowed member states to make exceptions for insurance contracts where gender is a determining factor in risk assessment, provided the differentiation was based on relevant and accurate actuarial and statistical data. This opt-out clause was particularly relevant for life insurance products such as outstanding balance insurance, where women, due to their (on average) lower mortality risk, traditionally benefited from lower premiums than men.[99]

The original Belgian Gender Act of 10 May 2007⁵⁸, which transposed the Gender Directive into Belgian law, did not apply this opt-out clause, prohibiting discrimination based on gender, including distinctions related to pregnancy, motherhood, gender change, gender identity and gender expression. However, the Act of 21 December 2007 amended this law by integrating the opt-out regime, allowing proportionate direct distinction in life insurance premiums and benefits based on gender, providing that gender is a determining factor in risk assessment and supported by relevant and accurate actuarial and statistical data⁵⁹. This amendment was challenged before the Belgian Constitutional Court by the Association belge des Consommateurs Test-Achats ASBL, a non-profit consumer organization, along with two private individuals. The applicants argued that the Belgian law, which implemented the derogation provided for in Article 5(2) of the Gender Directive, violated the principle

⁵⁵ Art. 4 (1) Gender Directive 2004/113/EC

⁵⁶ Art. 2, a) Gender Directive 2004/113/EC

(a) direct discrimination: where one person is treated less favourably, on grounds of gender, than another is, has been or would be treated in a comparable situation;

(b) indirect discrimination: where an apparently neutral provision, criterion or practice would put persons of one gender at a particular disadvantage compared with persons of the other gender, unless that provision, criterion or practice is objectively justified by a legitimate aim and the means of achieving that aim are appropriate and necessary.

⁵⁷ Art. 5(1) Gender Directive 2004/113/EC

⁵⁸ Wet van 10 mei 2007 ter bestrijding van discriminatie tussen vrouwen en mannen, *B.S.* 30 mei 2007/ Loi du 10 mai 2007 tendant à lutter contre la discrimination entre les femmes et les hommes, *M.B.* 30 mai 2007, [Justel databank](#)

⁵⁹ Art. 3 Wet van 21 december 2007 tot wijziging van de wet van 10 mei 2007 ter bestrijding van discriminatie tussen vrouwen en mannen wat betreft het geslacht in verzekeringsaangelegenheden, *B.S.* 31 december 2007/Loi du 21 décembre 2007 modifiant la loi du 10 mai 2007 tendant à lutter contre la discrimination entre les femmes et les hommes, pour ce qui est de l'appartenance sexuelle en matière d'assurance, *M.B.* 31 décembre 2007 [Justel databank](#)



of equality between men and women. In response, the Belgian Constitutional Court referred the question to the European Court of Justice (ECJ). In its judgment of March 1, 2011⁶⁰ the ECJ addressed the fundamental question of whether it is lawful for insurers to differentiate between men and women when calculating insurance premiums and benefits (for an extensive analysis of the Court's arguments see Goessens, E. and Baere, G.[100]). The Court ruled that **the use of gender as a factor in determining insurance premiums and benefits constitutes unlawful discrimination** under EU law. It emphasized that the principle of **equal treatment between men and women** is a fundamental right, enshrined in the Charter of Fundamental Rights of the European Union, particularly in Articles 21 and 23, which prohibit discrimination based on gender and mandate gender equality in all areas. The Court found that Article 5(2) of the Gender Directive, which allowed Member States to maintain gender-based differences in insurance pricing, undermined the Directive's core objective: the implementation of unigender premiums and benefits in insurance contracts.

A pivotal aspect of the Court's analysis was the **comparability of the situations of men and women** in the context of insurance. The Court affirmed that, for the purposes of applying the principle of equal treatment, **men and women must be regarded as being in comparable situations** with respect to insurance contracts. This conclusion was drawn from the structure and purpose of the Gender Directive, which aims to eliminate gender-based discrimination in access to and supply of goods and services, including insurance. The Court rejected the argument—advanced by the Council and supported by the insurance industry - that actuarial differences in risk profiles between men and women justified differential treatment. This argument was rooted in the insurance industry's “**group approach**” to equality (cfr. 4.4.2), whereby risks, premiums, and benefits are determined based on **group characteristics**. Under this model, individuals are treated according to the average characteristics of the group - here, male or female - to which they belong.[89] **From the insurer's perspective, women and men are not in comparable situations with regard to insurance contracts.** They rely on the statistically proven difference in life expectancy between men and women, which is why they base their premium-tariffs and benefits on gender-specific actuarial calculations. By using different mortality tables, the insurance industry aims to avoid a scenario in which one group - here, one gender - subsidizes the other. This approach is supported by studies such as those conducted by Oxford Economic Research Associates (Oxera), commissioned by insurance associations.[101, 102] While acknowledging that statistical data may reveal average differences in life expectancy or accident rates between genders, the Court emphasized that **such group-based generalizations cannot override the legal requirement to treat individuals equally**.

Special attention should also be given to the opinion of Advocate General Kokott⁶¹ who emphasized that many other economic, environmental and social factors, linked to personal habits and life styles (for example, the type of the professional activity, family and social environment, eating habits, consumption of stimulants and/or drugs, leisure- and sporting activities), have significant effects on life expectancy. In fact, as social change has eroded the traditional division of gender roles, it is no longer possible to establish a clear connection between gender and the effects of behavioural factors on a person's health and life expectancy. Any differentiation made for the purposes of actuarial calculations must therefore be based on objective criteria. As Advocate General Kokott emphasized, *“the use of a person's gender as a kind of substitute criterion for other distinguishing features is incompatible with the principle of equal treatment for men and women”*.

⁶⁰ ECJ 1 March 2011, C-236/09, ECLI:CE:ECHR:2023:0718JUD004925522, Association Belge des Consommateurs Test-Achats ASBL and Others v Conseil des ministres. [EUR-Lex - 62009CJ0236 - EN - EUR-Lex](#)

⁶¹ CJEU, Opinion of Advocate General Kokott delivered on 30 September 2010, Association Belge des Consommateurs Test-Achats ASBL and Others v Council of Ministers, C-236/09 [eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:62009CC0236](#). The Advocate General assists the Court of Justice of the European Union (CJEU) by providing impartial and independent opinions on cases. These opinions are influential but not binding.

As a result of the Court's ruling, from December 21, 2012, insurers across the EU were no longer permitted to apply different premiums based on gender. This implies that men and woman with the same characteristics- such as age and health status- must be charged the same price for identical insurance coverage.

Following the ECJ ruling, the European Commission issued **non-binding guidelines** to assist Member States and the insurance industry in complying with the ruling.⁶² The Commission outlined a **number of gender-related insurance practices that remain compatible with the unigender rule**. These include the use of gender-related information for internal purposes such as calculating reserves, setting internal pricing for risk assessment, determining reinsurance pricing, and gender-based marketing and advertising. Thus, if an insurance company has a customer base with an unequal distribution of men and women, this imbalance may be considered when calculating overall premiums, provided the premiums charged to individual men and women with the same risk profile remain equal.[103]

In its guidelines, the Commission also acknowledged that the shift to unigender premiums might lead to **price adjustments**, particularly for products like life insurance. For instance, women - who typically paid lower premiums due to their longer life expectancy - might experience premium increases, while men might benefit from lower rates. However, the Commission emphasized that **any increase in premiums must be justified and not based on arbitrary criteria**. To mitigate the risk of **market disruption**, the Commission encouraged insurers to innovate and develop competitive unigender products. It also stressed that **financial or administrative burdens** could not justify continued gender-based pricing, reaffirming that economic considerations alone do not override the principle of equal treatment.

In Belgium, it's **common practice amongst insurers** to use gender-specific data for internal actuarial modelling and risk management purposes, particularly in the context of the prudential framework of Solvency II regulation. To project future cash flows, including life insurance capitals in case of death of a policyholder, insurers prefer to use the most accurate data available, which involves gender-specific life tables (for more info see p. 153 of the supplement of the KCE report regarding the right to be forgotten and outstanding balance insurance: a proposition for type 1 diabetes[3]). Hence, while the insurers continue to differentiate between men and women in their internal models, they are required to apply average unigender tariffs to policyholders.

The (potential) impact of the Court's ruling has been widely discussed. The industry expressed concern about the risk of **adverse selection** (see supra 4.4.2). However, a study commissioned by the European parliament, argued that this risk was limited, especially since **all insurers would be subject to the same rules**, thereby **maintaining a level playing field**. [104] Moreover, the relevance of the adverse selection argument also must be assessed within the specific context of each insurance market, and it does not appear to apply uniformly across all types of insurance. [87, 105] For instance, in case of mortgages, where the insurance coverage is deemed essential, the impact of adverse selection is likely to be negligible, as demand in such markets tends to be rather price-inelastic. [89]

⁶² European Commission Guidelines on the Application of Council Directive 2004/113/EC to insurance, in the light of the judgment of the Court of Justice of the European Union in Case C-236/09 (Test-Achats), 2012 O.J. (C 11) 1, ¶ 25; <https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2012:011:0001:0011:en:PDF>



4.5.2 *Ban on discrimination based on genetic characteristics*

The prohibition of discrimination based on genetic characteristics is embedded in international human rights law, foundational legal instruments of the European Union, and national legal systems. In Europe, the cornerstone of this framework is the **Council of Europe's Convention on Human Rights and Biomedicine**, also known as the **Oviedo Convention**.⁶³ This treaty, along with its **Additional Protocol on Genetic Testing for Health Purposes**⁶⁴, explicitly prohibits discrimination based on genetic characteristics and restricts the use of genetic tests to medical purposes only. It clearly excludes their use in non-medical contexts, such as insurance underwriting. Complementing this framework, the **Council of Europe's Recommendation CM/Rec(2016)8 to the member States on the processing of personal health-related data for insurance purposes, including data derived from genetic tests**, calls on Member States to ban the use of genetic test results in insurance.⁶⁵ The Recommendation emphasizes the sensitive nature of genetic data and warns against the risk of social exclusion and unfair treatment if such data were allowed to influence access to financial services. The **Charter of Fundamental Rights of the European Union** reinforces these protections.⁶⁶ **Article 21** prohibits discrimination based on genetic features, while **Article 8** guarantees the right to the protection of personal data, including genetic and health-related information. These provisions support a **human rights-based approach** that prioritizes **individual** dignity and privacy. They uphold an ethical principle that no one should be penalized for traits or conditions over which they have no control.[86, 94]

Many EU member states have incorporated these principles into their national laws. However, approaches vary across countries regarding the extent to which insurers are permitted to access and use genetic information.[97]

Opponents of insurer access to genetic information emphasize the importance of protecting individuals from genetic discrimination and safeguarding their **privacy**. [106, 107] Genetic data is inherently sensitive, often revealing deeply personal and predictive information about an individual's- and their family members'- future health. Using such data in insurance could lead to exclusion, higher premiums, or denial of coverage based on factors beyond a person's control. Moreover, restricting the use of genetic information supports broader **public health goals**. If individuals fear that genetic test results could be used against them, they may avoid testing. This could hinder early diagnosis and treatment, as well as reduce participation in genetic research - ultimately undermining efforts to improve population health.[108, 109] The argument that an absolute ban on the use of genetic information undermines the element of randomness - or "chance" - essential to insurance contracts is countered by the fact that, even in cases of high genetic penetrance, significant uncertainty remains about when and how a condition will manifest.[110] Moreover, evidence suggests, that legislation limiting or banning the use of genetic information by insurers, has not led to significant financial instability in the insurance market.[93, 111]

⁶³ Art. 11 and 12 Convention of 4 April 1997 for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine, European Treaty Series - No. 164, <https://rm.coe.int/168007cf98>

⁶⁴ Additional Protocol of 27 November 2008 to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes, Council of Europe Treaty Series - No. 203, [CETS 203 - Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes](#)

⁶⁵ CM/Rec(2016)8 - Recommendation of 26 October 2016 of the Committee of Ministers to the member States on the processing of personal health-related data for insurance purposes, including data resulting from genetic tests (Adopted by the Committee of Ministers on 26 October 2016 at the 1269th meeting of the Ministers' Deputies, <https://search.coe.int/cm/?i=09000016806b2c5f>

⁶⁶ Charter of Fundamental Rights of the European Union, OJ C 326, 26.10.2012, p. 391–407, [EUR-Lex - 12012P/TXT - EN - EUR-Lex](#)

Advocates of insurer access to genetic information, particularly within the insurance industry, argue that allowing individuals with serious genetic conditions to obtain insurance without disclosure conflicts with the principle of risk-based pricing. They claim that restricted access to relevant risk information could undermine actuarial fairness^[112], potentially leading to adverse selection and financial imbalance.^[113] However, actuarial and economic models generally do not suggest widespread or severe anti-selection effects related to genetic testing.^[89, 114, 115] Moreover, proponents of insurer access argue that banning the use of genetic information actually reinforces the requirement of uncertainty in insurance contracts, which is a foundational element of insurability.^[116, 117]

Furthermore, concerns have been raised about **fairness**, suggesting that the ban on the use of genetic information could lead to **unequal treatment between individuals with genetic versus non-genetic conditions** that have similar health implications.^[118-120] This debate is closely tied to the concept of “**genetic exceptionalism**” - the idea that genetic data is fundamentally different from other types of medical information.^[121, 122] However, many of the characteristics attributed to genetic data - such as its predictive nature or immutability, the involuntary nature, the impact of a diagnosis on privacy and on the psychological health of patients - also apply to non-genetic health data.^[123] Therefore, it is difficult to sustain a clear distinction between genetic and non-genetic information, all the more so because most medical information can be considered at least partially genetic in nature. Using the predictive nature of medical information as a criterion, rather than its genetic nature, may offer a coherent solution in this regard. ^[123]

In **Belgium**, the use of genetic information in insurance is regulated under Article 58 of the Insurance Act 2014⁶⁷, which states that **genetic data may not be disclosed to the insurer**. Furthermore, medical examinations required for the conclusion or execution of an insurance contract **must be based solely on the current health status of the applicant. It explicitly prohibits the use of genetic testing techniques** intended to predict future health conditions.⁶⁸

However, the law does not provide a specific definition of what constitutes “genetic information” or “genetic testing techniques”. ^[123] The lack of statutory definitions does not promote legal certainty, as parties can determine their own contractual definitions.⁶⁹ Several proposals for definitions can be found in European and international binding and non-binding documents and in doctrine.^[124, 125] Legally binding definitions that can be periodically revised to accommodate technological and ethical developments would offer a more sound and sustainable regulatory approach.^[123]

By stating that no account may be taken of an individual's genetic profile at the time of concluding an insurance contract, the law effectively imposes an obligation on the insurer to spread genetic risk across the entire insured population within a given insurance branch. The legislator intends to ensure that the “genetically lucky” contribute to covering the risks of the “genetically unlucky”, thereby establishing a principle of ‘genetic solidarity’.^[126]

In the context of the Belgian legislation, however, there is ambiguity as to whether the ban on use of genetic information in insurance should be interpreted as **absolute** - covering all genetic data regardless of whether a condition has manifested - or **relative**, applying only to predictive or non-manifested conditions. **Manifested conditions** are those in which symptoms have already appeared in the individual. According to traditional insurance principles, these are no longer uncertain risks but known facts, and insurers should be entitled to consider such information in risk assessment. In contrast, **non-manifested conditions** refer to genetic predispositions or risks that have not yet

⁶⁷ Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014/ Loi du 4 avril 2014 relative aux assurances, *M.B.* 30 avril 2014

⁶⁸ Art. 61 Insurance Act 2014 Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014/ Loi du 4 avril 2014 relative aux assurances, *M.B.* 30 avril 2014

⁶⁹ “Assuralia”, the Belgian professional association of insurance companies refers to genetic data as “data related to your genes, DNA, genetic predispositions...”



resulted in symptoms and remain uncertain in terms of onset and severity. Without precise definitions in the law, it is unclear what exactly falls under the scope of the legal prohibition.

Some authors argue that the legislative intent behind the Belgian Insurance Act is clear⁷⁰: the law was designed to protect individuals from discrimination based on their genetic makeup, regardless of whether a condition has already manifested.[110] This interpretation supports an absolute prohibition, prioritizing social solidarity over actuarial fairness, affirming that insurance should not penalize individuals for genetic traits beyond their control. Others, however, interpret the intent of the legislator more narrowly, suggesting that the prohibition targets only predictive genetic information – that is, information related to non-manifested genetic conditions.[127]

Belgian courts uphold the relative interpretation of the ban on the use of genetic information in insurance. In a notable judgement involving three cases, the Court of Appeal, referred to the right to be forgotten legislation (Court of appeal Brussels[128], for a critical approach to this jurisprudence, see [110, 127, 129]) when interpreting the scope of applicant's disclosure obligations. Art. 61/2 § 1 of the 2014 Insurance Act states that⁷¹ persons who have been or are affected by a cancerous disease, regardless of its type, must notify their insurer of that disease when applying for outstanding balance insurance in accordance with article 58 of the Insurance Act. The Court of Appeal interprets this provision as confirmation by the legislator that the obligation to notify applies to any illness that may increase the mortality risk, **regardless of its origin**. Exempting applicants from disclosing genetic conditions, while still requiring disclosure of severe non-genetic conditions, would result in an unequal and discriminatory treatment. The Court of Appeal further notes that many forms of cancer have a genetic origin, reinforcing the relevance of genetic information in assessing mortality risk.

This relative interpretation is also supported by the insurance sector. In its guidance on the protection of health data, “Assuralia”, the Belgian professional association of insurance companies, explicitly states that **manifested genetic conditions** must be reported to the insurer, as they reflect the applicant's current health status.[130]

4.5.3 Differentiation based on age allowed, if justified

Differentiation based on age in insurance is generally allowed, but it is subject to certain conditions and ongoing legal and policy debates - especially at the European level. EU law currently does not prohibit age-based differentiation in insurance or other services outside the field of employment. Insurers can use age as a factor in setting premiums or determining eligibility, if such differentiation is justified.

In 2008, the European Commission proposed a new Equal Treatment Directive aimed at extending protection against discrimination based on age, disability, religion or belief, and sexual orientation to areas beyond employment, including insurance, education, and access to goods and services.⁷² However, this directive is still under discussion and has not yet been adopted. If enacted, it could impose new limitations or regulatory requirements on age-based differentiation in private

⁷⁰ Wetsontwerp op de landsverzekeringsovereenkomst – Memorie van Toelichting, KAMER 1990-91, 23 april 1991, nr. 1586/1/ Projet de loi sur le contrat d'assurance terrestre – Eposé des motifs, CHAMBRE 1990-91, n°. 1586 /1, [K20542377](#)

⁷¹ The obligation for applicants to declare their cancer history to insurers will be abolished as of 1st of June 2026, See art. 5 Wet van 20 januari 2025 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, *B.S.* 30 mei 2025/*Loi* du 20 janvier 2025 modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli, *M.B.* 30 mai 2025.

⁷² COM (2008) 426: Proposal for a Council Directive on implementing the principle of equal treatment between persons irrespective of religion or belief, disability, age or sexual orientation [EUR-Lex - 52008PC0426 - EN - EUR-Lex](#)

insurance. Nonetheless, it is expected to include exceptions for financial services- such as insurance- where differential treatment may still be allowed if justified.[87]

Belgium's **Anti-Discrimination Act of 10 May 2007** prohibits both **direct and indirect age discrimination** across a broad range of domains, including access to goods and services such as insurance. However, **exceptions are allowed** if the age-based treatment is **objectively justified** by a **legitimate aim**, and the means of achieving that aim are **appropriate and necessary** (see further in 4.7 on the three step test).⁷³ This means that insurers may differentiate based on age if they can demonstrate that the distinction is justified according to the legislation. For example, the use of relevant and reliable actuarial or statistical data proving that age is a prognostic factor for mortality, or arguments related to the financial sustainability, may serve as valid justification.[131-133]

In general, age-based premiums in life insurance are considered justified, as mortality risk tends to increase with age. Without segmentation based on age, younger individuals would have to bear a disproportional financial burden of covering the significantly higher mortality risk associated with older age groups.

4.6 The 'right to be forgotten' legislation and other solidarity measures

The challenge of balancing individual human rights with traditional risk-rating practices in private insurance is also at the root of the "Right to be forgotten" legislation.[56, 89, 90, 91, 92, 93] The right to be forgotten, particularly for cancer survivors, emerged in response to growing concerns about fairness, privacy, and equitable access to essential financial services, such as outstanding balance insurance. Although it is not mandatory to have outstanding balance insurance when taking out a mortgage loan, in practice, the absence of such coverage may lead to the bank refusing the loan or offering it under less favourable conditions. The core purpose of the right to be forgotten legislation is to prevent unfair treatment of applicants based on past health conditions that are no longer relevant to an individual's current risk profile.⁷⁴ In this context, several mechanisms have been introduced to protect applicants with an increased health risk, aiming to guarantee both transparency and accessibility in obtaining outstanding balance insurance.⁷⁵ The following sections outline the key measures that directly promote solidarity with applicants facing elevated health risk. These measures may support the rationale for applying segmentation strategies within the TC cohort.

⁷³ Art. 7 Wet van 10 mei 2007 ter bestrijding van discriminatie tussen vrouwen en mannen, *B.S.* 30 mei 2007/ Loi du 10 mai 2007 tendant à lutter contre la discrimination entre les femmes et les hommes, *M.B.* 30 mai 2007, [Justel databank](#)

⁷⁴ Wetsvoorstel tot wijziging van de wet van 25 juni 1992 op de landverzekeringsovereenkomst wat de schuldsaldoverzekeringen voor personen met een verhoogd gezondheidsrisico betreft, KAMER, 2008-09, 6 mei 2009, nr. 52-1977/001; /Proposition de loi modifiant la loi du 25 juin 1992 sur le contrat d'assurance terrestre en ce qui concerne les assurances de solde restant dû pour les personnes présentant un risque sanitaire accru, CHAMBRE, 2008-09, 6 mai 2009, nr. 52-1977/001. <https://www.dekamer.be/FLWB/pdf/52/1977/52K1977001.pdf>

⁷⁵ i.e. the use of medical questionnaires, the motivation duty for insurers in case of refusal or excess premium, the procedure of reevaluation by an reinsurer if the candidate insured disagrees with the excess premium, the intervention of the OBT/BST in case of refusal or excess premium >75%, the intervention of the Compensation fund for excess premiums between 125 and 800% - For an overview of these mechanisms and the history of the right to be forgotten in Belgium (see Background).



4.6.1 Limited waiting periods

Since 2025, Belgium's "Right to be forgotten" allows people who have been cancer-free for 5 years following the end of treatment to obtain outstanding balance insurance without being rejected or charged additional premiums due to their cancer history.⁷⁶ This marks a significant reduction of the waiting period - from 10 years, when the right to be forgotten was first introduced⁷⁷, shortened to 8 years in 2022.⁷⁸ The legislator justified this progressive reduction by the **positive evolution of the 5-year relative survival for the most frequently occurring cancers**.⁷⁹[134] At the same time, the reform aimed to enhance **solidarity between cancer survivors and other insured individuals, recognizing that it is abnormal and unacceptable that cured persons are deprived of life projects such as the purchase of their own property**.

Although the average relative survival of a cancer patient continues to improve, it remains lower than the survival in the general population.[135] Since insurance conditions cannot differ for subscribers with a history of cancer who have completed the 5-year remission period, individuals without a history of cancer will probably subsidise the former group.[136] At the time of the writing this report, there are **no (public) data on the impact of the right to be forgotten legislation on the premiums for outstanding balance insurance**. Individual insurers may accept applicants with a certain level of excess mortality without passing on additional costs to other policyholders.[137]

The legislation allows for waiting periods shorter than 5 years if such differentiation is objectively and reasonably justified based on scientific data, and from both a medical and actuarial perspective. The specific conditions and the respective differentiated waiting periods are specified in two lists, called "reference grids", published in Royal Decrees (also see 1.2).⁸⁰ It should be noted that, at the time of

⁷⁶ Art. 61/2, § 2, section 2 Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014/ *Loi du 4 avril 2014 relative aux assurances*, *M.B.* 30 avril 2014

⁷⁷ Wet van 4 april 2019 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen waarbij voor bepaalde persoonsverzekeringen een recht om vergeten te worden wordt ingevoerd, *B.S.* 18 april 2019/ *Loi du 4 avril 2019 modifiant la loi du 4 avril 2014 relative aux assurances et instaurant un droit à l'oubli pour certaines assurances de personnes*, *M.B.* 18 avril 2019

⁷⁸ Wet van 30 oktober 2022 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, *B.S.* 17 november 2022/ *Loi du 30 octobre 2022 modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli*, *M.B.* 17 novembre 2022

⁷⁹ Wetsvoorstel tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, *KAMER*, 2022-23, 21 oktober 2022, nr. 1639/005, p. 7/ *Proposition de loi modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli*, *CHAMBRE*, 2022-23, 21 octobre 2022, n° 1639/005, p. 7

⁸⁰ Koninklijk besluit van 26 mei 2019 tot vaststelling van een referentierooster met betrekking tot het recht om vergeten te worden in het kader van bepaalde persoonsverzekeringen bedoeld in artikel 61/3 van de wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 14 juni 2019 /*Arrêté royal du 26 mai 2019 déterminant une grille de référence relative au droit à l'oubli en certaines assurances de personnes visée à l'article 61/3 de la loi du 4 avril 2014 relative aux assurances*, *M.B.* 14 juin 2019 ; Koninklijk besluit van 7 juni 2023 tot wijziging van het koninklijk besluit van 26 mei 2019 tot vaststelling van een referentierooster met betrekking tot het recht om vergeten te worden in het kader van bepaalde persoonsverzekeringen bedoeld in artikel 61/3 van de wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 17 juli 2023/*Arrêté royal du 7 juin 2023 modifiant l'arrêté royal du 26 mai 2019 déterminant une grille de référence relative au droit à l'oubli en certaines assurances de personnes visée à l'article 61/3 de la loi du 4 avril 2014 relative aux assurances*, *M.B.* 17 juillet 2023.

It has to be noted that the reference tables assume absence of other risk factors or pathologies in the application of the waiting periods and additional premium modalities. However, candidate insured are, irrespective whether they had a cancer history or not, submitted to the general obligation to report other risk factors or pathologies (that might be – but not necessarily - a sequel of the cancer) (Art. 58 Insurance

writing the report, the reference grids published in the relevant Royal Decrees still include waiting periods of up to eight years. An update is necessary (i.e. maximum waiting period of 5 years). An (unofficial) adapted consolidated version of the reference grid is available on the website of the Federal Public Service Economics.⁸¹

4.6.2 Abolition of the obligation to declare cancer history

The obligation to declare a history of cancer to insurance companies has been a point of discussion on several occasions. The argument used by insurers and upheld in the explanatory memorandum of the Act of 4 April 2019, was to maintain this obligation even after the period foreseen in the 'right to be forgotten' legislation. This was to ensure that applicants would still declare pathologies related to the long-term effects of cancer and its treatment.⁸² Cancer treatment can have side effects that persist for years or even a lifetime. For example, chemotherapy may cause permanent damage to the heart, lungs, or kidneys in certain cases. Rather than placing the burden on the applicant to refrain from reporting certain medical antecedents, the legislator chose to make the insurance company responsible for disregarding certain medical histories, i.e. the history of cancer. In this way, the insured is protected from sanctions related to withholding or inaccurately disclosing information.⁸³

The obligation **for applicants to declare their cancer history to insurers will be abolished as of 1st of June 2026**.⁸⁴ The rationale behind this change is that the obligation to declare cancer history undermines the effectiveness of 'the right to be forgotten'. However, side effects resulting from cancer treatment must still be reported. The law also foresees that insurers should inform prospective policy holders via a standardized information form on the rules related to the (non-) obligation to declare, the Price Monitoring Office for outstanding balance insurance policies (see 1) and the Compensation Fund (see 4.6.3).⁸⁵

It needs to be stressed that the abolishment of the duty to declare a cancer history only applies if a period of 5 years has passed after the successful completion of active treatment, without any relapse. This implies that for cases where shorter waiting periods are defined in the reference grids, declaration of cancer history would be still obligatory. Preparatory work does not give any justification for this differential treatment.

law 4 April 2014) and when requested by the insurer lifestyle and/or behavioural risks. Medical questionnaires used by insurers typically query potential lifestyle and/or behavioural risk factors (e.g. tobacco use, alcohol consumption, body mass index). Based on the assessment of these elements conditions to subscribe, an outstanding balance insurance can individually differ from the conditions defined in the reference tables.

⁸¹ [Referentierooster kankeraandoeningen | FOD Economie](#)

⁸² Wetsvoorstel tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen waarbij voor bepaalde persoonsverzekeringen een recht om vergeten te worden wordt ingevoerd, KAMER, 6 februari 2019, nr. 3524/001, p. 5-6/Proposition de loi modifiant la loi du 4 avril 2014 relative aux assurances qui instaure un droit à l'oubli pour certaines assurances de personnes, CHAMBRE, 6 février 2019, n° 3524/001, p. 5-6

⁸³ Art. 59 and 60 Wet van 4 april 2014 betreffende de verzekeringen, B.S. 30 april 2014/ Loi du 4 avril 2014 relative aux assurances, M.B. 30 avril 2014

⁸⁴ Wet van 20 januari 2025 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, B.S. 30 mei 2025/Loi du 20 janvier 2025 modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli, M.B. 30 mai 2025

⁸⁵ Art. 4 Wet van 20 januari 2025 tot wijziging van de wet van 4 april 2014 betreffende de verzekeringen met het oog op het uitbreiden van het recht om vergeten te worden, B.S. 30 mei 2025/Loi du 20 janvier 2025 modifiant la loi du 4 avril 2014 relative aux assurances en vue d'étendre le droit à l'oubli, M.B. 30 mai 2025



According to representatives of the insurance sector⁸⁶, the legislator deliberately entrusted insurers - rather than the prospective policyholder or their treating physician - with the responsibility for determining whether and from when the “right to be forgotten” applies. They argue that, given the technical nature of the applicable conditions, the risk of errors would be considerably higher if that assessment were left to patients or physicians, and that such errors could trigger legal sanctions that ultimately harm the prospective insured person.

4.6.3 *Capped excess premiums*

Another layer of solidarity has been **introduced through a cap on the excess premium** that may be charged to applicants with an increased health risk.⁸⁷ Patients with a history of cancer who have not yet completed the waiting period - and patients with chronic diseases - may only be charged a capped excess premium or may be refused coverage. A Compensation Fund (*Compensatie Kas – Caisse de Compensation*) covers excess premiums ranging 125% to 925% in the context of a mortgage loan for the first and only residence. Insurers and credit providers are responsible for covering any premium amount above the 125% threshold. The 125% cutoff represents a compromise between the initial proposal from insurers (200%) and the counterproposal of patient and consumer representatives (50%) [138]. The interventions of the Compensation Fund are financed equally: 50% by credit institutions and mortgage companies, and 50% by insurance companies, based on their turnover.⁸⁸ Any amount exceeding 925% of the basic premium must be paid by the client. There is **no (public) data on the impact** of the Compensation Fund’s solidarity mechanism **on the premiums paid by policy holders for outstanding balance insurance**. In 2023, the Compensation Fund paid out 1.7 million Euro, which represents only a very small fraction of the total turnover of insurance companies, credit institutions and mortgage providers.[139] It remains unclear whether these cost are passed on to the clients, e.g. through increased pricing of other insurance products or through higher premiums for the pool of outstanding balance insurance subscribers. A general increase in premiums was observed in a comparable case involving the solidarity mechanism of natural disaster insurance, which is part of fire insurance.[140].

4.6.4 *The financial burden of solidarity measures: a challenging discussion*

Some authors have criticized the solidarity mechanisms introduced by the Belgian legislator in the context of outstanding balance insurance, arguing that they shift the financial burden of social responsibility onto insurers - and indirectly to the group of insured without a cancer history or with a more favourable prognosis - in situations where redistribution between good and bad risks is intended. They question whether alternative corrective mechanisms might have been more effective.[87, 105] Several proposals have been made in which the financial burden of solidarity would be borne by the government, ranging from insurance vouchers financed through tax revenues[141] to partial or full coverage of the excess premiums[142] for high-risks individuals, possibly via the social security system.[96] In such a model, the costs would be covered by the government – and thus by society as a whole - rather than by insurers, who may pass on the additional costs to the pool of outstanding

⁸⁶ Personal communication of the representative of insurers at the OBT-BST

⁸⁷ Koninklijk besluit van 10 april 2014 tot regeling van sommige verzekeringsovereenkomsten tot waarborg van de terugbetaling van het kapitaal van een hypothecair krediet, *B.S.* 10 juni 2014/ Arrêté royal du 10 avril 2014 réglementant certains contrats d'assurance visant à garantir le remboursement du capital d'un crédit hypothécaire, *M.B.* 10 juin 2014

⁸⁸ Art. 27 Koninklijk besluit van 10 april 2014 tot regeling van sommige verzekeringsovereenkomsten tot waarborg van de terugbetaling van het kapitaal van een hypothecair krediet, *B.S.* 10 juni 2014/ Arrêté royal du 10 avril 2014 réglementant certains contrats d'assurance visant à garantir le remboursement du capital d'un crédit hypothécaire, *M.B.* 10 juin 2014

balance insurance policy holders. This is the model often used in **public or social insurance systems**, such as national health services.

However, statutory health insurance systems differ fundamentally from private insurance. In public schemes, solidarity is a constitutive legal principle supported by income-related contributions, broad risk pooling, and an explicit redistributive mandate. Private insurance, by contrast, is organised under contractual freedom and actuarial equivalence, with individualized risk assessment and premiums. While the legislator may introduce targeted solidarity mechanisms - such as the right to be forgotten to prevent unjustified differentiation - such interventions must remain proportionate and exceptional. This directly links to the subsequent question of whether outstanding balance insurance should be regarded as an essential social good. Only if society deems the product sufficiently fundamental to warrant public financing would a shift from private to collective responsibility be coherent.

The decision to classify a private insurance product as essential may appear arbitrary, or even potentially inequitable or discriminatory. Would it be justifiable to define outstanding balance insurance as a social priority, while many people with a history of cancer continue to face significant barriers in accessing rental housing? Is it legitimate to give priority to government funding for outstanding balance insurance in the current context of widespread budgetary constraints across various social sectors, where cost-cutting measures are a pressing reality?

Since outstanding balance insurance is an almost necessary condition for purchasing a home, one might also question whether all citizens have an absolute right to the possibility of homeownership. This issue can be linked to the right to adequate housing, which citizens hold in relation to the government.^[96] This right is embedded in several international⁸⁹ and national legal frameworks.⁹⁰ Although this does not imply that the government must guarantee homeownership for every citizen, it does require ensuring access to safe, affordable, and adequate housing - whether through renting, social housing, or other means. In the realisation of this constitutional duty, the government has a large political margin of decision.

4.7 No legislative guidance on cohort segmentation

The legislation provides no guidance on how cohort segmentation should be conducted for the purpose of defining waiting periods in the reference grids. The inclusion criteria or characteristics specified in the reference grids are limited to **age categories** and/or **the type of cancer**.⁹¹ However, the law does not further specify what is meant by “the type of cancer”. The law nor the preparatory works provide any further guidance regarding the definition of subgroups within a cohort of cancer patients. The law merely states that adjusted waiting periods may be established insofar as they are medically and insurance-technically objective and reasonably justified based on scientific evidence.⁹²

⁸⁹ E.g. Art. 25(1) **Universal Declaration of Human Rights**, [OHCHR | Universal Declaration of Human Rights - English](#); art. 34(3) **Charter of Fundamental Rights of the European Union**, [europa.eu](#)

⁹⁰ Art. 23, 3rd section, 3^o Belgian Constitution

⁹¹ Art. 61/3 § 1 Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014/ *Loi du 4 avril 2014 relative aux assurances*, *M.B.* 30 avril 2014

⁹² Art. 61/3 § 1 Wet van 4 april 2014 betreffende de verzekeringen, *B.S.* 30 april 2014/ *Loi du 4 avril 2014 relative aux assurances*, *M.B.* 30 avril 2014



5 STUDY QUESTIONS AND GENERAL METHODS

5.1 Research question 1: Net Survival

What is the long-term net survival of adults diagnosed with a first primary malignant thyroid carcinoma in Belgium?

Method:

Data from the Belgian Cancer Registry (BCR) for individuals diagnosed with thyroid cancer between 2004 and 2023 are used. Access to BCR data requires approval from the Information Security Committee, which evaluates proportionality and ensures strict protection of individual privacy. Upon approval, KCE receives anonymized data.

Vital status is included in the BCR dataset, obtained via the Crossroads Bank for Social Security ('Kruispuntbank van de Sociale Zekerheid' – 'Banque Carrefour de la Sécurité Sociale', KSZ-BCSS). The dataset includes vital status up to 1 May 2025. Net survival is estimated using Statbel life tables⁹³ (the Belgian statistical office) matched to the cancer cohort on sex, age, calendar year and region. Statbel tables are preferred over the XK and NBB tables because they reflect the general population, whereas insurance-specific tables are adjusted to policyholder profiles (see 3.4). Net survival is calculated using the Pohar-Perme estimator.[73]

Inclusion criteria:

- Individuals diagnosed with a first primary malignant thyroid carcinoma (ICD-10: C73, D09.3) during the incidence period 2004-2023.
- Only invasive (behaviour code 3) and in situ (behaviour code 2) tumours are included. (Benign and borderline lesions - behaviour codes 0 and 1 - are not required to be reported to BCR.)
- Belgian residents with a known social security number (INSZ)
- Age ≥18 years at diagnosis (aligned with adult eligibility for loans).

Exclusion criteria:

- History of prior primary invasive tumours
- Cases with non-specified tumours, i.e. not attributable to an organ or histology.

Time horizon:

Net survival is assessed for the entire follow-up period (up to 21.3 years after diagnosis), which aligns closely with typical mortgage durations in Belgium, where the standard maximum term is 20 years.⁹⁴

⁹³ [Mortaliteit | Statbel](#)

⁹⁴ Source: IA-BE (Institute of Actuaries in Belgium) training

5.2 Research question 2: Time-to-Cure

Assuming the cure hypothesis holds, what is the estimated time to statistical cure (TTC) for the entire cohort, and can clinically distinct subgroups with shorter TTC be identified?

“Time-to-cure” definition

- TTC-estimate (TTC-hat) is defined as the time since thyroid cancer diagnosis at which the estimated 1-year conditional net survival (1-yCNS) first exceeds 99% and remains above this threshold for the remainder of follow-up.

The 95% confidence interval (CI) for the TTC-hat is defined as:

- Lower bound: the time at which the upper bound of the 1-yCNS curve first exceeds 99%.
- Upper bound: the time at which the lower bound of the 1-yCNS curve first exceeds 99%.
- TTC-confirmed is defined as the upper bound of the 95% CI of TTC-hat. This represents the conservative, statistically verified time point by which the cohort can be considered statistically cured with 95% confidence.

Method:

Net survival is graphically assessed for the presence of statistical cure, i.e. a plateau in the curve indicating that excess mortality has approached zero. This plateau provides the first indication of when disease-related excess mortality may no longer be present. If the assumption of cure holds, the excess mortality hazard is estimated using flexible parametric non-mixture cure models. Model adequacy is visually assessed by comparing the predicted net survival function to the non-parametric Pohar-Perme estimator. Model estimates are used to generate the continuous 1-year conditional net survival function.

Time-to-cure is evaluated in the entire cohort and for clinically relevant subgroups, including differentiated, medullary and anaplastic thyroid carcinoma. Within each subgroup, analysis is further stratified by age (<55 vs ≥55 years) and the presence of distant metastasis clinically confirmed at diagnosis.

Results are presented for men and women combined, consistent with Belgian legislation governing insurance underwriting (see Chapter 4).

5.3 Research question 3: Standardized Mortality Ratio

What is the standardized mortality ratio for the entire thyroid cancer cohort and for the clinically distinct subgroups?

Method:

The standardized mortality ratio (SMR) is defined as the ratio of the observed number of deaths in a study population to the expected number of deaths, and is a widely used actuarial indicator of relative mortality risk.^{95 96 97} Observed deaths in the cohort are compared with expected deaths calculated from Statbel life tables matched on sex, age, calendar year, and region. SMRs are calculated for the entire cohort and clinically relevant subgroups defined in Research question 2. Analyses are performed up to 21.3 years of follow-up, both without a waiting period and with waiting periods of 1 to 5 years (see 6.2.4.2).

⁹⁵ <https://lifeexpectancyexpertise.ca/life-expectancy-calculation-methodology/>

⁹⁶ <https://scispace.com/pdf/evidence-based-risk-assessment-4u7uy31umf.pdf>

⁹⁷ https://link.springer.com/chapter/10.1007/978-1-349-14499-0_4



The excess mortality ratio (EMR), calculated as $SMR-1$, determines the excess premium rate (see 3.4). In this analysis, SMR and EMR serve as external validation metrics for the TTC-based cure estimates, enabling comparison between actuarial risk measures and epidemiological survival-based modelling.

From a statistical perspective, mortality comparable to that of the general population is considered confirmed when the SMR approaches 1.0 and its 95% confidence interval includes 1 or lies entirely below 1. In Belgian insurance practice, some residual excess mortality is permitted. EMR values are therefore evaluated against the 25% negligibility threshold set by the Price Monitoring Committee, corresponding to a point estimate $SMR \leq 1.25$.

5.4 Transferring scientific evidence into policy recommendations

Depending on the segmentation strategy, different subgroups may exhibit shorter or longer TTC estimates. Pooling a proportionally large subgroup with a favourable prognosis (e.g., differentiated thyroid carcinoma) with a smaller subgroup associated with poorer outcomes (e.g., medullary thyroid carcinoma) can produce an aggregated Time-to-cure estimate that penalizes one group while benefiting the other, when this estimate is subsequently translated into waiting periods for obtaining the right to be forgotten. It may also mask true differences between subgroups because the smaller subgroup's effect is diluted within the combined analysis.

Determining the most appropriate level of segmentation - whether based on clinical risk, biological distinctiveness, prevalence, or considerations of fairness and proportionality in insurance underwriting - extends beyond statistical evidence alone. Such decisions require a consensus-driven process involving all relevant stakeholders, including patient organizations, clinical experts, and insurers. To support this process, scenario-based results derived from the various segmentation approaches will be synthesized and presented in a structured written consultation. Stakeholders will be invited to rank the proposed scenarios and provide clear justification for their choices. The outcomes of this consultation will serve as the foundation for policy recommendations regarding potential revisions of the current reference grids for individuals with a history of thyroid carcinoma.

6 DATA ANALYSIS PLAN

6.1 Data selection

The initial BCR selection included all cases of primary malignant thyroid carcinoma (ICD-10: C73, D09.3; behaviour codes 2 and 3) among Belgian residents diagnosed between 2004 and 2023. Patients without a national social security number (INSZ/NISS) were excluded, as no vital status could be retrieved for these individuals. Further exclusion criteria are described in Chapter 5. The variables extracted from BCR are listed in Appendix 3.1.

6.2 Data analysis

6.2.1 Descriptive statistics

The thyroid cancer (TC) cohort is described using counts and percentages stratified by sex, age group, period of diagnosis, tumour histology, stage and presence of metastases clinically confirmed at diagnosis. For final T and N staging, the combined clinical and pathological diagnosis was shown, whenever available. For distant metastases, evidence from either clinical or pathological sources is considered sufficient.⁹⁸ The number and percentage of patients with subsequent malignancies within the first five years after the thyroid cancer diagnosis are reported by histological subtype, as such malignancies influence all-cause mortality and must be disclosed to the credit insurer during the waiting period of up to five years in Belgium.

6.2.2 Net survival

Net survival is estimated as described in Chapter 5, using the *rs.surv* function from the *relsurv* package in R.[143] A graphical inspection of the net survival curves is performed to evaluate the plausibility of the cure assumption, which is a prerequisite for applying cure models.[85] Because Pohar-Perme estimates may become unstable when the number of individuals at risk becomes small, potentially restricting reliable non-parametric estimation to shorter follow-up durations than those available in the dataset, decisions regarding the maximal follow-up time used in the analysis are guided by a visual assessment of net survival curves, including standard errors or confidence intervals.

6.2.3 Cure models

6.2.3.1 Application of cure models to estimate conditional net survival

A prerequisite for any cure model is the presence of a cure plateau in the net survival curve,[85] together with the usual survival modelling assumption of non-informative censoring. The plausibility of cure will be visually assessed using the Pohar-Perme estimator.

If the assumption of cure can be accepted, the net survival will be modelled with flexible parametric non-mixture cure models on the log cumulative excess hazard scale using restricted cubic splines to estimate the baseline log cumulative excess hazard.[64] In this framework, the total cumulative hazard, $H(t)$, is the sum of the expected cumulative hazard, $H^*(t)$, and the cumulative excess hazard, $\Lambda_e(t)$:

$$H(t) = H^*(t) + \Lambda_e(t). \quad (1)$$

⁹⁸

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The cumulative excess hazard on the log scale is then modelled as:

$$\ln(\Lambda_e(t)) = s(x; \gamma_0), \quad (2)$$

with $x = \ln(t)$ and $s(x; \gamma_0)$ a restricted cubic spline, or natural spline, defined as:

$$s(x; \gamma_0) = \gamma_{00} + \gamma_{01}v_1(x) + \gamma_{02}v_2(x) + \dots + \gamma_{0K-1}v_{K-1}(x), \quad (3)$$

Where K is the number of knots, and v_l are the spline basis functions. The first spline basis function is simply $v_1 = x$, while for $l=2$ up to $K-1$:

$$v_l(x) = (x - k_l)_+^3 - \tau_l(x - k_1)_+^3 - (1 - \tau_l)(x - k_K)_+^3, \quad (4)$$

with $u_+ = u$ if $u > 0$ and $u_+ = 0$ if $u \leq 0$, k_1 the position of the first knot and k_K the position of the last knot, and $\tau_l = (k_K - k_l)/(k_K - k_1)$. A set of covariates z can be added to the model:

$$\ln(\Lambda_e(t; z)) = s(x; \gamma_0) + \beta^T z. \quad (5)$$

Covariates in the model can be categorical or continuous. This last expression is a proportional excess hazards model, i.e. the covariate effects do not depend on time. Population-based survival studies often show non-proportional covariate effects. Non-proportional terms can be accounted for by including interactions between covariates and splines for time, the final model then becomes:

$$\ln(\Lambda_e(t; z)) = s(x; \gamma_0) + \beta^T z + \sum_{i=1}^I s(x; \gamma_i) z_i, \quad (6)$$

with I the number of time-dependent covariates and $s(x; \gamma_i)$ the spline function for the i^{th} time-dependent effect.

When cure is reached, the excess hazard is zero, and the cumulative excess hazard will be constant after this time. Cure can therefore be incorporated in the flexible parametric survival model by constraining the log cumulative excess hazard to be linear with zero slope after the last knot. More technical details on the effective implementation can be found in Andersson et al. (2011). [64] We use the function `stpm2` from the R package `rstpm`, which is a re-implementation of Stata's 'stpm2'.

Andersson et al. demonstrated that the flexible parametric non-mixture cure model is fairly robust to the number and location of the knots used for the natural splines. We apply either the software default setting or follow their recommendations: (1) placing knots over the whole follow-up period, positioning the last knot at the last observed death time (or slightly beyond), and (2) using the centiles of the distribution of the log death times to determine the knot positions, e.g. 0, 25, 50, 75, 95 and 100 centiles. Furthermore, models with different number of knots can be evaluated with a likelihood ratio test. Predicted net survival curves will visually be compared with the non-parametric Pohar-Perme curve to evaluate the model fit.

The post-estimation functionality of the `predict` function in the `rstpm2` package is used to estimate the net survival for any given combination of covariate strata, with standard errors and confidence intervals generated directly by the software. The cured fraction equals the net survival at the longest available follow-up time. Predicted marginal net survival for the full cohort, or for specific subcohorts, is obtained as a weighted sum of the predicted net survival curves across the relevant covariate level combinations. The standard error of the marginal estimate is derived via matrix multiplication using the delta method (see Appendix 4.1).

The estimated model parameters are then used to calculate the annual conditional net survival (CNS) as a function of time. The relation between net survival probability (NS) and (cumulative) excess hazard is:

$$NS(t) = \exp(-\Lambda_e(t)) = \exp\left(-\int_0^t \lambda_e(u) du\right), \quad (7)$$

with $\Lambda_e(t)$ the cumulative excess hazard up to time t and $\lambda_e(t)$ the excess hazard at time t . The conditional 1 year NS at time t can be obtained from (7) by integrating only over the interval $[t, t+1]$:

$$CNS(t, t+1) = \exp\left(-\int_t^{t+1} \lambda_e(u) du\right) = \exp\left(-(\Lambda_e(t+1) - \Lambda_e(t))\right), \quad (8)$$

Cumulative excess hazard estimates at any time since diagnosis can be obtained from the model parameters, the delta rule is applied to propagate the standard errors. The standard error on the conditional net survival is used to construct a 95% confidence interval assuming asymptotic normality. The resulting 1-year conditional net survival as a function of time since diagnosis will be presented in a graph and a summary at specific time points will be given in a table. The maximum time displayed is limited by either the maximum available follow-up or the reliable range resulting from the Pohar-Perme estimation.

Missing data is not expected to pose a problem for the net survival modelling in the full cohort. The essential variables required for the analysis (age at diagnosis, sex, region of residence, vital status and survival time) are expected to be available for all included patients.

6.2.3.2 Model building procedure

Covariates in the flexible parametric model – clinical prognostic group, age group, and distant metastasis - are added sequentially in the model building procedure. For each covariate, a potential non-proportional effect is examined before adding the next covariate to the model. Non-proportionality is accounted for by including an interaction term between the covariate and the time spline. The presence of non-proportional effects is assessed using a likelihood ratio test (LRT) comparing models with and without the time-dependent interaction. The LRT statistic is calculated as twice the difference in log-likelihood between both models and is compared with a chi-square distribution with degrees of freedom equal to the difference in the number of model parameters.

After all main covariates (and their potential non-proportional effects) have been included in the model, interactions between the main terms are assessed in the same way, using LRTs.

Model fit is visually assessed by comparing the model predicted net survival with the Pohar-Perme estimates, both within specific strata and for the overall (marginal) net survival.

6.2.4 Standardized Mortality Ratio

6.2.4.1 Construction of the periodic person-years life table

The initial data obtained from the Belgian Cancer Registry include, for each patient, the date of diagnosis, the date at which follow-up ended, and the patient's vital status at the end of follow-up (dead or alive, the latter used as censoring indicator). A key feature of prospective epidemiological studies is the representation of follow-up time across multiple time scales, which allows reference



mortality rates from the Belgian general population - provided by Statbel⁹⁹ - to be matched on attained age, sex, region, and calendar year.

To enable this alignment, the original cohort dataset is split into subintervals defined by calendar year, age, and follow-up time, using annual time breaks (see Figure 13). This restructuring results in a person-year dataset, in which each individual contributes one record per year of observation. For each calendar year, we derive the number of patients under observation (person-years), their corresponding attained age, and the number of deaths occurring during that year. All computations are performed in R using the Epi package, specifically the Lexis function.

6.2.4.2 Incorporating waiting periods into SMR estimation

In this analysis, SMRs are calculated over follow-up periods of up to 5, 10, 15, and 21.3 years (entire follow-up), broadly corresponding to common mortgage durations, both with and without the application of a waiting period ranging from 1 to 5 years. Conditional SMRs quantify the long-term mortality experience among individuals who have already survived a defined period after diagnosis, relative to the mortality expected in the general population with similar demographic characteristics.

At waiting time 0, all individuals diagnosed with thyroid cancer (TC) are included. For waiting times 1, 2, 3, 4, and 5 years, we construct landmark cohorts defined as:

- Survived at least WT years after diagnosis (WT = 1,2,3,4,5), and
- Had not developed a new primary tumour within that same WT-year period.

Figure 13 – Construction of the periodic life table

3 patients followed up during 16, 7 and 8 years respectively, and one of them died

Year	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Patient 1	Diag, A=32	A=33	A=34	A=35	A=36	A=37	A=38	A=39	A=40	A=41	A=42	A=43	A=44	A=45	A=46	D=0 A=47
Patient 2			Diag, A=20	A=21	A=22	A=23	A=24	A=25	Lost, A=26							
Patient 3							Diag, A=71	A=72	A=73	A=74	A=75	A=76	A=77	D=1, A=78		
Number of patients	1	1	2	2	2	2	3	3	3	2	2	2	2	2	1	1
Number of death	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
Number of patients/year	31		Number of death on the period		1		Observed mortality rate		1/31							

Individuals who died or developed a second primary tumour before completing the waiting period were excluded from the corresponding conditional cohort. This is consistent with the Belgian RTBF framework, which requires individuals to remain cancer-free during the waiting period.

For a given waiting time (WT), follow-up commences exactly WT years after diagnosis, and subjects are censored at the predefined end of the follow-up period (see Figure 14). Consequently, the number

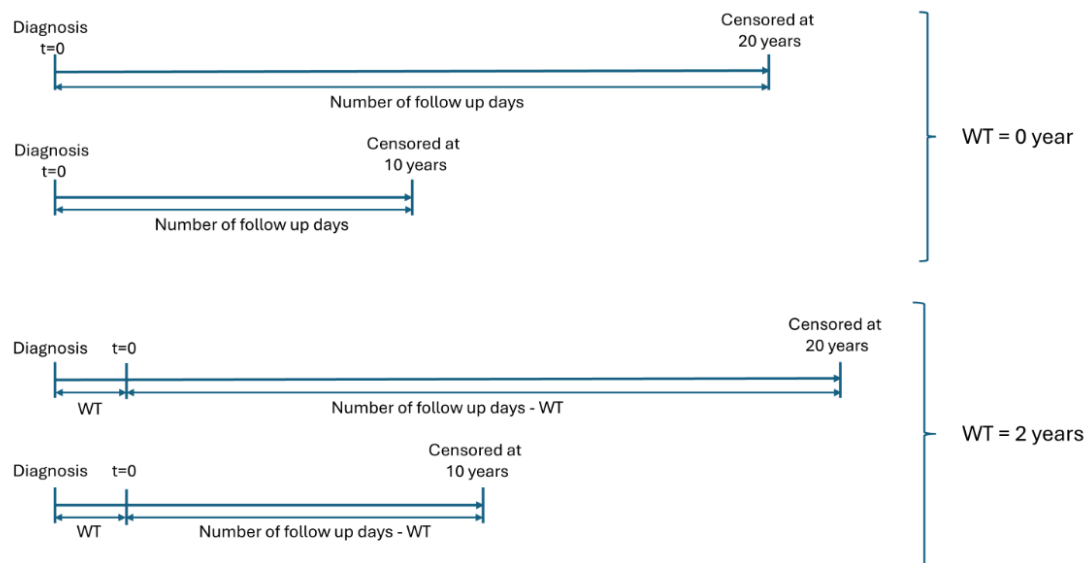
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of subjects from the TC cohort contributing to each analysis varies across WT scenarios. The choice of waiting time determines the number of person-years at risk in the TC cohort at the beginning of the follow-up period, whereas the choice of follow-up duration determines the number of subjects censored at the end of the follow-up period.

The maximum follow-up period (up to 21.3 years) was used as the reference scenario, as it includes the largest number of events and therefore yields the most stable SMR estimates. This choice is consistent with the follow-up horizon applied in TTC modelling. For the calculation of conditional SMRs for the entire observation period, the analysis follow-up was shortened by the applied waiting period (1–5 years), and no patients were censored at the end of follow-up.

Figure 14 – Calculation of follow up duration based on the predefined follow-up period and waiting time



WT: waiting time

6.2.4.3 SMR estimation

In the SMR analysis, the number of deaths in the TC cohort is compared with that expected based on the general-population mortality rates. The expected number of deaths is calculated by multiplying the Statbel mortality rates (matched on age, sex, region, and calendar year) by the corresponding person-years at risk accumulated by the TC cohort.

For each relevant subgroup, the crude observed number of deaths in the thyroid cancer cohort (A) and the expected number of deaths (E) were summed to produce comparable group-level estimates. The SMR was defined as: $SMR = A/E$.

Under the assumption that the observed number of deaths follows a Poisson distribution with mean E , large-sample theory implies that the following test statistic is approximately distributed with mean 0 and variance 1: $\frac{(A-E)}{\sqrt{E}} \sim N(0,1)$

A 95% confidence interval (CI) for the SMR is calculated using the standard Wald approximation: $95\%CI = \exp \left[\ln(SMR) \pm 1.96 \left(\frac{1}{A^{1/2}} \right) \right]$.

This approximation is considered reliable when the expected number of deaths is sufficiently large ($E > 5$). These formulas correspond to standard large-sample methods for SMR estimation based on the Poisson distribution.[144-146] For each subgroup, the SMR and its 95% confidence interval are



calculated. Strata with $E \leq 5$ were flagged as potentially unstable because the Poisson assumptions may not hold.

Because crude mortality rates in some thyroid cancer subgroups fluctuate substantially from year to year as a result of small sample sizes, a Poisson generalized linear model (GLM) stratified by calendar year, age, sex, and region, was used to smooth mortality rates in the TC cohort. In this model-based approach, mortality in the TC cohort is represented by an estimated average number of deaths (A), obtained by multiplying the mortality rates predicted by the Poisson regression by the corresponding person-years at risk. For each analysis category, model-based estimates of A and the corresponding expected number of deaths (E) were summed to obtain group-level SMRs ($SMR = A/E$). A 95% CI for the SMR was computed as $95\%CI = \exp \left[\ln(SMR) \pm 1.96 \left(\frac{SE(A)}{E} \right) \right]$ where $SE(A)$ denotes the standard error of the predicted number of deaths, derived from the Poisson regression model.

As differences between SMRs based on smoothed and crude mortality rates were minimal - particularly in groups with a large number of cases - the primary analyses were based on observed deaths, with SMRs derived from predicted death counts used as a sensitivity analysis.

7 RESULTS

KEY POINTS

- Belgian Cancer Registry cohort**
 The analysis was based on 15,713 adults with primary thyroid carcinoma from the Belgian Cancer Registry, with up to 21 years follow-up, providing a robust basis for Time-to-Cure (TTC) and SMR estimation.
- Excellent overall prognosis driven by differentiated thyroid carcinoma (DTC)**
 DTC constituted ~93% of all cases and showed near-perfect long-term net survival, with 1-year conditional net survival (CNS) >0.99 from diagnosis and Time-to-Cure (TTC) of 0 years. For all thyroid carcinomas combined, TTC was <1 year and fell to 0 years after excluding anaplastic cases (~3%).
- Medullary thyroid carcinoma (MTC)** showed gradually improving conditional survival; however, statistical cure could not be demonstrated before 5 years post-diagnosis in any of the predefined subgroups.
- Anaplastic thyroid carcinoma (ATC)** showed no evidence of statistical cure, consistent with the absence of sustained long-term survival.
- Distant metastasis (M1) at diagnosis identifies a small but high-risk subgroup.**
 In DTC, metastatic disease clinically confirmed at diagnosis (~2%) showed **no evidence of a statistical cure and very low cured fractions**, contrasting sharply with the excellent outcomes observed in DTC without distant metastasis apparent at diagnosis.
- Strong concordance between TTC and SMR results**
 TTC estimates closely matched the time required to reach actuarially negligible excess mortality ($SMR \leq 1.25$) across all subgroups: ≤ 1 year for the full cohort and 0 years for (a) thyroid carcinomas excluding anaplastic histology, (b) differentiated thyroid carcinoma (DTC), and (c) DTC without distant metastasis clinically confirmed at diagnosis.
 No evidence of cure before 5 years post-diagnosis was demonstrated under either method for MTC, ATC, and DTC with distant metastasis clinically confirmed at diagnosis when these subgroups were analysed separately.

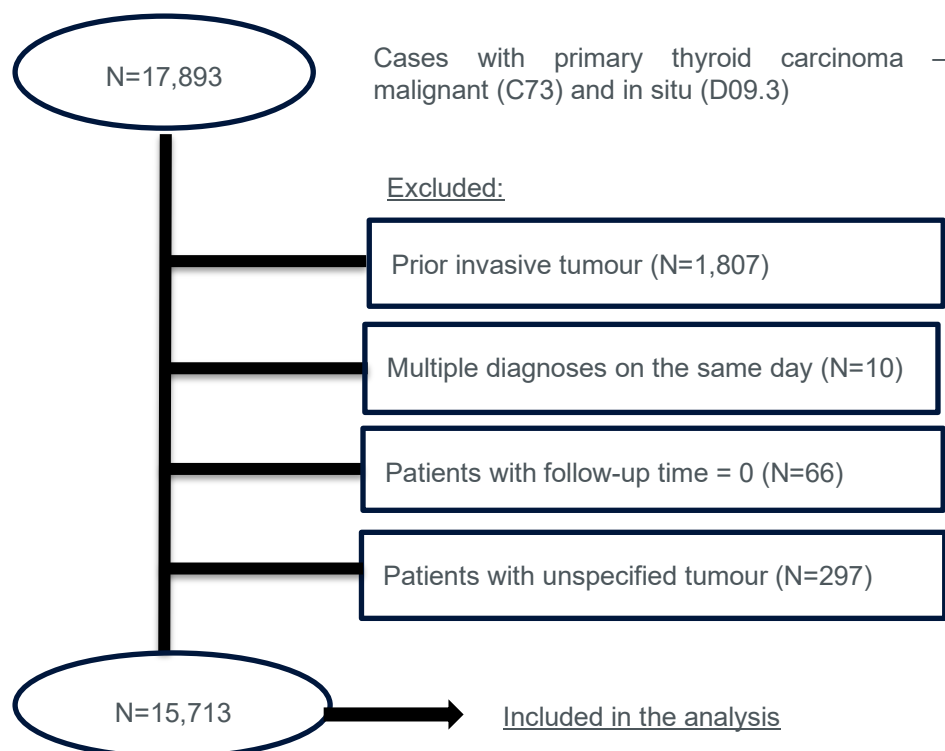
7.1 Description of the thyroid cancer cohort

7.1.1 Included population

A total of 17,893 cases of primary thyroid carcinoma diagnosed between 2004 and 2023 were identified in the BCR database (see Appendix 3.2 for the full overview of histological codes). We excluded individuals with a prior invasive tumour (10.1%), cases with zero days of follow-up (0.4%), cases with multiple diagnoses on the same day (0.06%), and tumours with unspecified histology (1.7%). The final study cohort comprised 15,713 adults with a first primary thyroid cancer diagnosis and adequate follow-up for survival analyses (see Figure 15).



Figure 15 – Study cohort selection flowchart



7.1.2 Cohort characteristics

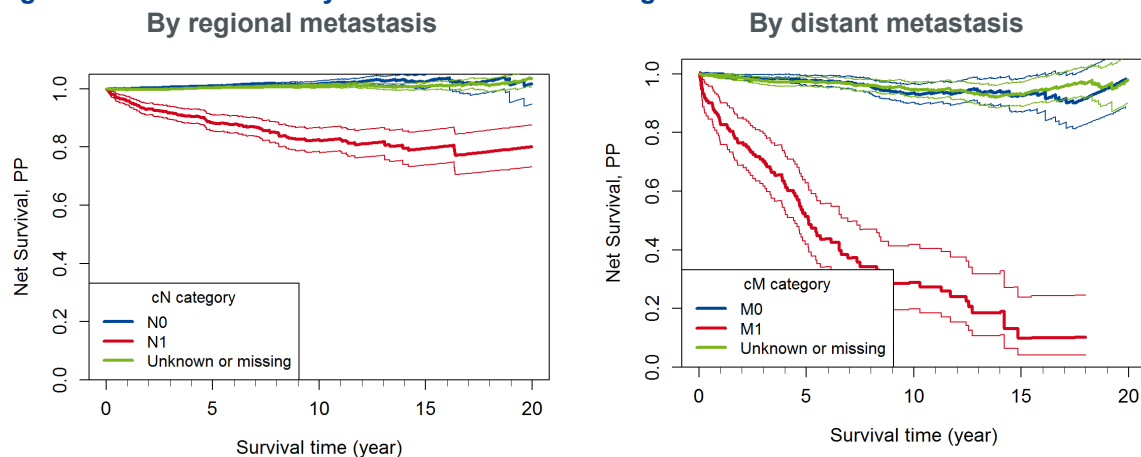
Among the 15,713 included subjects, 2,306 deaths occurred over a median follow-up of 9.11 years (range: 0.00–21.33). The cohort was predominantly female (74.6%), and most were diagnosed between 35 and 64 years of age (63.3%) (see Table 3). Over half of all diagnoses occurred in the period 2014–2023. Papillary thyroid carcinoma was the most common histological subtype (80.6%), followed by follicular carcinoma (10.9%). Overall, differentiated thyroid carcinoma (DTC) accounted for 93.2% of cases. Most patients presented with early-stage disease, with 65.9% classified as Stage I and only 7.5% as Stage IV. However, due to stage reclassification introduced in the seventh and eighth editions of the TNM system, a fully consistent staging framework cannot be applied across the entire observation period (see 3.5). Only ten subjects (0.06%) were diagnosed with in situ thyroid carcinoma.

Information on nodal status and distant metastasis was missing for a substantial proportion of records (61.9% and 58.1%, respectively). Regional lymph node metastasis (N1) was recorded in 6.7% and distant metastasis (M1) in 3.3%. The frequent use of “unknown” coding for nodal and metastatic status in population-based cancer registries may be explained by the fact that in routine clinical practice, many patients with low-risk or early-stage DTC do not undergo comprehensive nodal or distant metastatic staging.[8] In DTC, the BCR predominantly captures macroscopic metastases detectable at diagnosis by conventional anatomic imaging modalities, such as CT. In contrast, (micro)metastatic disease identified only on post-RAI WBS – a more sensitive functional imaging modality – is typically not evident at diagnosis and is therefore recorded as negative or unknown (see also 3.5). An exploratory net survival analysis in the entire cohort stratified by metastatic status demonstrated no observable differences in survival patterns between patients recorded as metastasis-free (N0/M0) and those with unknown or missing nodal or metastatic status (NX/MX) (see Figure 16). This finding is consistent with previous reports demonstrating the excellent prognosis of patients with RAI-avid pulmonary (micro)metastatic disease.[34, 45] Accordingly, for subsequent analyses, patients with negative and unknown metastatic status were merged into a single group.

Table 3 – Description of the study population (N=15,713)

Characteristics	N	%
Total	15,713	100.0
Sex		
Males	3,998	25.4
Females	11,715	74.6
Age at diagnosis (years)		
18–24	547	3.5
25–34	1,842	11.7
35–44	3,127	19.9
45–54	3,624	23.1
55–64	3,186	20.3
65–74	2,154	13.7
≥75	1,233	7.8
Period of diagnosis		
2004-2013	7,116	45.3
2014-2023	8,597	54.7
Histology		
Papillary	12,658	80.6
Follicular	1,715	10.9
Medullary	655	4.2
Anaplastic	416	2.6
Oncocytic	269	1.7
Combined prognostic group		
Stage I	10,351	65.9
Stage II	1,275	8.1
Stage III	1,030	6.6
Stage IV	1,173	7.5
Unknown or missing	1,812	11.9
Presence of regional lymph node metastasis		
N0/NX	14,668	93.3
N1	1,045	6.7
Presence of distant metastasis		
M0/MX	15,188	96.7
M1	525	3.3

N0/M0 = no clinically confirmed regional (N0) or distant (M0) metastases. NX/MX= metastatic status unknown or missing. N1/M1 = presence of clinically confirmed regional (N1) or distant (M1) metastases.

**Figure 16 – Net Survival by metastatic status at diagnosis**

Results of the Pohar-Perme estimator. Thinner lines represent the 95% CI.

N0/M0 = no clinically confirmed regional (N0)/ distant (M0) metastases.

N1/M1 = presence of clinically confirmed regional (N1)/ distant (M1) metastases.

Age patterns varied substantially across the histological subtypes (see Table 4).

Table 4 – Description of the study population by histological subtype

	Papillary		Follicular		Oncocytic		Medullary		Anaplastic	
Characteristics	N	%	N	%	N	%	N	%	N	%
Total	12,658	100.0	1,715	100.0	269	100.0	655	100.0	416	100.0
Sex										
Males	2,917	23.0	529	30.8	108	40.1	273	41.7	171	41.1
Females	9,741	77.0	1,186	69.2	161	59.9	382	58.3	245	58.9
Age at diagnosis (years)										
18–24	467	3.7	65	3.8	5	1.9	10	1.5	0	0.0
25–34	1,598	12.6	190	11.1	14	5.2	40	6.1	0	0.0
35–44	2,711	21.4	287	16.7	29	10.8	95	14.5	5	1.2
45–54	3,091	24.4	329	19.2	49	18.2	131	20.0	24	5.8
55–64	2,585	20.4	321	18.7	61	22.7	159	24.3	60	14.4
65–74	1,531	12.1	308	18.0	61	22.7	141	21.5	113	27.2
75+	675	5.3	215	12.5	50	18.6	79	12.1	214	51.4
Period of diagnosis										
2004–2013	5,603	44.3	854	49.8	93	34.6	343	52.4	223	53.6
2014–2023	7,055	55.7	861	50.2	176	65.4	312	47.6	193	46.4
Tumour behaviour										
In situ	10	0.1	0	0.0	0	0.0	0	0.0	0	0.0
Malignant	12,648	99.9	1,715	100.0	269	100.0	655	100.0	416	100.0
Combined prognostic group										
Stage I	9,234	72.9	786	45.8	128	47.6	203	31.0	0	0.0
Stage II	835	6.6	295	17.2	51	19.0	94	14.4	0	0.0
Stage III	714	5.6	200	11.7	43	16.0	73	11.1	0	0.0
Stage IV	401	3.2	177	10.3	20	7.4	190	29.0	385	92.5
Unknown or missing	1,472	11.7	257	15.0	27	10.0	95	14.5	31	7.5

Presence of regional lymph node metastasis										
N0/NX	11,969	94.6	1,658	96.7	254	94.4	520	79.4	267	64.2
N1	689	5.4	57	3.3	15	5.6	135	20.6	149	35.8
Presence of distant metastasis										
M0/MX	12,497	98.7	1,599	93.2	253	94.1	592	90.4	247	59.4
M1	161	1.3	116	6.8	16	5.9	63	9.6	169	40.6
Presence of subsequent tumour within 5 years since diagnosis thyroid carcinoma										
No	12,091	95.5	1,623	94.6	259	96.3	608	92.8	404	97.1
Yes	567	4.5	92	5.4	10	3.7	47	7.2	12	2.9

N0/M0 = no clinically confirmed regional (N0)/ distant (M0) metastases.

N1/M1 = presence of clinically confirmed regional (N1)/ distant (M1) metastases

Papillary, follicular and oncocytic carcinomas were most frequently diagnosed in mid-life, whereas medullary carcinoma peaked at somewhat older ages. Anaplastic thyroid carcinoma occurred predominantly in the elderly, with more than half of patients aged ≥ 75 years at diagnosis. Early-stage presentation was common in DTC, - Stage I accounted for most papillary, follicular and oncocytic cases, whereas medullary carcinoma showed a wider distribution across stages. In contrast, all anaplastic carcinomas were classified as Stage IV according to the TNM classification definition.

Patterns of metastasis also differed: nodal involvement was relatively uncommon in DTC but occurred frequently in medullary and anaplastic tumours, and distant metastases were rare except in anaplastic carcinoma, where 41% of patients presented with metastatic disease at diagnosis. Subsequent primary tumours within five years after the TC diagnoses occurred in 4% to 5% of DTC and 7% of MTC.

7.2 Net survival

7.2.1 Maximum age at diagnosis eligible for inclusion

Following the recommendation of Perme and Pavlic, a maximum age at diagnosis was set for the net survival analysis to ensure stable and interpretable estimates.[143] To support this decision, the *net expected sample size* - defined as the number of individuals still at risk at each time point after accounting for expected population mortality - was calculated as a function of age at diagnosis (see Table 5). Given the limited sample size in the oldest age groups and the relatively short life expectancy of individuals aged ≥ 75 at diagnosis, we restricted the cohort analysis to cases diagnosed between ages 18 and 74.

Table 5 – Net expected sample size as a function of time since diagnosis, by age at diagnosis

Age	0	1	3	5	10	15	20	LE
<45	5516	5511	5501	5489	5451	5394	5307	47.
45-54	3624	3613	3590	3563	3476	3347	3154	33.4
55-64	3186	3163	3113	3055	2868	2597	2203	24.4
65-74	2154	2116	2033	1938	1633	1222	747	16.3
75-84	1019	970	86	755	461	209	62	9.7
85+	214	185	134	92	26	4	0	5.1

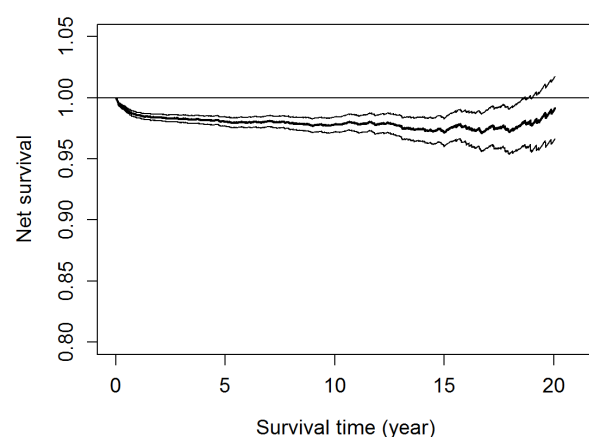
LE=average Life Expectancy at diagnosis



7.2.2 Pohar-Perme Net Survival estimates

Net Survival was estimated in the full cohort after excluding individuals diagnosed at age ≥ 75 years (Figure 17).

Figure 17 – Net Survival in the full cohort, age 18-74



Results of the Pohar-Perme estimator. Thinner lines represent the 95% CI.

Table 6 – Net survival probability in the full thyroid carcinoma cohort, by time since diagnosis

Time after diagnosis (Years)	Number at risk	PP (%)	95% CI
1	14,142	98.6	[98.3, 98.8]
2	13,480	98.4	[98.1, 98.7]
3	12,605	98.3	[98.0, 98.6]
4	11,689	98.2	[97.8, 98.5]
5	10,903	98.0	[97.7, 98.4]
6	10,157	98.0	[97.5, 98.4]
7	9,356	98.1	[97.6, 98.5]
8	8,505	97.9	[97.4, 98.4]
9	7,689	97.7	[97.2, 98.3]
10	6,811	97.8	[97.2, 98.4]
11	5,989	97.9	[97.2, 98.6]
12	5,194	97.8	[97.1, 98.6]
13	4,488	97.6	[96.8, 98.5]
14	3,776	97.5	[96.5, 98.4]
15	3,126	97.1	[96.0, 98.3]
16	2,512	97.6	[96.3, 98.9]
17	1,935	97.4	[95.9, 99.0]
18	1,419	97.3	[95.5, 99.1]
19	934	97.7	[95.6, 99.9]
20	526	99.0	[96.5, 101.5]

Results of the Pohar-Perme estimator (PP)

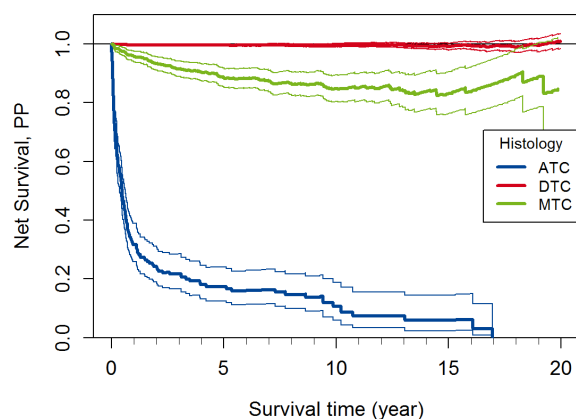
The net survival curve shows only a very small gradual decline over time, with values consistently between 97% and 99% across the entire follow-up (see Table 6). This pattern reflects minimal excess mortality associated with thyroid cancer and supports the appropriateness of a cure-model framework for this cohort. The slight upward fluctuations observed at the extreme end of follow-up are attributable to the known instability of the Pohar–Perme estimator when the number at risk becomes very small and the excess hazard is close to zero; these fluctuations should therefore be interpreted as methodological artifacts rather than true improvements in net survival.

7.3 Time-to-cure

7.3.1 Development of the non-mixture flexible parametric cure model

The development of the non-mixture flexible parametric cure model followed a structured series of model building steps, including the valuation of alternative covariate structures. Full technical specifications are provided in Appendix 4.1. In brief, net survival was first examined by stratifying the full cohort according to clinically relevant variables (see Figure 16, Figure 18 and Figure 19). In DTC, net survival consistently approached 100% throughout follow-up, ATC demonstrated a rapid, continuous decline, with no indication of long-term stabilization, MTC displayed more gradual decline. Individuals <55 years exhibited minimal decline in net survival, whereas those ≥55 years showed a steeper and more persistent reduction. Age was subsequently evaluated both categorically and continuously.

Figure 18 – Net Survival in differentiated (DTC), medullary (MTC) and anaplastic (ATC) thyroid carcinoma



Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Covariates potential interactions, and non-proportionality (time dependence) terms were assessed for their contribution to model fit using maximum likelihood-ratio tests (see Appendix 4.1). The model was further evaluated through visual comparison of the predicted net survival curves with the empirical Pohar-Perme curves.

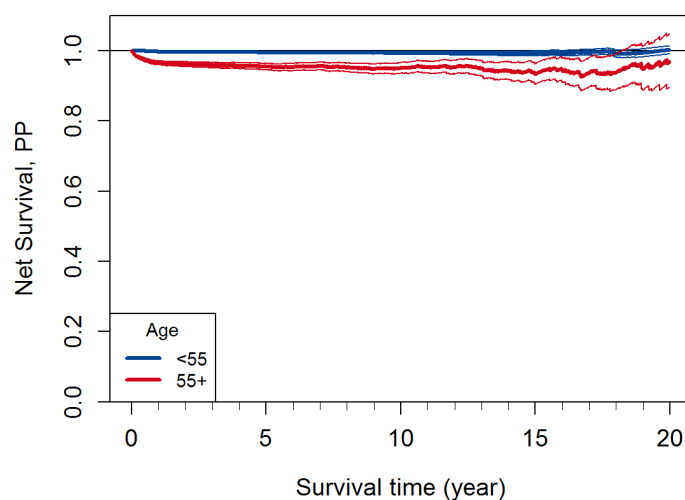
The final model demonstrated a very good agreement with the Pohar-Perme estimator (see Figure 20). The selected covariate structure included:

- TNM-based prognostic group: DTC, MTC, ATC
- Age: 4 categories (<45, 45-54, 55-64, 65-74)
- Distant metastasis at diagnosis: M0/MX vs M1.



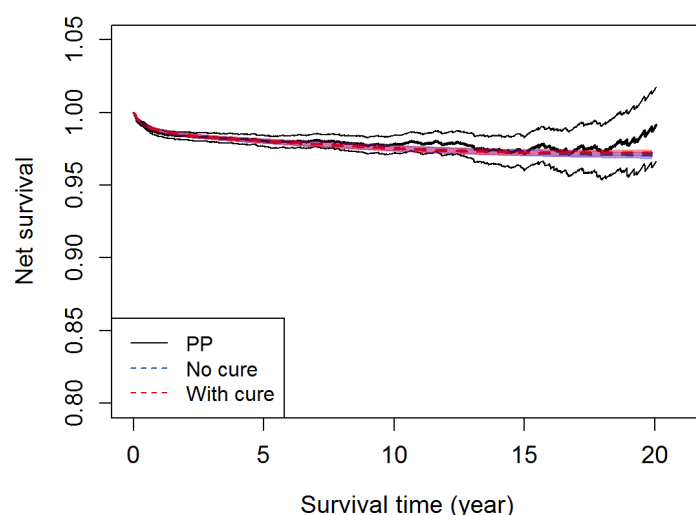
Model predictions for the predefined subgroups, i.e. age <55 vs ≥55 years, are obtained as a weighted average of the predicted net survival curves corresponding to the covariate strata represented within each subgroup. The weight assigned to each covariate combination equals the proportion of patients in that combination within the subgroup. Results per each of the 4 age categories are presented in Appendix 4.2 and can be used to evaluate the goodness-of-fit.

Figure 19 – Net Survival in the thyroid carcinoma cohort, by age group (<55 vs ≥55 years)



Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Figure 20 – Net Survival in the thyroid carcinoma cohort: Pohar-Perme estimator and model prediction



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: net survival prediction from the selected cure model, shaded areas represent the 95% CI.

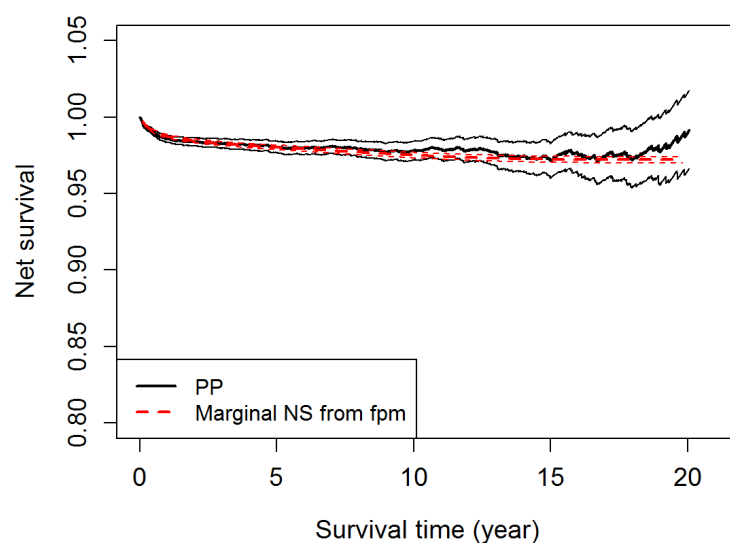
Notably, the cure model and the corresponding non-cure model yielded nearly identical net survival curves, indicating that the cure fraction in this thyroid carcinoma cohort is very high.

7.3.2 Time-to-Cure in all thyroid carcinomas

Marginal net survival for full thyroid carcinoma cohort represents a weighted average of cure-model-predicted net survival functions across all covariate strata, obtained via matrix multiplication. The resulting predicted curve shows excellent agreement with the empirical Pohar–Perme estimator (see Figure 21).

The predicted marginal 1-year CNS (1-yCNS) exceeds 0.99 from the first year after diagnosis onward (see Figure 22 and Table 7). At diagnosis, the 1-yCNS is 0.988 (95%CI: 0.986-0.989), narrowly missing the predefined cure threshold of >0.99 including the upper CI bound. The marginal TTC for the full cohort is therefore <1 (95%CI: 0-0.1), indicating that the cohort reaches statistical cure within the first year after diagnosis. The estimated cure fraction is 0.97 (95%CI: 0.97-0.97).

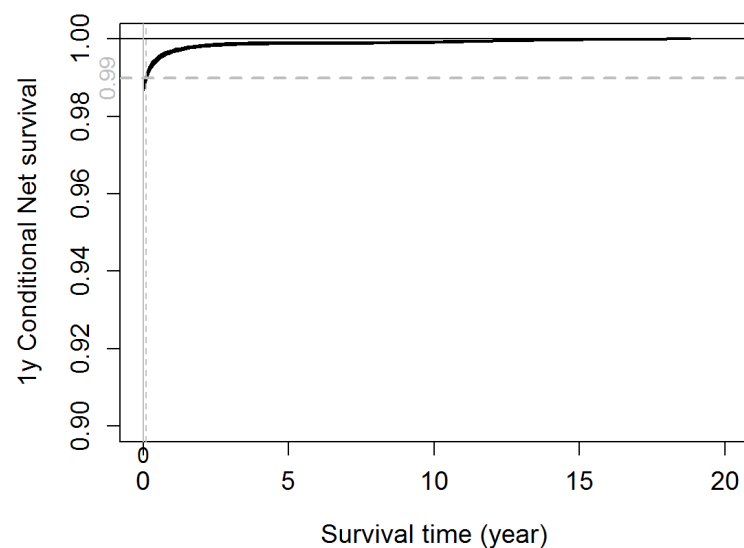
Figure 21 – Marginal Net Survival in all thyroid carcinomas: Pohar-Perme estimator and weighted average of predicted net survival across covariate strata



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: weighted average of predicted net survival curves per covariate stratum obtained with the non-mixture flexible parametric cure model (fpm), shaded areas represent the 95% CI.



Figure 22 – All thyroid carcinomas: predicted marginal 1-year Conditional Net Survival



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

Table 7 – Predicted marginal 1-year Conditional Net Survival for all thyroid carcinomas, by time since diagnosis

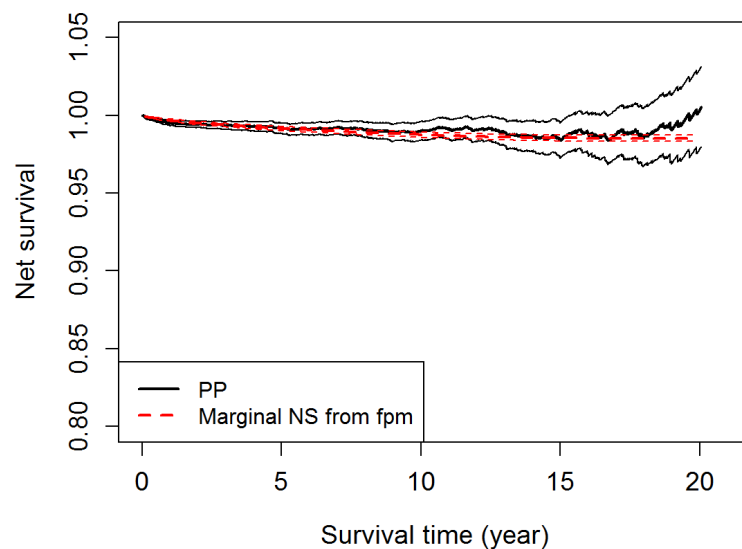
Time after diagnosis (Years)	1-yCNS	95%CI
0	0.988	[0.986, 0.989]
1	0.997	[0.997, 0.997]
2	0.998	[0.998, 0.998]
3	0.999	[0.998, 0.999]
4	0.999	[0.999, 0.999]
5	0.999	[0.999, 0.999]
6	0.999	[0.999, 0.999]
7	0.999	[0.999, 0.999]
8	0.999	[0.999, 0.999]
9	0.999	[0.999, 0.999]
10	0.999	[0.999, 0.999]
11	0.999	[0.999, 1]
12	0.999	[0.999, 1]
13	1.000	[0.999, 1]
14	1.000	[1, 1]
15	1.000	[1, 1]
16	1.000	[1, 1]
17	1.000	[1, 1]
18	1.000	[1, 1]
19	NA	[NA, NA]

1-yCNS=1-year Conditional Net Survival

7.3.3 Time-to-Cure excluding anaplastic histology

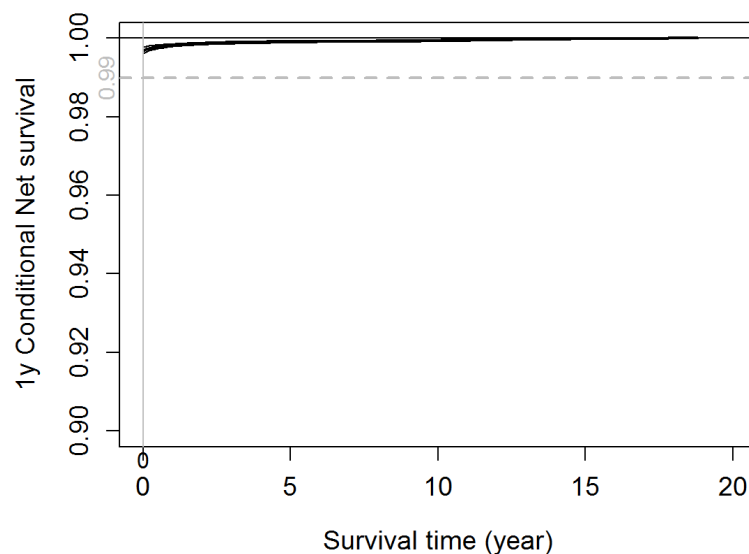
After excluding ATC, the histological type with the most unfavourable prognosis, the predicted net-survival curve for the remaining cohort again shows very good concordance with the Pohar–Perme estimator (see Figure 23).

Figure 23 – Marginal Net Survival in thyroid carcinoma excluding anaplastic histology: Pohar-Perme estimator and weighted average of predicted net survival across covariate strata



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: weighted average of predicted net survival curves per covariate stratum obtained with the non-mixture flexible parametric cure model (fpm), shaded areas represent the 95% CI.

Figure 24 – Predicted marginal 1-year Conditional Net Survival: thyroid carcinoma excluding anaplastic histology



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI



The corresponding marginal 1-yCNS lies consistently above 0.99 from year 0 onward, including the upper bound of the 95% CI (see Figure 24 and Table 8). The marginal TTC estimate for this restricted cohort is 0 years (95%CI: 0-0), indicating immediate cure at diagnosis. The estimated cure fraction is 0.99 (95%CI: 0.98-0.99).

Table 8 – Predicted marginal 1-year Conditional Net Survival in thyroid carcinoma excluding anaplastic histology, by time since diagnosis

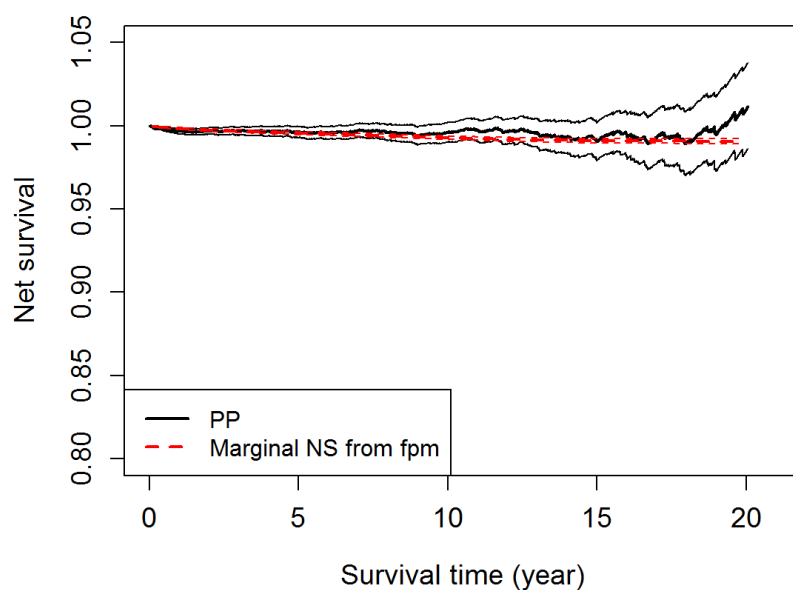
Time after diagnosis (Years)	1-yCNS	95%CI
0	0.997	[0.996, 0.998]
1	0.998	[0.998, 0.999]
2	0.999	[0.998, 0.999]
3	0.999	[0.999, 0.999]
4	0.999	[0.999, 0.999]
5	0.999	[0.999, 0.999]
6	0.999	[0.999, 0.999]
7	0.999	[0.999, 0.999]
8	0.999	[0.999, 0.999]
9	0.999	[0.999, 1]
10	0.999	[0.999, 1]
11	0.999	[0.999, 1]
12	1.000	[0.999, 1]
13	1.000	[1, 1]
14	1.000	[1, 1]
15	1.000	[1, 1]
16	1.000	[1, 1]
17	1.000	[1, 1]
18	1.000	[1, 1]
19	NA	[NA, NA]

1-yCNS=1-year Conditional Net Survival

7.3.4 Time-to-Cure in differentiated thyroid carcinoma

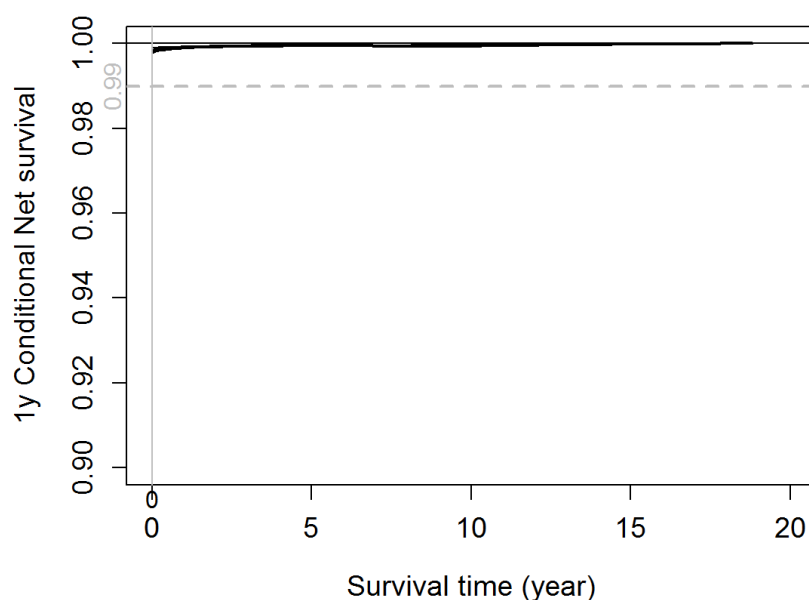
Predicted marginal net survival in DTC closely aligned with the Pohar–Perme estimator (see Figure 25), indicating a good overall fit of the cure model.

Figure 25 – Marginal Net Survival in differentiated thyroid carcinoma: Pohar-Perme estimator and weighted average of predicted net survival across covariate strata



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: weighted average of predicted net survival curves per covariate stratum obtained with the non-mixture flexible parametric cure model (fpm), shaded areas represent the 95% CI.

Figure 26 – Predicted marginal 1-year Conditional Net Survival: differentiated thyroid carcinoma



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

The predicted marginal 1-year Conditional Net Survival (1-yCNS) remained exceptionally high throughout follow-up, consistently exceeding 0.99 from the time of diagnosis onwards (see Figure 26 and Table 9). The corresponding marginal TTC estimate for DTC is 0 years (95%CI: 0-0), indicating



immediate statistical cure at diagnosis. The cure fraction was similarly very high: 0.99 (95%CI: 0.99-0.99).

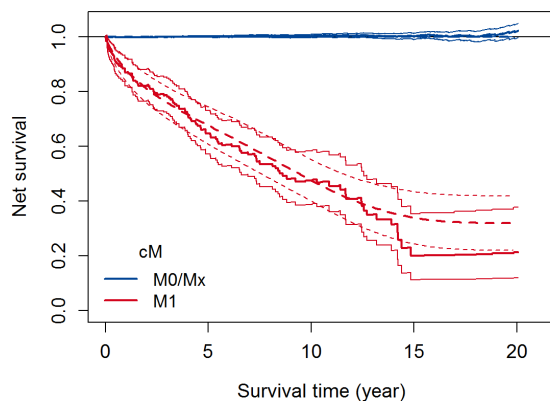
Table 9 – Predicted marginal 1-year Conditional Net Survival in differentiated thyroid carcinoma, by time since diagnosis

Time after diagnosis (Years)	1-yCNS	95%CI
0	0.998	[0.998, 0.999]
1	0.999	[0.999, 0.999]
2	0.999	[0.999, 0.999]
3	0.999	[0.999, 1]
4	0.999	[0.999, 1]
5	0.999	[0.999, 1]
6	0.999	[0.999, 1]
7	0.999	[0.999, 1]
8	0.999	[0.999, 1]
9	0.999	[0.999, 1]
10	0.999	[0.999, 1]
11	1.000	[0.999, 1]
12	1.000	[0.999, 1]
13	1.000	[1, 1]
14	1.000	[1, 1]
15	1.000	[1, 1]
16	1.000	[1, 1]
17	1.000	[1, 1]
18	1.000	[1, 1]
19	NA	[NA, NA]

7.3.4.1 Time-to-Cure in differentiated thyroid carcinoma by age and distant metastasis at diagnosis

Distant metastasis (M1) detected at diagnosis by conventional imaging techniques (post-RAI WBS-detected (micro)metastatic disease not included) had a marked negative impact on net survival in DTC (see Figure 27). Age-related differences were minimal among patients without clinically confirmed distant metastasis at diagnosis (M0/Mx), whereas in patients with M1 DTC, older age was associated with noticeably poorer outcomes (see Figure 28).

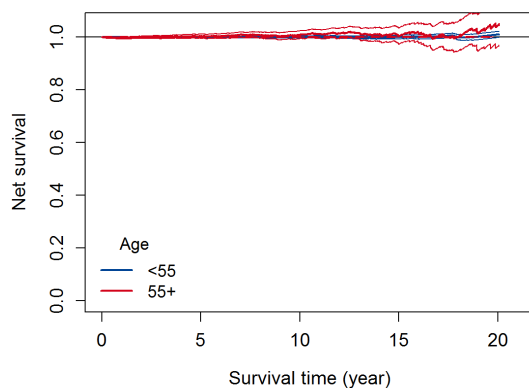
Figure 27 – Marginal Net Survival in differentiated thyroid carcinoma, by distant metastasis at diagnosis



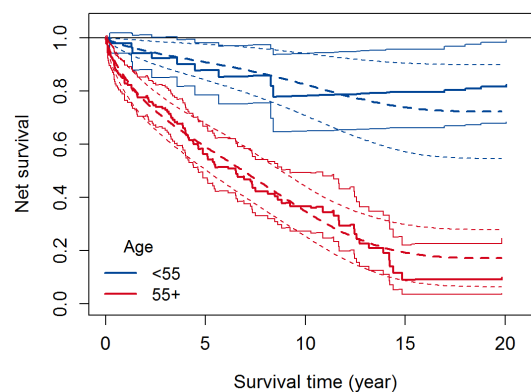
Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Figure 28 – Marginal Net Survival in differentiated thyroid carcinoma (DTC), by distant metastasis and age (<55 vs ≥55)

a) DTC without clinically confirmed distant metastasis at diagnosis (M0/MX)



b) DTC with distant metastasis clinically confirmed at diagnosis (M1)



Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Across both age categories, individuals without clinically confirmed metastasis at diagnosis achieved immediate statistical cure, with TTC estimates consistently equal to 0 and upper CI bounds also equal to 0. Cure fractions reached 100% in all M0/MX groups (see Table 10). In contrast, patients presenting with distant metastasis (M1) exhibited substantially prolonged TTCs and markedly reduced probabilities of cure. For both M1 age groups, no evidence of a statistical cure was observed within five years after diagnosis. Results were stable across analyses using two and four age categories (see Appendix 4.2).



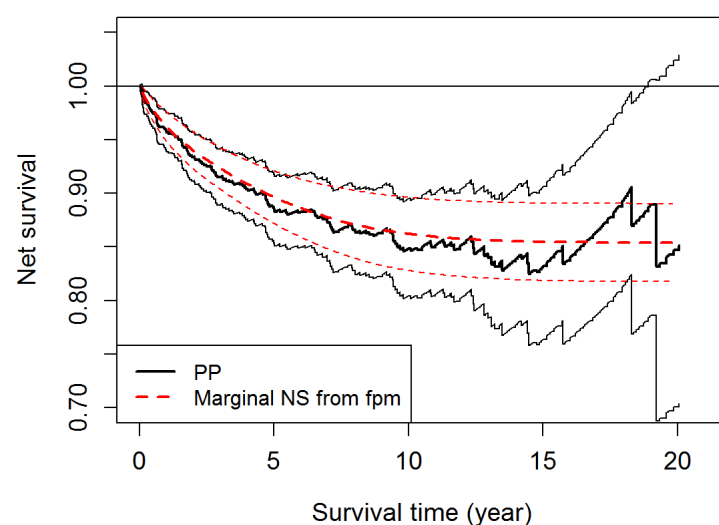
Table 10 – Predicted Time-to-Cure (TTC) in differentiated thyroid carcinoma, by age and distant metastasis

Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
<i>Differentiated thyroid carcinoma</i>						
All	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	13,516	1,078	9.68 (0.00, 20.05)
<55	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	8,785	268	10.25 (0.01, 20.05)
≥55	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	4,731	810	8.71 (0.00, 20.05)
All	M1	16.7 (15.3, 17.2)	0.32 (0.22, 0.42)	186	104	4.64 (0.01, 20.05)
<55	M1	15.2 (0, 16.3)	0.72 (0.55, 0.90)	50	9	7.13 (0.20, 20.05)
≥55	M1	17.4 (15.7, 17.9)	0.17 (0.06, 0.28)	136	95	4.01 (0.01, 19.83)

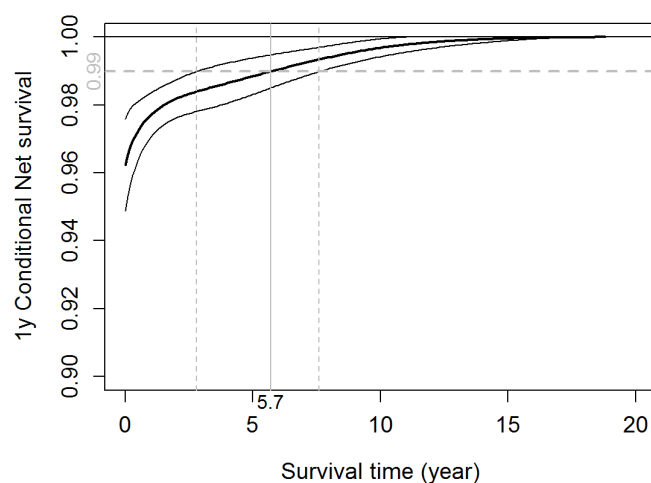
7.3.5 Time-to-Cure in medullary thyroid carcinoma

Modelled marginal net survival for MTC closely matched the Pohar–Perme estimator (see Figure 29), supporting the adequacy of the flexible parametric cure model.

Figure 29 – Marginal Net Survival in medullary thyroid carcinoma: Pohar-Perme estimator and weighted average of predicted net survival across covariate strata



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: weighted average of predicted net survival curves per covariate stratum obtained with the non-mixture flexible parametric cure model (fpm), shaded areas represent the 95% CI.

Figure 30 – Predicted marginal 1-year Conditional Net Survival: medullary thyroid carcinoma

Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

Conditional net survival improved steadily over time (see Figure 30). The marginal 1-yCNS at diagnosis was 0.96, surpassing the 0.99-threshold approximately 6 years post-diagnosis (Table 11). The overall marginal TTC estimate for MTC was 5.7 years (95%CI: 2.8–7.6), the corresponding cure fraction 0.85 (95%CI: 0.82–0.89).

Table 11 – Predicted marginal 1-year Conditional Net Survival in medullary thyroid carcinoma, by time since diagnosis

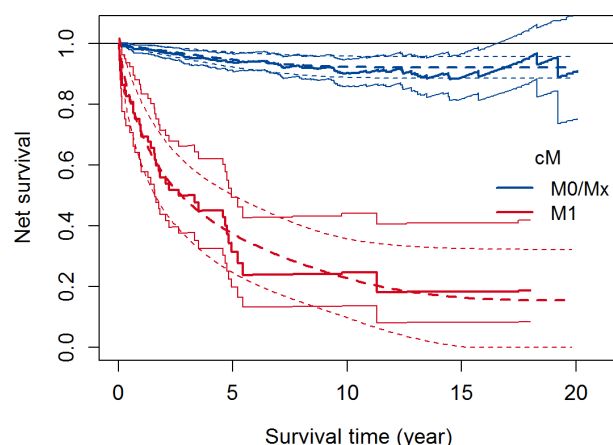
Time after diagnosis (Years)	1-yCNS	95%CI
0	0.962	[0.949, 0.976]
1	0.977	[0.971, 0.984]
2	0.982	[0.976, 0.988]
3	0.984	[0.978, 0.99]
4	0.986	[0.981, 0.992]
5	0.988	[0.983, 0.994]
6	0.990	[0.986, 0.995]
7	0.992	[0.988, 0.996]
8	0.994	[0.991, 0.997]
9	0.996	[0.993, 0.999]
10	0.997	[0.994, 0.999]
11	0.998	[0.996, 1]
12	0.998	[0.997, 1]
13	0.999	[0.998, 1]
14	0.999	[0.998, 1]
15	1.000	[0.999, 1]
16	1.000	[0.999, 1]
17	1.000	[1, 1]
18	1.000	[1, 1]
19	NA	[NA, NA]



7.3.5.1 Time-to-Cure in medullary thyroid carcinoma by age and distant metastasis at diagnosis

Also in MTC, metastatic spread was a key determinant of survival (see Figure 31). Patients aged ≥ 55 years showed somewhat poorer net survival than younger individuals, particularly in the metastatic subgroup (see Figure 32).

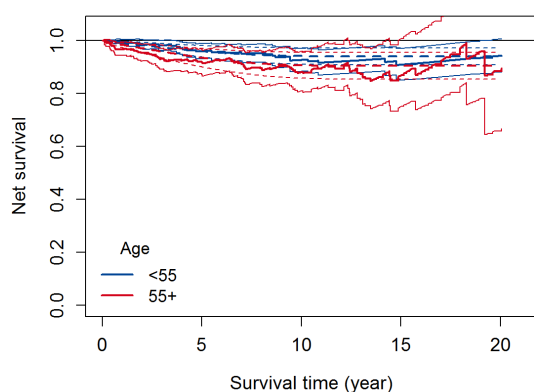
Figure 31 – Marginal Net Survival in medullary thyroid carcinoma, by distant metastasis



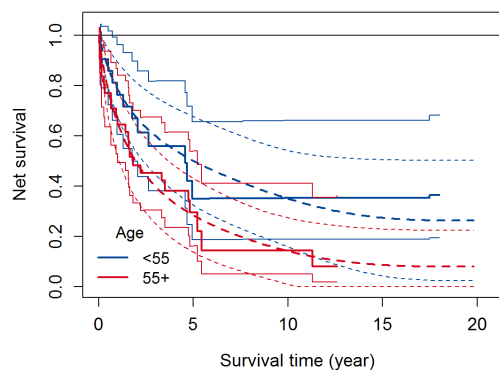
Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Figure 32 – Marginal Net Survival in medullary thyroid carcinoma (MTC), by distant metastasis and age (<55 vs ≥ 55)

a) MTC without clinically confirmed distant metastasis at diagnosis (M0/MX)



b) MTC with clinically confirmed distant metastasis at diagnosis



Results of the Pohar-Perme estimator (PP), thinner lines represent the 95% CI

Among patients with MTC and without clinically evident distant metastasis at diagnosis (M0/MX), confirmed time to cure (TTC) was reached approximately six years after diagnosis, occurring around five years in younger patients (<55 years) and seven years in those aged 55 years or older (see Table 12). The cure fraction was consistently high, averaging 0.92. In contrast, for individuals with clinically confirmed distant metastasis, TTC estimates were >16 years and cure fractions low, declining sharply with age - from 0.26 in patients <55 years to 0.08 among those ≥ 55 years. Results using four age categories showed similar trends; the youngest MTC M0/MX group (<45 years) showed a more rapid achievement of statistical cure (<1 year) (see Appendix 4.2). However, overall, the wide confidence

intervals - particularly in M1 subgroups with limited sample sizes - preclude confirming the TTC estimates for MTC with statistical certainty.

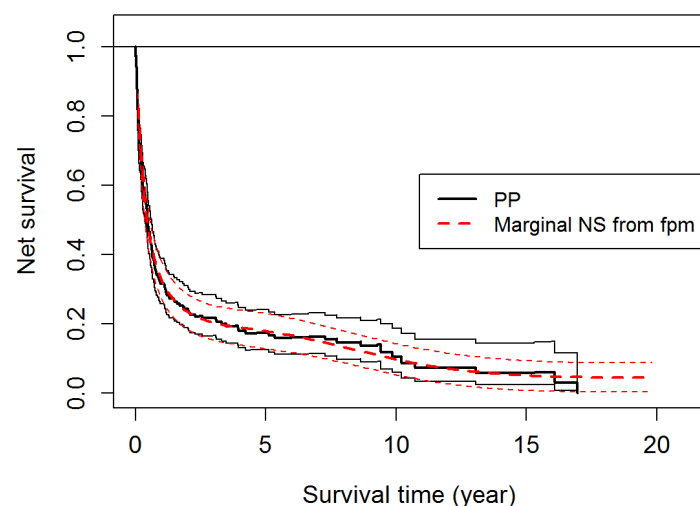
Table 12 – Predicted Time-to-Cure (TTC) in medullary thyroid carcinoma, by age and distant metastasis

Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
Medullary thyroid carcinoma						
All	M0/MX	3.3 (0, 6.1)	0.92 [0.89, 0.96]	525	103	9.50 [0.11, 20.05]
<55	M0/MX	0.0 (0, 4.9)	0.94 (0.91, 0.97)	255	24	11.08 (0.25, 20.05)
≥55	M0/MX	4.9 (0, 7.1)	0.90 (0.85, 0.96)	270	79	8.41 (0.11, 20.05)
All	M1	16.6 (7.4, 17.6)	0.16 (0.0, 0.32)	51	36	2.07 (0.20, 18.00)
<55	M1	16.2 (6.9, 17.4)	0.26 (0.02, 0.50)	21	12	2.63 (0.11, 18.00)
≥55	M1	17.1 (7.3, 18.0)	0.08 (0.0, 0.22)	30	24	1.73 (0.02, 12.59)

7.3.6 Time-to-Cure in anaplastic thyroid carcinoma

For ATC, the predicted marginal net survival aligned well with the Pohar–Perme estimator (see Figure 33), despite the limited follow-up typical of this aggressive disease.

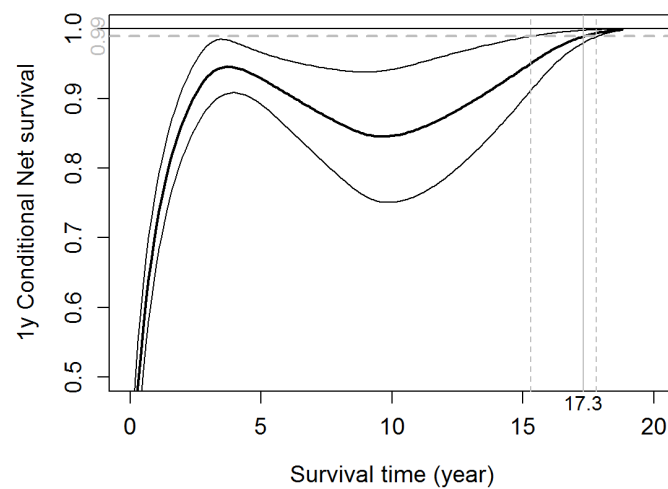
Figure 33 – Marginal Net Survival in anaplastic thyroid carcinoma: Pohar-Perme estimator and weighted average of predicted net survival across covariate strata



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: weighted average of predicted net survival curves per covariate stratum obtained with the non-mixture flexible parametric cure model (fpm), shaded areas represent the 95% CI.



Figure 34 – Predicted marginal 1-year Conditional Net Survival: anaplastic thyroid carcinoma



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

The 1-yCNS at diagnosis was extremely low (0.33) but improved markedly over the following years, reaching 0.99 only after 18 years post-diagnosis (see Figure 34 and Table 13). The estimated marginal TTC was 17.3 years (95%CI: 15.3–17.8). The cure fraction remained very small: 0.05 (95%CI: 0.0–0.09).

Table 13 – Predicted marginal 1-year Conditional Net Survival in anaplastic thyroid carcinoma, by time since diagnosis

Time after diagnosis (Years)	1-yCNS	95%CI
0	0.327	[0.274, 0.381]
1	0.718	[0.662, 0.773]
2	0.865	[0.816, 0.915]
3	0.933	[0.888, 0.978]
4	0.945	[0.908, 0.981]
5	0.929	[0.892, 0.966]
6	0.907	[0.858, 0.955]
7	0.884	[0.822, 0.947]
8	0.864	[0.788, 0.941]
9	0.849	[0.759, 0.938]
10	0.846	[0.751, 0.942]
11	0.856	[0.762, 0.951]
12	0.873	[0.785, 0.961]
13	0.895	[0.818, 0.971]
14	0.918	[0.856, 0.98]
15	0.943	[0.899, 0.987]
16	0.968	[0.942, 0.993]
17	0.985	[0.973, 0.997]
18	0.995	[0.992, 0.999]
19	NA	[NA, NA]

7.3.6.1 Time-to-Cure in anaplastic thyroid carcinoma by age and distant metastasis at diagnosis

Given the extremely poor prognosis of ATC, median follow-up times were short across all strata, limiting estimation precision. No subgroup - regardless of age or metastatic status - reached confirmed statistical cure within 18 years after diagnosis (see Table 14). Estimated cure fractions were uniformly low, ranging from approximately 0.30 in the small subset of younger patients (<55 years) to (almost) 0 in older adults. Consequently, observed TTC values primarily reflect parametric model behaviour rather than any meaningful long-term survival plateau.

Table 14 Predicted Time-to-Cure (TTC) in anaplastic thyroid carcinoma, by age and distant metastasis

Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
<i>Anaplastic thyroid carcinoma</i>						
All	M0/MX	17.2 (14, 17.8)	0.07 (0.01, 0.13)	124	105	0.68 (0.01, 16.95)
<55	M0/MX	16.7 (8.2, 17.5)	0.30 (0.08, 0.53)	19	10	5.96 (0.47, 16.95)
≥55	M0/MX	17.8 (12.1, 18.3)	0.02 (0.0, 0.07)	105	95	0.51 (0.01, 16.08)
All	M1	17.9 (13.2, 18.4)	0.01 (0.0, 0.04)	78	72	0.25 (0.01, 8.63)
<55	M1	17.9 (1.8, 18.4)	0.09 (0.01, 0.83)	10	7	0.54 (0.01, 2.97)
≥55	M1	18.5 (13.5, NA)	0.0 (0.0, 0.0)	68	65	0.24 (0.01, 8.63)

7.4 Standardized mortality ratios

7.4.1 SMR in the full thyroid carcinoma cohort

At diagnosis (WT = 0), the overall SMR in the cohort is 1.41 (95% CI: 1.34–1.48), indicating a 41% higher mortality compared with the Belgian general population. With a one-year waiting time, the SMR decreases to 1.20 (95% CI: 1.13–1.27). For waiting times beyond one year, the SMR continues to decline, ranging from 1.15 at WT=2 to 1.07 at WT=5. At WT = 5 years, the 95% confidence interval includes 1, indicating that mortality in the cohort is no longer significantly different from population mortality. According to the actuarial acceptability criterion ($SMR \leq 1.25$), the threshold is already met at WT = 1 year (see Table 15).

Table 15 – Standardized mortality ratios by waiting time in the full thyroid cancer cohort (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
0	14 480	149 676	1 498.0	1 061.9	1.41 [1.34;1.48]
1	14 296	134 047	1 179.0	982.5	1.20 [1.13;1.27]
2	13 238	119 415	1 051.0	911.0	1.15 [1.08;1.22]
3	12 284	105 428	936.0	835.3	1.12 [1.05;1.19]
4	11 300	92 482	833.0	761.6	1.09 [1.02;1.17]
5	10 474	80 588	738.0	691.3	1.07 [0.99;1.14]

WT: waiting time, SMR: standard mortality ratio, TC: thyroid cancer, CI: confidence interval



7.4.2 SMR in the full cohort excluding anaplastic thyroid carcinoma

When anaplastic thyroid carcinoma (ATC) is excluded, the remaining cohort shows only a modest increase in mortality compared with the Belgian general population (Table 16). At diagnosis (WT = 0), the SMR is 1.25 (95%CI: 1.18–1.32). With increasing waiting time, the SMR values decline progressively, reaching 1.06 at WT = 5 years. At WT=5, the 95% confidence interval includes 1, indicating no statistically significant excess mortality. From an actuarial perspective (SMR≤1.25), negligible excess mortality is already observed at diagnosis.

Table 16 – Standardized mortality ratios by waiting time in the cohort excluding anaplastic histology (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
0	14 278	149 199	1 321	1055.9	1.25 [1.18;1.32]
1	13 921	133 777	1 141	978.8	1.17 [1.10;1.23]
2	13 197	119 222	1 029	908.3	1.13 [1.06;1.20]
3	12 251	105 276	919	833.1	1.10 [1.03;1.17]
4	11 279	92 364	823	759.9	1.08 [1.01;1.16]
5	10 456	80 495	728	689.9	1.06 [0.98;1.13]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.

7.4.3 SMR in differentiated thyroid carcinoma

At diagnosis, patients with DTC exhibit a modestly elevated mortality, with an SMR of 1.19 (95% CI: 1.12–1.25) (Table 17). The SMR decreases steadily with longer waiting times, ranging from 1.12 at WT = 1 year to 1.04 at WT = 5 years. From WT = 3 years onward, confidence intervals include 1, suggesting no statistically detectable excess mortality. According to the actuarial criterion, excess mortality in DTC is negligible at diagnosis.

Table 17 – Standardized mortality ratios by waiting time in differentiated thyroid cancer (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
0	13 702	143 528	1 182	995.6	1.19 [1.12;1.25]
1	13 395	128 796	1 036	924.3	1.12 [1.05;1.19]
2	12 710	114 803	939	857.8	1.09 [1.02;1.16]
3	11 795	101 360	845	786.5	1.07 [1.00;1.15]
4	10 864	88 932	759	717.5	1.06 [0.98;1.13]
5	10 083	77 486	677	650.9	1.04 [0.96;1.12]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.

7.4.3.1 SMR in differentiated thyroid carcinoma stratified by distant metastasis

Among patients with DTC without clinically confirmed distant metastasis (M0/MX), mortality at diagnosis is only slightly elevated, with an SMR of 1.10 (95% CI: 1.03–1.16) (Table 18). As waiting time increases, the SMR declines further, ranging between 1.05 and 1.00 across WT = 1–5. From WT = 1 year onward, the confidence intervals include 1, indicating mortality similar to that of the general population.

In contrast, DTC with clinically confirmed distant metastasis at diagnosis (M1) - post-RAI WBS-detected (micro)metastatic disease not included - shows markedly elevated SMRs across all waiting times, ranging from 7.65 at diagnosis to 6.11 at WT = 5 years, reflecting substantial excess mortality throughout the follow-up.

From an actuarial perspective, excess mortality in M0/MX DTC is negligible at diagnosis, whereas in M1 DTC, the threshold is not approached at any waiting time.

Table 18 – Standardized mortality ratio by waiting time in differentiated thyroid cancer, stratified by distant metastasis (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Differentiated Thyroid Carcinoma without clinically confirmed distant metastasis at diagnosis					
0	13 516	142 319	1078	982.0	1.10 [1.03;1.16]
1	13 240	127 799	960	912.9	1.05 [0.99;1.12]
2	12 569	113 992	874	848.6	1.03 [0.96;1.10]
3	11 675	100 692	791	778.8	1.02 [0.94;1.09]
4	10 767	88 385	715	711.0	1.01 [0.93;1.08]
5	10 005	77 038	644	645.5	1.00 [0.92;1.07]
Differentiated Thyroid Carcinoma with clinically confirmed distant metastasis at diagnosis					
0	186	1 209	104	13.6	7.65 [6.18;9.12]
1	155	997	76	11.4	6.67 [5.17;8.17]
2	141	811	65	9.2	7.07 [5.35;8.78]
3	120	668	54	7.8	6.92 [5.08;8.77]
4	97	547	44	6.5	6.77 [4.77;8.77]
5	78	448	33	5.4	6.11 [4.03;8.20]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.

7.4.3.2 SMR in differentiated thyroid carcinoma without clinically confirmed distant metastasis at diagnosis, stratified by age

In DTC without clinically confirmed distant metastasis at diagnosis (M0/MX), patterns are similar for patients diagnosed before age 55 and those diagnosed between 55 and 74 years. Across all waiting times, SMRs range from 0.94–1.10, with confidence intervals that include 1 in most cases. (Table 19 and Figure 35).

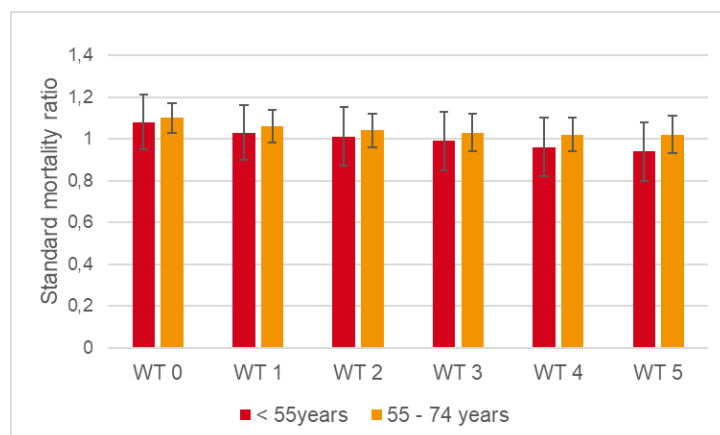
Table 19 – Standardized mortality ratios in differentiated thyroid cancer without clinically confirmed distant metastasis at diagnosis (M0/MX), by age: <55 vs 55-74 years (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Diagnosis before age 55 years					
0	9 126	96 391	268	247.8	1.08 [0.95;1.21]
1	8 676	87 287	242	234.7	1.03 [0.90;1.16]
2	7 971	78 331	222	220.6	1.01 [0.87;1.14]
3	7 190	69 713	203	205.5	0.99 [0.85;1.12]
4	6 440	61 698	183	190.3	0.96 [0.82;1.10]
5	5 748	54 210	165	175.5	0.94 [0.80;1.08]
Diagnosed between 55 and 74 years of age					
0	4 390	45 928	810	734.1	1.10 [1.03;1.18]
1	4 564	40 512	718	678.2	1.06 [0.98;1.14]
2	4 598	35 661	652	628.0	1.04 [0.96;1.12]
3	4 485	30 979	588	573.3	1.03 [0.94;1.11]
4	4 327	26 687	532	520.6	1.02 [0.94;1.11]
5	4 257	22 828	479	469.9	1.02 [0.93;1.11]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.



Figure 35 – Standardized mortality ratios in differentiated thyroid cancer without clinically confirmed distant metastasis at diagnosis, by age (<55 vs 55-74 years)



WT: waiting time

7.4.4 SMR in medullary thyroid carcinoma

In MTC, mortality is elevated at all waiting times. At diagnosis, the SMR is 2.31 (95% CI: 1.92–2.69). Although the SMR declines with increasing waiting time - from 1.93 at WT = 1 year to 1.31 at WT = 5 years, values remain well above the actuarial acceptability threshold of 1.25 (Table 20).

Table 20 – Standardized mortality ratios by waiting time in medullary thyroid cancer (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
0	576	5 671	139	60.3	2.31 [1.92;2.69]
1	526	4 981	105	54.5	1.93 [1.56;2.30]
2	487	4 419	90	50.5	1.78 [1.41;2.15]
3	456	3 916	74	46.5	1.59 [1.23;1.95]
4	415	3 432	64	42.4	1.51 [1.14;1.88]
5	373	3 009	51	39.0	1.31 [0.95;1.67]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.

7.4.4.1 SMR in medullary thyroid carcinoma stratified by distant metastasis

Stratification by metastatic status reveals two distinct mortality patterns in MTC. Among individuals without clinically confirmed distant metastasis, SMRs remain elevated up to five years after diagnosis, declining from 1.76 at WT=0 to 1.24 at WT=5 (Table 21). Although the point estimate at WT=5 meets the actuarial threshold, the CI is wide (95% CI: 0.89–1.60), and the Poisson-model-based SMR does not confirm this finding (SMR = 1.80, 95% CI: 1.38–2.22; Appendix 4.3.2), indicating instability likely due to small sample size.

In patients with registered distant metastasis at diagnosis, SMRs are extremely high, ranging between 12.50 and 20.00 at all waiting times. These estimates are based on small expected death counts (≤ 5), leading to unstable CIs, but the pattern clearly indicates very poor long-term survival.

Table 21 – Standardized mortality ratios by waiting time in medullary thyroid cancer, stratified by distant metastasis (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Medullary Thyroid Carcinoma without clinically confirmed distant metastasis at diagnosis					
0	525	5 468	103	58.5	1.76 [1.42;2.10]
1	493	4 833	86	53.2	1.62 [1.27;1.96]
2	461	4 304	77	49.4	1.56 [1.21;1.91]
3	435	3 827	64	45.8	1.40 [1.06;1.74]
4	399	3 364	56	41.9	1.34 [0.99;1.69]
5	364	2 957	48	38.6	1.24 [0.89;1.60]
Medullary Thyroid Carcinoma with clinically confirmed distant metastasis at diagnosis					
0	51	203	36	1.8	20.00 [13.47;26.53]
1	33	148	19	1.3	14.62 [8.04;21.19]
2	26	115	13	1.0	13.00 [5.93;20.07]
3	21	89	10	0.8	12.50 [4.75;20.25]
4	16	68	8	0.5	16.00 [4.91;27.09]
5	9	52	2	0.4	20.00 [-7.72;47.72]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

7.4.4.2 SMR in medullary thyroid carcinoma without clinically confirmed distant metastasis, stratified by age at diagnosis

Table 22 – Standardized mortality ratios by waiting time in medullary thyroid cancer without clinically confirmed distant metastasis, by age: <55 vs 55-74 (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Diagnosis before age 55 years					
0	268	2 798	24	8.3	2.89 [1.73;4.05]
1	246	2 516	21	7.8	2.69 [1.54;3.84]
2	227	2 270	19	7.3	2.60 [1.43;3.77]
3	212	2 034	16	6.8	2.35 [1.20;3.51]
4	184	1 807	14	6.4	2.19 [1.04;3.33]
5	157	1 595	11	5.9	1.86 [0.76;2.97]
Diagnosed between 55 and 74 years of age					
0	257	2 670	79	50.2	1.57 [1.23;1.92]
1	247	2 317	65	45.4	1.43 [1.08;1.78]
2	234	2 034	58	42.1	1.38 [1.02;1.73]
3	223	1 793	48	38.9	1.23 [0.88;1.58]
4	215	1 557	42	35.5	1.18 [0.83;1.54]
5	207	1 362	37	32.8	1.13 [0.76;1.49]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer.

Among patients with medullary thyroid carcinoma (MTC) without clinically confirmed distant metastasis (M0/MX) diagnosed before age 55, the SMRs remain markedly elevated ranging between 1.86 and 2.89 across all waiting times (Table 22), with wide confidence intervals reflecting reduced statistical precision. Although the 95% confidence interval includes 1 at WT = 5 years, this should *not* be interpreted as evidence that mortality has returned to population levels.

In older patients (55–74 years), the SMR at diagnosis is 1.57 and falls below the actuarial threshold at WT=3 years. However, this pattern lacks clinical plausibility and is not supported by model-based SMRs, where SMRs remain elevated (1.80–3.32; Appendix 4.3.2). Here, confidence intervals are wide and reflect low precision rather than a true decline in excess mortality.

7.4.5 SMR in anaplastic thyroid carcinoma

At diagnosis, the SMR in ATC is 29.50 (95% CI: 25.15–33.85), reflecting a nearly 30-fold excess mortality compared with the general population (Table 23). From WT = 1 year onward, expected deaths falls below five, violating Poisson assumptions. SMR values at later waiting times must therefore be interpreted with caution due to statistical instability. Nevertheless, all point estimates remain markedly elevated, clearly indicating persistently poor relative survival over the full follow-up period. Due to small subgroup sizes and very low number of expected deaths, no further stratification (e.g., by age or metastasis) is presented for ATC.

Table 23 – Standardized mortality ratios by waiting time in anaplastic thyroid carcinoma (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Anaplastic thyroid carcinoma					
0	202	477	177	6.0	29.50 [25.15;33.85]
1	62	270	38	3.6	10.56 [7.20;13.91]
2	41	193	22	2.7	8.15 [4.74;11.55]
3	33	152	17	2.2	7.73 [4.05;11.40]
4	21	118	10	1.7	5.88 [2.24;9.53]
5	18	93	10	1.4	7.14 [2.72;11.57]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Overall, model-based SMRs were consistent with those based on observed deaths (Appendix 4.3.2). As discussed above, meaningful discrepancies were limited to small MTC subgroups with very low expected death counts, where statistical instability is expected. Analyses based on shorter follow-up periods (up to 5, 10, and 15 years) show broadly similar patterns to those observed in the full follow-up (Appendix 4.3.3). However, shorter horizons yield fewer deaths and therefore wider confidence intervals, greater variability, and earlier inclusion of 1 within the confidence intervals, reflecting reduced statistical power rather than true epidemiologic differences.

7.5 Concordance between Time-to-Cure and SMR results

The Time-to-Cure (TTC) estimates derived from the non-mixture parametric flexible cure model show a high level of concordance with the time required to reach the actuarially accepted excess-mortality threshold of $\leq 25\%$, corresponding to an SMR point estimate of ≤ 1.25 (see Table 24).

For the overall thyroid carcinoma cohort, both approaches indicate that excess mortality becomes negligible within 1 year after diagnosis. When anaplastic thyroid carcinoma - a subgroup representing 2.7% of the cohort and associated with extremely poor prognosis - is excluded, statistical cure occurs immediately at diagnosis. Negligible excess mortality is also observed in the DTC cohort. This finding is driven by ~98% of DTC cases without distant metastasis clinically confirmed at diagnosis (M0/MX), which demonstrate statistical cure at diagnosis in both age groups. In contrast, the remaining ~2% of DTC patients with distant metastases detected at diagnosis by conventional imaging do not reach negligible excess mortality threshold by either method. Notably, (micro)metastases detectable only on post-RAI WBS, are not included in this classification.

Table 24 – Time-to-Cure and Time to reach $SMR \leq 1.25$ for full thyroid carcinoma cohort and clinically distinct subgroups

Population*	Percentage of cohort	Time-to-Cure confirmed (Years, <5)	Time to $SMR \leq 1.25^{**}$ (Years, <5)
All thyroid carcinomas	100%	<1	1
Thyroid carcinomas excluding anaplastic	~97%	0	0
Differentiated thyroid carcinomas (DTC)	~93%	0	0
⇒ <i>DTC without distant metastasis apparent at diagnosis</i>	~91%	0	0
➤ Age <55 years	~56%	0	0
➤ Age ≥55 years	~35%	0	0
⇒ <i>DTC with clinically confirmed distant metastasis at diagnosis</i>	~2%	NA	NA
Medullary thyroid carcinomas (MTC)	~4%	NA	NA
⇒ <i>MTC without metastasis</i>	~4%	NA	NA
⇒ <i>MTC with metastasis</i>	<1%	NA	NA
Anaplastic thyroid carcinoma	~3%	NA	NA

NA=Not applicable, i.e. no cure/ negligible excess mortality could be confirmed before 5 years post-diagnosis

*Individuals diagnosed with thyroid carcinoma between ages 18 and 74 years.

**SMRs values were assessed by simulating waiting periods from 0 up to 5 years post-diagnosis.

For medullary thyroid carcinoma, statistical cure could not be confirmed before 5 years post-diagnosis for any of the predefined subgroups, and the SMR-based assessment yielded concordant results. No evidence of cure was observed for anaplastic thyroid carcinoma.



8 DISCUSSION

KEY POINTS

- Methodological novelty**
 This study is the first to explicitly cross-validate cure-model-based Time-to-Cure estimates with actuarially relevant SMR-based excess-mortality thresholds, ensuring methodological alignment with insurance practice. Excess mortality across waiting periods from 0 to 5 years was quantified using conditional SMRs, calculated for landmark cohorts restricted to individuals alive at the end of each respective waiting period.
- Importance of cohort segmentation strategy**
 Segmentation strategy substantially influences TTC and SMR outcomes: although small high-risk groups, such as individuals with distant metastasis clinically confirmed at diagnosis, do not influence aggregate time to negligible mortality, their markedly poorer prognosis becomes pronounced in subgroup analyses.
- Stakeholder consultation on waiting-time scenarios**
 The choice between pooling and stratifying risks in life insurance underwriting goes beyond scientific interpretation and requires consideration of clinical practice as well as ethical, equity, and actuarial principles. Patient and consumer organisations, the national insurance industry, and clinical experts ranked four RTBF waiting-time scenarios derived from the study results, each reflecting a different balance between solidarity and risk differentiation. Most stakeholders favored the most granular stratification, in particular supporting waiver of the waiting period for differentiated thyroid carcinoma without distant metastases at diagnosis, while excluding small subgroups that did not demonstrate statistical cure within five years.
- Limitations inherent to registry-based analysis**
 Cancer registries capture patient status at diagnosis rather than longitudinally, precluding dynamic risk assessment over time. In addition, incomplete histological detail, staging inconsistencies over time, and small sample sizes in rare subgroups constrain the granularity of subgroup analyses but do not materially affect the robustness of the study's overall conclusions.
- Transferability of methods in RTBF context**
 The strong concordance between TTC and SMR-based estimates supports the use of the conservative statistical-cure definition applied in this study, which requires annual conditional net survival - including the lower bound of the 95% confidence interval - to exceed and consistently maintain the 99% threshold. This alignment in outcomes reinforces the applicability and transferability of the proposed methodological framework to future RTBF-related research.

8.1 Methodological novelty

Time-to-cure analysis has become an important tool in several countries to inform policy decisions on the waiting periods required before individuals with a history of cancer become eligible for the right to be forgotten. However, because the RTBF framework is relatively new within Europe, there is not yet a consolidated consensus on best methodological practice. Before conducting our analysis, we carried out a methodological exploration consisting of a literature review and consultations with biostatistical and actuarial experts (see Chapter 3). This process highlighted several key challenges.

First, the definition of statistical cure is not uniform. Although TTC is typically anchored to a predefined net survival threshold indicating when excess mortality becomes negligible, the literature applies a wide range of thresholds - from 90% to 99%. Variability in these cut-offs can lead to substantially different TTC estimates.[2, 50, 59]

Second, traditional TTC analyses were not developed with actuarial practice in mind. Historically, TTC models aimed to describe overall trends in cancer survivorship for the scientific community, rather than to support insurance-related risk assessment.

The methodological contribution of this work lies in the explicit cross-validation framework developed to evaluate Time-to-Cure (TTC) estimates. To our knowledge, this is the first study to systematically compare TTC estimates derived from cure models with SMR-based results, broadly used in actuarial risk assessment, specifically for updating RTBF reference grids.

We adopted a deliberately stringent definition of statistical cure: the point at which the annual conditional net survival (CNS) exceeds 99%, including the lower bound of its 95% confidence interval, and remains above that threshold throughout the entire follow-up period. TTC was considered confirmed only when the lower confidence limit permanently crossed and sustained the 99% CNS threshold.

To align SMR estimation with RTBF logic, we implemented a landmark-based SMR approach, calculating SMR at successive waiting periods (1–5 years). For each waiting period, landmark cohorts were defined as individuals alive and free of subsequent primary tumours at the start of the waiting period, thereby mitigating the influence of early cancer-related mortality on survivor risk profiles.

Finally, TTC estimates were benchmarked against the maximum level of excess mortality considered negligible by national insurance industry ($EMR \leq 25\%$, corresponding to $SMR \leq 1.25$). This integrated approach enhances the robustness and interpretability of TTC-based waiting-time recommendations in the RTBF context and strengthens their policy relevance.

8.2 Interpretation of results

Time to reach statistical cure and time to achieve an $SMR \leq 1.25$ were highly consistent across all predefined strata in thyroid cancer. At the same time, our findings highlight that the choice of cohort segmentation strategy has a marked impact on the resulting estimates.

Across all thyroid carcinomas combined, annual net survival was extremely high - ranging from 97% to 99% - and TTC was confirmed within one year post-diagnosis. This is broadly consistent with previous work, although earlier TTC analyses stratified results by age and rarely reported marginal TTC for the full cohort. For example, based on Italian cancer registry data, mixture cure models estimated $TTC < 1$ year in women diagnosed before age 55 and men diagnosed before age 45, findings that informed the 2024 Italian RTBF reference grid. [56]¹⁰⁰ Analyses using non-mixture cure models applied to the French FRANCIM registries yielded $TTC = 0$ years in men diagnosed under age 45 and women under age 65.[59, 78] Earlier Belgian work similarly identified $TTC < 1$ year for women at any age and for men diagnosed before age 50.[60]

In this study, we applied a more granular stratification strategy based on clinical subgroups defined by the TNM classification—differentiated, medullary, and anaplastic thyroid carcinoma - and incorporated age and distant metastasis status as additional prognostic variables. Sex was intentionally excluded because it is not an independent prognostic factor for survival,[8] and its use is restricted under Belgian underwriting legislation.

Because of the extremely poor prognosis associated with ATC, we analyzed the restricted cohort after exclusion of ATC and found a TTC of 0. Consistently, the actuarial threshold of negligible excess mortality ($SMR \leq 1.25$) was reached immediately at diagnosis in this subgroup. This improvement in time-to-cure is expected, given the very short median survival in ATC (~4 months),[13, 20] meaning most ATC cases do not survive beyond the first year.

¹⁰⁰ Personal communication with the corresponding author G. Dal Maso.



The negligible excess mortality observed from the time of diagnosis in the overall cohort is explained by the predominance of DTC, which represents ~93% of all cases and is generally associated with excellent prognosis. In the aggregate DTC group, both the TTC and the time to reach $SMR \leq 1.25$ were zero. However, these aggregate results mask the substantially poorer outcomes observed in the small subgroup with distant metastases clinically confirmed at diagnosis (~2%). When analysed separately, statistical cure could not be confirmed in the DTC M1 subgroup. These findings are consistent with SEER-based analysis reporting $TTC = 0$ for localized and regional thyroid carcinoma, but a markedly prolonged TTC of 26.1 years for metastatic disease.[79] Age stratification did not alter the findings in DTC without clinically confirmed distant metastasis at diagnosis, reinforcing the very favourable prognosis for this group, regardless of age at diagnosis.

In medullary thyroid carcinoma (MTC), TTC of less than one year was observed only in the youngest subgroup (<45 years) without distant metastasis, consistent with previous evidence identifying age a favourable prognostic factor in MTC.[32] However, this early TTC was not reproduced in the broader 18–55-year age group, and statistical cure before five years after diagnosis could not be confirmed in any of the predefined subgroups. Some MTC subgroups exhibited unstable or implausible trajectories in the raw SMR estimates, whereas the Poisson-modeled SMRs produced smoother and more interpretable excess-mortality patterns that aligned with clinical expectations. This underscores the importance of cross-validating SMRs derived from observed death counts with Poisson-modeled SMRs in small cohorts, where sparse events may lead to unstable or misleading estimates.

In anaplastic thyroid carcinoma, statistical cure could not be demonstrated in any subgroup, reflecting its short median survival. The TTC confidence intervals were wide across multiple subgroups of MTC and ATC, reflecting underlying sample constraints and reducing the precision and interpretability.

It is important to emphasize that the concept of time to statistical cure refers to the point at which the mortality of a patient group becomes comparable to that of the general population. This does not necessarily correspond to clinical cure as defined in clinical practice (e.g. based on imaging or tumour markers). Patients may therefore still exhibit signs of residual disease without an associated increase in mortality. Consequently, the notion of “immediate statistical cure” (i.e. a TTC of 0 years) should not be interpreted as indication that all patients are clinically cured at the time of diagnosis or treatment. Rather, it reflects that, from that time point onward, no excess mortality can be demonstrated at the population level.

This distinction is particularly relevant in thyroid cancer, where patients may exhibit biochemical or structural evidence of disease without a measurable impact on long-term mortality. Furthermore, the high degree of overdiagnosis in differentiated thyroid carcinoma underscores the importance of RTBF policies that avoid unnecessary waiting time for individuals with excellent prognosis.

TTC and SMR provide complementary perspectives on excess mortality. TTC, derived from flexible excess-hazard models, smooths short-term variability and offers a stable indication of when cancer-related excess mortality becomes negligible. SMRs, in contrast, reflect the observed mortality experience relative to the general population and are therefore more sensitive to short-term fluctuations and real-world heterogeneity. The close agreement between TTC estimates and the SMR-based actuarial threshold ($SMR \leq 1.25$) strengthens confidence in the robustness of the findings. Although no consensus exists on what level of excess mortality should be considered negligible, our cross-validation demonstrates that the stringent cure definition used here corresponds closely to the threshold typically applied in insurance practice. This alignment underscores the suitability of our approach and supports its potential applicability to other cancer types and broader RTBF policy contexts.

8.3 Limitations

This study benefits from a rich data source: the Belgian national cancer registry, which captures nearly all (~99%) cancer diagnoses nationwide since 2004 and enabled the analysis of more than 15,000 cases of thyroid carcinoma with up to 21 years of follow-up. Despite these strengths, several limitations must be acknowledged.

First, full granularity in cohort stratification was not feasible. Constraints stemmed both from conventions of the cancer registry's data collection protocol and from the evolving diagnostic and prognostic classification systems for thyroid cancer. As discussed in Section 3.5, several clinically meaningful sub-entities - such as poorly differentiated thyroid carcinoma or high-grade DTC - could not be reliably distinguished from the broader DTC category. Similarly, aggressive histological variants such as hobnail papillary carcinoma or widely invasive follicular carcinoma could not be isolated. While this limits the precision of subgroup analyses, these entities are extremely rare, and meaningful statistical inference might not have been possible even with complete classification. Given that the TNM 8th edition currently groups differentiated thyroid carcinomas into a single category, our segmentation strategy remains aligned with standard epidemiological and clinical practice.

Second, changes in the TNM classification over time limited consistent staging across the full follow-up period. The 8th edition of the TNM system downstaged about one third of thyroid carcinoma cases compared to previous editions, making longitudinal staging inconsistent across the 21-year observation window. This precluded staging from being used as a stable prognostic variable throughout the entire study period.

The segmentation strategy therefore reflects a pragmatic balance between clinical relevance and feasibility. While finer segmentation (e.g., by molecular markers, treatment information and response or detailed pathological criteria) could theoretically yield deeper prognostic discrimination, these variables were not available in a systematic way in population-based cancer registry data. The adopted segmentation - based on major clinical groups, distant metastasis, and age - allowed differentiation of clinically distinct profiles while maintaining sufficient statistical power for cure modelling and SMR estimation.

Moreover, for the group diagnosed with DTC before the age of 55, which constitutes the majority of the cohort and represents the primary target population in the context of mortgage lending and credit life insurance, the results provide a meaningful assessment of differences in time to statistical cure across TNM stages, stratified by the presence of distant metastases at diagnosis.

Further, RTBF legislation defines the waiting period as a period without cancer recurrence. However, cancer registries do not systematically capture disease recurrence or progression. Consequently, individuals continue to contribute person-time to the analyses regardless of recurrence status. This limitation may result in more conservative estimates of the time to achieve negligible excess mortality, as undetected recurrences cannot be accounted for during the waiting period. More generally, the lack of longitudinal clinical data in cancer registries precludes dynamic risk assessment over time, restricting risk stratification to information captured at diagnosis.

Finally, although flexible natural spline excess-hazard models used for the TTC analysis are transparent, reproducible and well suited to population-based survival analyses, any model-based estimates should be interpreted with appropriate caution. Visual assessment of model fit and systematic cross-validation against SMRs derived from observed death counts were therefore integral to our analytical approach.

Overall, these limitations are intrinsic to conducting a population-based, long-term analysis within a real-world cancer registry context but do not undermine the validity of the study's central findings.



8.4 Policy implications

8.4.1 Evidence-based waiting period scenarios: solidarity versus risk differentiation

As outlined above, the strategy used to segment the cohort has a direct and substantial impact on time-to-cure estimates. Pooling subgroups with markedly different prognoses can mask important clinical heterogeneity, resulting in TTC estimates that are largely driven by outcomes in the numerically dominant subgroup. Conversely, stratifying subgroups preserves prognostic differences but may lead to greater complexity in policy implementation. In the context of life-insurance underwriting, this trade-off necessitates a stakeholder perspective to account for clinical practice, actuarial fairness, and ethical and equity considerations. Based on the study results, four policy scenarios are proposed as a basis for structured consultation.

Scenario 1 - Uniform 1-year waiting period for all thyroid cancers

All individuals with history of thyroid cancer would be considered statistically cured one year after diagnosis.

Scenario 2 - Immediate statistical cure (0-year waiting period) for all thyroid cancers except anaplastic thyroid carcinoma

All thyroid cancers except anaplastic thyroid carcinoma would be considered statistically cured immediately at diagnosis. ATC is excluded because of its extremely poor prognosis.

Scenario 3 - Immediate statistical cure (0-year waiting period) for differentiated thyroid carcinoma

Individuals diagnosed with differentiated thyroid carcinoma – comprising primarily papillary and follicular types - would be considered statistically cured immediately at diagnosis. Anaplastic and medullary thyroid carcinomas are not eligible, as statistical cure was not demonstrated in these histological types before 5 years post-diagnosis.

Scenario 4 - Immediate statistical cure (0-year waiting period) for differentiated thyroid carcinoma without distant metastasis clinically confirmed at diagnosis

Individuals with differentiated thyroid carcinoma without distant metastasis clinically confirmed at diagnosis would be considered statistically cured immediately at diagnosis. Anaplastic, medullary thyroid carcinomas and differentiated carcinoma with clinically confirmed distant metastasis at diagnosis would not be eligible, as statistical cure was not demonstrated before 5 years post-diagnosis.

Selecting Scenario 1 instead of Scenarios 2-4 reflects a solidarity-oriented policy approach: individuals with DTC would be assigned a longer waiting period than suggested by their statistical cure estimates, thereby supporting a harmonized rule across all thyroid cancer subtypes.

The distinction between Scenarios 2, 3 and 4 requires a policy decision on whether smaller subgroups with substantially poorer prognosis (e.g. metastatic DTC) should be explicitly separated into higher-risk categories with longer waiting periods. Although these subgroups represent only a small proportion of the cohort, and their inclusion does not materially influence the aggregate TTC or SMR-based estimates, their distinct prognosis becomes evident when examined separately, which may justify differentiated treatment in certain policy frameworks.

Table 25 illustrates how each scenario translates into waiting periods if mapped onto the TNM-8 classification.

Table 25 – Waiting period scenarios for thyroid cancer mapped onto the TNM-8 classification

Thyroid cancer TNM-stage at diagnosis	Current reduced waiting period (years)	Evidence-based waiting period (years)			
		Scenario 1	Scenario 2	Scenario 3	Scenario 4
Differentiated thyroid carcinoma <55 years					
Stage I: any T, any N, M0	3	1	0	0	0
Stage II: any T, any N, M1	NA	1	0	0	NA
Differentiated thyroid carcinoma ≥55 years					
Stage I: T1/T2, N0/NX, M0	3	1	0	0	0
Stage II: T1/T2, N1, M0 T3a/T3b, any N, M0	3	1	0	0	0
Stage III: T4a, any N, M0	5*	1	0	0	0
Stage IVA: T4b, any N, M0	NA	1	0	0	0
Stage IVB: anyT, any N, M1	NA	1	0	0	NA
Medullary thyroid carcinoma					
Stage I: T1, N0, M0	NA	1	0	NA	NA
Stage II: T2/T3, N0, M0	NA	1	0	NA	NA
Stage III: T1-3, N1a, M0	NA	1	0	NA	NA
Stage IVA: T4a, any N, M0 T1-3, N1b, M0	NA	1	0	NA	NA
Stage IV B: T4b, any N, M0	NA	1	0	NA	NA
Stage IVC: any T, any N, M1	NA	1	0	NA	NA
Anaplastic thyroid carcinoma					
Stage IVA-IVC	NA	1	NA	NA	NA

NA= no reduced waiting periods applicable; the general waiting period of 5 years applies.

*For DTC≥55 years, Stage III, the initially adopted waiting period of 6 years was reduced to 5 years in January 2025, when general waiting period in cancer was brought down from 8 to 5 years.

8.4.2 Stakeholder consultation on scenario preferences

Determining the most appropriate scenario, based on clinical risk, prevalence, or principles of equity and proportionality, extends beyond purely scientific exercise. For this reason, a written consultation was conducted with relevant stakeholders, including representatives of patient and consumer organisations, insurers, and clinical experts.

Patients and consumers were represented by the cancer advocacy organization *Kom op tegen kanker*, the Flemish patient organization *Vlaams Patiëntenplatform*, and the Belgian consumer organization *TestAankoop/Test-Achats*. The *Ligue des Usagers des Services de Santé*, a French-speaking patient advocacy organisation, declined to participate, citing a lack of medical expertise. *Assuralia*, the professional association representing insurance companies in Belgium, responded on behalf of the national insurance industry. Clinicians were invited based on their established expertise in thyroid cancer treatment and research; three medical doctors contributed to the consultation. Stakeholders



were asked to rank the scenarios (1 = most preferred; 4 = least preferred) and to justify their ranking (see Appendix 5 for the consultation template).

The clinicians independently arrived at an identical ranking, expressing a clear preference for Scenario 4. Their ranking corresponded with that of the insurers. In contrast, patient and consumer organisations expressed divergent preferences, with each organisation prioritising a different scenario (see Table 26). The Belgian consumer organisation proposed an alternative to the four scenarios presented, advocating for a system modelled on the French framework¹⁰¹, where individuals with a past cancer diagnosis are exempt from disclosing that history to insurers provided certain criteria are met.

Table 26 – Stakeholder ranking of the waiting period scenarios for right to be forgotten in thyroid cancer

Waiting period scenarios	Patients and consumers			Insurers	Clinicians
	A	B	C		
<i>Scenario 1: Uniform 1-year waiting period for all thyroid cancers</i>	4	4	1	4	4
<i>Scenario 2: 0-year waiting period for all thyroid cancers except anaplastic</i>	3	1	2	3	3
<i>Scenario 3: 0-year waiting period for differentiated thyroid carcinoma</i>	2	2	4	2	2
<i>Scenario 4: 0-year waiting period for differentiated thyroid carcinoma without distant metastasis clinically confirmed at diagnosis</i>	1	3	4	1	1

A=Kom op tegen kanker; B=Vlaams Patiëntenplatform; C= TestAankoop/Test-Achats

1 = most preferred; 4 = least preferred

For Scenario 1, concerns were expressed by most stakeholders that a 1-year waiting period would be unfair to the majority of individuals with thyroid carcinoma, who exhibit no or only negligible excess mortality at diagnosis. At the same time, it was emphasized that for small subgroups with a poorer prognosis - such as anaplastic thyroid carcinoma - a waiting period of 1 year would be overly optimistic and not proportionate to their actual mortality risk.

Scenario 4 was preferred by the majority of stakeholders and was considered the most equitable option. It was emphasized that removing the waiting period for the homogeneous group with an excellent prognosis - namely, patients with thyroid carcinoma without clinically confirmed distant metastases at diagnosis – while maintaining it for subgroups without demonstrated statistical cure within 5 years after diagnosis, represents the most appropriate approach from both a clinical and actuarial perspective. This approach was also considered to align most closely with the objective of the reference tables, namely, to provide exceptions to the general waiting period for cancer subtypes with very favourable survival. Full responses to the consultation are available upon request.

Indeed, in the case of thyroid cancer, pooling subgroups with different risk profiles has a limited impact on aggregate TTC estimates, reflecting the relatively small size of the high-risk subgroup; in settings where higher-risk cases constitute a larger share of the population, pooling strategies may have more pronounced implications for waiting periods. Furthermore, supporting the waiver of waiting periods for

¹⁰¹ Art. 10 [LOI n° 2022-270 du 28 février 2022 pour un accès plus juste, plus simple et plus transparent au marché de l'assurance emprunteur \(1\) - Légifrance](#)

metastatic disease in thyroid cancer, but not in other cancers, may be perceived as inequitable and establish a politically sensitive precedent.

When Scenario 4 is translated into TNM-based stages of thyroid carcinoma, the proposed adjustments to waiting periods are as follows (see Table 27):

Table 27 – Proposed reduced waiting periods for thyroid carcinoma according to the TNM-8 classification

Thyroid cancer TNM-stage at diagnosis	Proposed waiting period (from diagnosis)	Current waiting period (from end of active treatment and without relapse)
Differentiated thyroid carcinoma <55 years:		
Stage I	0 years	3 years
Differentiated thyroid carcinoma ≥55 years:		
Stage I of II	0 years	3 years
Stadium III of IVA	0 years	5 years*

* Since January 2025, the waiting period for all cancer survivors has been reduced to 5 years.

For other subtypes, including anaplastic and medullary thyroid carcinoma, as well as differentiated thyroid carcinoma with clinically confirmed distant metastases (M1) at diagnosis, no reduction of the current 5-year waiting period is proposed under Scenario 4.

8.4.3 Start of waiting periods

Under current Belgian legislation, RTBF waiting periods are calculated from the end of active treatment, provided that no recurrence occurs. However, because patient status at diagnosis is the only status systematically recorded in the Belgian Cancer Registry, the available evidence is based on time to statistical cure measured from the date of diagnosis rather than from the end of treatment. In addition, in population-based analyses, it is difficult to account for the variable duration of individual treatments. To better align legislation with the available evidence base and to provide greater clarity for both patients and insurers, the KCE has already recommended in its previous RTBF report that waiting periods should start from the date of diagnosis.[2]



■ APPENDICES

APPENDIX 1. THYROID CANCER – HISTOLOGICAL SUBTYPES

Table 28 – Histological subtypes of thyroid carcinoma – variants, key characteristics, prevalence and 10-year overall survival estimates

Histological type	Description	10-year OS	Prevalence
Papillary Thyroid Carcinoma			
Papillary carcinoma, classic variant¹⁰²	Classic form of PTC is an indolent tumour with papillary architecture and characteristic nuclear features ^[147] .	~93 ^[8]	~65% (78-80% of all PTC ^[147])
Papillary carcinoma, infiltrative follicular variant¹⁰³	As per 2022 WHO Classification of Thyroid Tumours (5th edition), separated from invasive encapsulated follicular variant (IEFV-PTC, new diagnostic type). Infiltrative growth, risk of nodal metastasis and BRAF V600E mutation. Worse prognosis than IEFV-PTC, but better than tall cell or hobnail variants.	~80%-85%	~1.5% (1.7% of all PTC ^[148])
Papillary carcinoma, oxyphilic (oncocytic) cell¹⁰⁴	Hürthle cell-like features, but must be distinguished from Oncocytic TC (new diagnostic type). Cancer specific and overall mortality is similar to classical PTC and FTC ^[149, 150]	>85%	<1% ^[149]
Papillary carcinoma, Tall cell¹⁰⁵	Most common aggressive variant of PTC, often associated with BRAF V600E mutations. Usually diagnosed at older age (41-66 years) ^[151] . More frequent ETE and N1 and/or M1 at presentation compared to classic PTC. ^[151]	72% ^[152] to 85% ^[153]	4-9% (5-11% of all PTC) ^[151]
Papillary carcinoma, Columnar cell¹⁰⁶	Rare aggressive variant, associated with BRAF mutations. Advanced clinical stage at presentation: ETE and N1 in up to 55%, M1 in up to 5%. Minimally invasive and encapsulated variants have a better prognosis than infiltrative variant. ^[151]	75% ^[154] to 89% ^[151, 155]	~0.1% (0.15%-0.2% of all PTC ^[151])
Papillary Thyroid Carcinoma,	Rare and aggressive subtype: high mitotic activity and frequent TERT promoter and TP53 mutations, ^[156] ETE and N1 in up to 68% at presentation. ^[157]	~64% ^[151]	<1% (~1% of all PTC) ^[157]

¹⁰² [Pathology Outlines - Papillary thyroid carcinoma - classic](#)

¹⁰³ [Pathology Outlines – Follicular variant](#)

¹⁰⁴ [Pathology Outlines – Oncocytic](#)

¹⁰⁵ [Pathology Outlines – Tall cell](#)

¹⁰⁶ [Pathology Outlines – Columnar cell](#)

Hobnail Variant (HV-PTC)107			
Papillary carcinoma, Diffuse Sclerosing Variant108	Aggressive type, high rates of N1 (up to 80%), M1 (~10%), frequent ETE and lymphovascular invasion at presentation.[158] Despite its aggressive features, mortality rates are similar to classic PTC when treated appropriately.[158, 159] Mixed survival results: some studies report same mortality as classic PTC, with good treatment, [158, 159], others worse OS [160]	79%[152]	<2% (0.7%[161] to 1.8%[162])
Papillary Thyroid Carcinoma, Solid/ trabecular Variant109	Uncommon PTC subtype in which > 50% of tumour has solid, trabecular or insular growth but lacks diagnostic features of a higher-grade tumour. Frequently associated with BRAF V600E mutations. More common in children and adolescents, especially after radiation exposure (e.g., post-Chernobyl).[163] The solid variant should be distinguished from PDTC, which have similar insular, solid, and trabecular growth patterns and a lower survival rate.[164] Limited data, but similar to classical PTC[165, 166]	>85%	<2% (1-3% of PTC[167])
Papillary Thyroid Carcinoma, Warthin-like Variant	Very rare type. Prognosis is similar to classic PTC [168]	>85%	Very rare
Papillary microcarcinoma (PTMC)110	PTC ≤1 cm in size, often incidental and indolent. As per 2022 WHO Classification of Thyroid Tumours (5th edition), PTMC is no longer considered a separate subtype of PTC as it refers to any papillary thyroid carcinoma measuring ≤1 cm, regardless of histological subtype.	91%[169]	~38% (~45% of PTC[170])
Other well-differentiated thyroid carcinomas			
Papillary carcinoma, encapsulated invasive follicular variant111	A new diagnostic type (IEFV-PTC) as per WHO classification (2022). The distinction from FTC is based entirely on nuclear morphology.[20] Long-term survival is comparable with classic PTC and FTC. [20, 26] Minimally Invasive and Encapsulated Angioinvasive subtypes have a better prognosis than widely invasive (rare).	87%-91%	~6% (~7% of all PTC[148])
Follicular Thyroid Carcinoma	Minimally Invasive (mi): encapsulated tumour, often asymptomatic, 10-year OS:~98% [171] Encapsulated Angioinvasive: less common than mi-FTC, 10-year OS: >85% [171]	87%[27]	~4%[20]

107 [Pathology Outlines – Hobnail](#)

108 [Pathology Outlines – Diffuse sclerosing](#)

109 [Pathology Outlines - Solid / trabecular](#)

110 [Pathology Outlines – Microcarcinoma](#)

111 [Pathology Outlines - Invasive EFVPTC](#)



	Widely Invasive: most rare type, extensive infiltration into thyroid and beyond, 10-year OS: 77% [171]		
Oncocytic carcinoma of the thyroid	A new diagnostic type (OCA) as per WHO classification (2022). Oncocytic follicular cell-derived neoplasms (with more than 75% oncocytic cells) without the typical nuclear features of PTC and high-grade characteristics. Compared to non-oncocytic thyroid carcinomas, it has a higher level of aggressiveness.[28] In widely invasive OCA, older age (≥55 years), ETE, and (distant) metastasis are more often at presentation, negatively affecting survival[171].	82%[27]	~3%[27, 28]
High-grade non-anaplastic follicular-derived thyroid carcinomas			
Poorly differentiated thyroid carcinoma (PDTC)¹¹²	Solid/trabecular/insular growth, necrosis, mitoses, TP53, TERT mutations, advanced TNM at diagnosis. Prognostic factors: age ≥55, TNM stage at diagnosis—especially M1 and ETE.[172]	50%-60% [20]	1%-15% [173]
Differentiated High-Grade Thyroid Carcinoma (DHGTC)¹¹³	A new diagnostic type as per WHO classification (2022). Retains features of PTC, FTC, or OCA, but shows ≥5 mitoses per 2 mm² and/or tumour necrosis. At presentation, often associated with older age (>55 y.), locally advanced disease, including gross ETE, M1 in up to 25%.[174, 175]	50-60%[20, 174]	<3%[176]
Medullary thyroid carcinoma			
Medullary thyroid carcinoma	Originates from parafollicular C cells of the thyroid; produces calcitonin (used as a tumour marker). Prognostic factors: tumour size, lymph node involvement, calcitonin doubling time, Ki-67 index, age, stage at diagnosis, hereditary vs sporadic form[32]. 10-year OS is ~100% (stage I), ~93% (stage II), ~71% (stage III), ~21% (stage IV).	78%[33]	2-3%[32]
Anaplastic thyroid carcinoma			
Anaplastic thyroid carcinoma	Extremely aggressive, undifferentiated tumour, often presents with local invasion and distant metastases	<10% (8.9%[152])	~1%[20]

¹¹² [Pathology Outlines - Poorly differentiated thyroid carcinoma](#)

¹¹³ [Pathology Outlines - Differentiated high grade thyroid carcinoma / high grade differentiated thyroid carcinoma \(HGDTC\)](#)



APPENDIX 2. REVIEW OF TIME-TO-CURE METHODS

Appendix 2.1. Methods

We searched PubMed, Embase, EconLit, and Scopus for English-language papers (2010–2024) from Western countries that estimate TTC using population-based cancer registries. Snowballing identified additional papers. We excluded studies that did not estimate TTC or did not sufficiently describe modelling methods for reproducibility. We extracted cancer types, outcomes, model types, parameter estimation and model validation approaches, subgroup/covariate strategies, and software. Results specific to thyroid cancer TTC were captured separately.

Appendix 2.2. Summary of the included studies

Appendix 2.2.1. Mixture cure models (MCMs)

Study	Registry country	Types of cancer	Number of cases		Registration period	Time-to-cure definition	Software
Dal Maso 2014[50]	Italy	26 types	818,902		1985–2005	Time to reach 5-year CNS of >95%	SAS NLIN procedure
Dal Maso 2019[56]		30 types	>500,000		1985–2011		
Toffolutti 2023[58]		62 types	>3 million		≤40 years		
Dal Maso 2024[74]		Breast colorectal	806,410	422,407	≤40 years		
Guzzinati 2024[76]		28 types	>4 million		≤40 years		
Bucchi 2024[75]		vulvar squamous cell carcinoma	>6,000?		1978–2017		
Giudici 2024[177]		gynecological cancers (uterine and ovarian)	146, 678		≤40 years		
Dal Maso 2020[70]	EUROCARE-5 (17 European countries)	32 types	7.2 million		1990–2008	Not performed: mean survival time of survival distribution for the uncured is reported	SAS NLIN procedure
Silversmit 2016[61]	Belgium	cervix, colon, corpus uteri, skin melanoma, pancreas, stomach and oesophagus	94,891		1999–2011		



Appendix 2.2.2. Non-mixture cure models (NMCMS)

Study	Registry country	Types of cancer	Number of cases	Registration period	Time-to-cure definition	Type of NMCM	Software	Distribution
Boussari 2018[59]	France	Pancreas breast colorectal thyroid	8,169 71,947 46,371 8,762	1995-2010 FU:2013	Time to cure Cure probability ≥ 0.95 (cure probability is the ratio between the cure proportion and the net survival[78])	Flexible parametric	Stata for flexible parametric survival models (stpm2)	The log baseline cumulative excess hazard is written as a restricted cubic spline of the log time
Romain 2019[78]		27 types	335,358	1995-2009				
Mounier 2021[77]		Acute myeloid leukemia	9,453	1995-2015				
Xia 2022[79]	U.S.	46 types	8,978,721	1975-2018			???	
Boussari 2021[65]	France	Simulation + real data: testicular women pancreatic women colon	3,021 3,239 5,032	1995-2010 FU:2013	Time-to-null-excess-hazard (TNEH)	Non-mixture: new beta-TNEH regression model	R (???)	Model: Beta Expected hazard: Weibull

Appendix 2.2.3. Other methods

Study	Registry country	Types of cancer	Number of cases	Registration period	Time-to-cure definition	Type of model	Software	Distribution
Jacobsen (2020)[82]	Denmark	colon	42,380	2000-2016	Time to reach the mortality risk equal to that of general population	1)NMCM (flexible parametric); 2)A novel flexible mixture model (combining regular MCM with spline-based survival models); 3) MCM	R-package cuRe (https://github.com/LasseHjort/cuRe)	1 and 2: restricted cubic splines; 3) Weibull
Soetewey 2020[60]	Belgium	Melanoma thyroid	19,848 9,146	2004-2016 (2018FU)	Time to cure probability ≥ 0.95 (as Boussari 2018)	5 models were fitted, non-linear non-proportional gave the best fit	flexrsurv package in R	uni- or multidimensional penalized spline
Soetewey 2024[72]	Belgium	Melanoma thyroid breast	29,213 12,241 119,553	2004-2020 (2022FU)	N.A. Alternative reference: additive correction for premium calculation (based on the survival probability in general population)	No cure model. Conditional annual survival probability in cancer cohort estimated with flexible parametric model	Mexhaz package in R	exponential of B-splines



APPENDIX 3. BELGIAN CANCER REGISTRY DATA

Appendix 3.1. Variables extracted from the Belgian Cancer Registry for analysis of the thyroid cancer cohort

Variable	Description
<i>cls_ag</i>	Age at incidence date
<i>cls_cg</i>	Clinical stage (cTNM)
<i>cls_dg</i>	ICD-10 diagnosis code
<i>cls_pg</i>	Pathological stage (pTNM)
<i>combstad</i>	Combined stage
<i>combStadkort</i>	Final consolidated stage based on first clinical and first pathological stage
<i>cStadkort</i>	Combination of clinical TNM categories into prognostic groups
<i>fld_bh</i>	Tumour behaviour
<i>fld_cm</i>	Presence or absence of distant metastases based on evidence at treatment start
<i>fld_cn</i>	Presence and extent of regional lymph node metastases
<i>fld_ct</i>	Size of the primary tumour based on pre-treatment evidence
<i>fld_df</i>	Degree of differentiation
<i>fld_dp</i>	Basis for diagnosis
<i>fld_mp</i>	Histology: full ICD-O-3 code
<i>fld_pm</i>	Presence of distant metastases based on pre-treatment evidence, supplemented or adjusted by surgical or pathological findings
<i>fld_pn</i>	Presence and extent of regional lymph node metastases based on pre-treatment evidence, supplemented or adjusted by surgical or pathological findings
<i>fld_pt</i>	Size of the primary tumour based on pre-treatment evidence, supplemented or adjusted by surgical or pathological findings
<i>fld_sx</i>	Sex at birth
<i>fld_tp</i>	Organ or tissue of tumour origin

INSZ	Patient's social security registration number
multiple	Tumour location in the sequence of malignant tumours in the patient
pStadkort	Combination of pathological TNM categories into prognostic groups
region	Region of residence at diagnosis
regist	Incidence date
regist_mm	Month of incidence date
fld_vs	Vital status at last observation (alive, deceased, or lost to follow-up)
surv_dd	Survival time in days since diagnosis
totaltum	Total number of malignant tumours in the patient
cls_ag_lod	Age (in completed years) at date of last vital status observation
regist_lod	Calendar year at date of last vital status observation
ad hoc variable	Other invasive tumour within 5 years before the incidence of the selected thyroid cancer
ad hoc variable	Other invasive tumour within 8 years after the incidence of the selected thyroid cancer
ad hoc variable	Incidence date of the most recent prior invasive tumour (excluding basal and squamous cell carcinoma of the skin) preceding the selected thyroid cancer
ad hoc variable	Incidence date of the most recent invasive tumour (excluding basal and squamous cell carcinoma of the skin) following the selected thyroid cancer



Appendix 3.2. Histology codes of thyroid carcinoma cases identified in the Belgian cancer registry over the incidence years 2004-2023

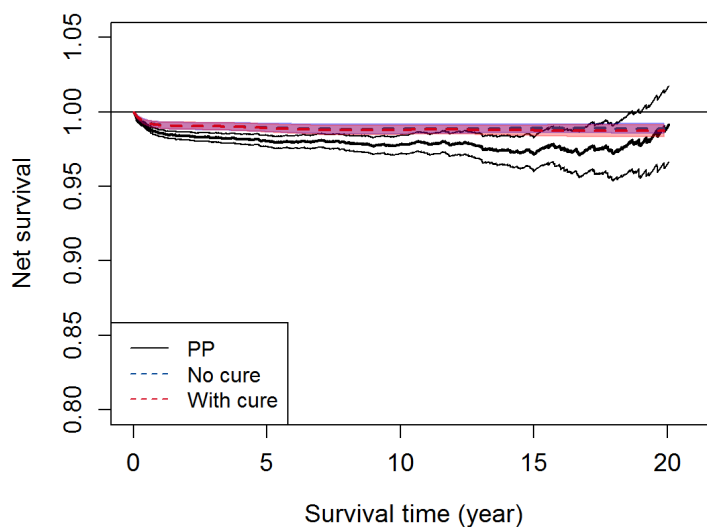
	Papillary	Follicular	Medullary	Anaplastic	Oncocytic	Non-specified
Histology codes	12658	1715	655	416	269	297
8000	0	0	0	0	0	45
8001	0	0	0	0	0	1
8010	0	0	0	0	0	60
8012	0	0	0	0	0	6
8013	0	0	0	0	0	1
8020	0	0	0	82	0	0
8021	0	0	0	303	0	0
8041	0	0	0	0	0	1
8050	4	0	0	0	0	0
8052	0	0	0	0	0	1
8070	0	0	0	26	0	0
8071	0	0	0	5	0	0
8140	0	0	0	0	0	123
8240	0	0	0	0	0	1
8243	0	0	0	0	0	1
8245	0	0	0	0	0	1
8246	0	0	0	0	0	3
8249	0	0	0	0	0	1
8260	5332	0	0	0	0	0
8265	2	0	0	0	0	0
8290	0	0	0	0	269	0
8310	0	0	0	0	0	3
8323	0	0	0	0	0	1
8330	0	1028	0	0	0	0
8331	0	48	0	0	0	0
8332	0	15	0	0	0	0
8335	0	504	0	0	0	0
8337	0	84	0	0	0	0
8339	0	36	0	0	0	0
8340	4132	0	0	0	0	0
8341	2690	0	0	0	0	0
8342	116	0	0	0	0	0
8343	282	0	0	0	0	0
8344	67	0	0	0	0	0
8345	0	0	631	0	0	0
8346	0	0	10	0	0	0
8347	0	0	14	0	0	0
8350	33	0	0	0	0	0
8430	0	0	0	0	0	10
8480	0	0	0	0	0	2
8550	0	0	0	0	0	1
8572	0	0	0	0	0	1
8574	0	0	0	0	0	1
8589	0	0	0	0	0	1
8680	0	0	0	0	0	1
8693	0	0	0	0	0	1
8800	0	0	0	0	0	4
8801	0	0	0	0	0	1
8803	0	0	0	0	0	1
8805	0	0	0	0	0	1
8830	0	0	0	0	0	1
8890	0	0	0	0	0	5
8940	0	0	0	0	0	1
8980	0	0	0	0	0	2
9080	0	0	0	0	0	1
9120	0	0	0	0	0	13

APPENDIX 4. RESULTS

Appendix 4.1. Model development

Adequacy of the cure-model predictions were visually assessed by comparison to the empirical net-survival curve (Pohar-Perme method). As a first step, predictions from a covariate-free model were considered (see Figure 36). The model without covariates did not reproduce the empirical pattern satisfactorily: predicted survival was systematically overestimated, indicating persistent and non-random deviation from observed data. This misfit demonstrates that the cohort contains meaningful heterogeneity in factors influencing excess mortality. Consequently, incorporating clinically relevant covariates was essential to improve model performance and better reflect underlying survival dynamics.

Figure 36 – Net survival: Pohar-Perme estimator and model prediction



Full line: Pohar-Perme estimate, thinner lines represent the 95% CI. Dashed line: net survival prediction from a model without covariates, shaded areas represent the 95% CI.

Inclusion of the prespecified covariates - clinical subgroup (*histo*), age at diagnosis (*age*), and distant metastasis (*cM*) at diagnosis - significantly improved the model. Likelihood-ratio tests provided strong evidence for non-proportional hazard effects (*nph*) associated with clinical subgroup and distant metastasis. Furthermore, significant effect modification was detected through interactions between clinical subgroup and age, and between clinical subgroup and distant metastasis (see Table 29).



Table 29 – Evaluating covariates for inclusion in cure models (maximum likelihood ratio estimation)

Base model	Extra term	LRT p-value
<i>histo</i>	nph(histo)	0.0407
<i>histo + nph(histo)</i>	age	0.0001
<i>histo + nph(histo) + age</i>	nph(age)	1.0000
<i>histo + nph(histo) + age</i>	cM	0.0000
<i>histo + nph(histo) + age + cM</i>	nph(cM)	0.0007
<i>histo + nph(histo) + age + cM + nph(cM)</i>	age:histo	0.0000
<i>histo + nph(histo) + age + cM + nph(cM) + age:histo</i>	cM:histo	0.0000
<i>histo + nph(histo) + age + cM + nph(cM) + age:histo + histo:cM</i>	age:cM	0.2058

The $-2 \times \log$ -likelihood for this model is 10546.65.

Next, age at diagnosis was evaluated both as a categorical and a continuous covariate. Two categorical specifications were considered:

- (1) two groups (<55, 55–74 years), and
- (2) four groups (<45, 45–54, 55–64, 65–74 years).

When added to the model, the comparison of these two categorical specifications using a likelihood ratio test (LRT) showed a preference for the four-category (p-value <0.0001). A continuous age effect was also assessed by introducing a cubic spline with three degrees of freedom. Because the continuous and four-group categorical models are not nested, an LRT cannot be used; however, both models contain the same number of parameters, allowing comparison via their $-2 \times \log$ -likelihood values (equivalent to AIC in this context). The difference between the two specifications was minimal ($-2 \times \log$ -likelihood=10878.71 for the continuous vs. $-2 \times \log$ -likelihood=10872.74 for the four-category model), indicating no clear advantage of the continuous versus the categorical covariate. The four-category age structure (<45, 45–54, 55–64, 65–74) was retained for subsequent modelling.

For reporting purposes, results were aggregated according to the predefined two-group age structure. The aggregated net survival results are obtained as a weighted average of the predicted net survival curves per clinical subgroup-age-cM combination, $\widehat{NS}(h, a, m)$, with the fraction of observations per stratum, $f_{h,a,m}$, as weight. For the full cohort marginal result, a summation over all covariate levels is performed:

$$\widehat{NS}_w(t) = \sum_{h=1}^3 \sum_{a=1}^4 \sum_{m=1}^2 f_{h,a,m} \widehat{NS}(h, a, m). \quad (9)$$

To obtain the result for the <55 year age group for example, the summation for the age dimension is limited to the two youngest age groups: $\widehat{NS}_w(t) = \sum_{h=1}^3 \sum_{a=1}^2 \sum_{m=1}^2 n_{h,a,m} \widehat{NS}(h, a, m)$. The delta rule based on matrix multiplication was used to obtain the standard error on the aggregated survival result.

Let β be the vector of estimated model parameters and Σ_β the corresponding covariance matrix, and X the design matrix containing all covariate combinations needed on a set of time values (from 0 to 20 years in steps of 0.1 for example). The predicted log (cumulative excess hazard) matrix and its covariance matrix is given by

$$\begin{aligned} \log(H_e) &= X\beta \\ \Sigma_{\log(H_e)} &= X\Sigma_\beta X^T \end{aligned} \quad (10)$$

So:

$$H_e = \exp(X\beta)$$

$$\Sigma_{H_e} = J_{H_e} \Sigma_{\log(H_e)} J_{H_e}^T \quad (11)$$

with J_{H_e} the Jacobian matrix $J_{H_e} = \text{diag}(\exp(X\beta))$.

Another exponential transformation is needed to obtain the matrix with net survival predictions:

$$NS = \exp(-H_e)$$

$$\Sigma_{NS} = J_{NS} \Sigma_{H_e} J_{NS}^T \quad (12)$$

These matrices allow to make the weighted average given in (9) and obtain the standard error. A normal approximation is applied to construct the 95% confidence intervals.

The predicted marginal net survival for the full cohort can also be obtained with the `predict` function in the `rstpm2` package. The matrix multiplication approach gave the same result for the full cohort as the `predict` function.

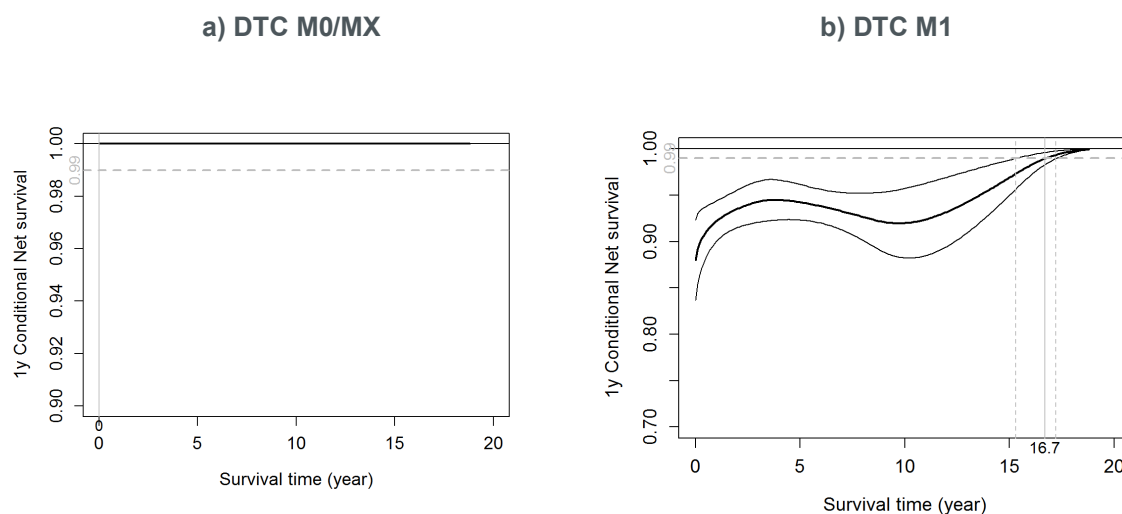
Appendix 4.2. Time-to-Cure Results

Table 30 – Predicted marginal 1-year Conditional Net Survival in differentiated thyroid carcinoma with and without clinically confirmed distant metastasis, by time since diagnosis

Time after diagnosis (Years)	DTC M0/MX		DTC M1	
	1-yCNS	95%CI	1-yCNS	95%CI
0	1.00	[1, 1]	0.880	[0.837, 0.923]
1	1.00	[1, 1]	0.922	[0.9, 0.944]
2	1.00	[1, 1]	0.935	[0.915, 0.956]
3	1.00	[1, 1]	0.943	[0.921, 0.965]
4	1.00	[1, 1]	0.945	[0.923, 0.966]
5	1.00	[1, 1]	0.942	[0.923, 0.962]
6	1.00	[1, 1]	0.938	[0.92, 0.956]
7	1.00	[1, 1]	0.933	[0.912, 0.953]
8	1.00	[1, 1]	0.927	[0.901, 0.952]
9	1.00	[1, 1]	0.921	[0.889, 0.953]
10	1.00	[1, 1]	0.920	[0.882, 0.957]
11	1.00	[1, 1]	0.924	[0.885, 0.963]
12	1.00	[1, 1]	0.932	[0.895, 0.97]
13	1.00	[1, 1]	0.943	[0.91, 0.976]
14	1.00	[1, 1]	0.956	[0.929, 0.982]
15	1.00	[1, 1]	0.969	[0.95, 0.988]
16	1.00	[1, 1]	0.982	[0.971, 0.993]
17	1.00	[1, 1]	0.992	[0.987, 0.997]
18	1.00	[1, 1]	0.998	[0.996, 0.999]
19	NA	[NA, NA]	NA	[NA, NA]



Figure 37 – Predicted marginal 1-year Conditional Net Survival: differentiated thyroid carcinoma, stratified by distant metastasis



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

Table 31 – Predicted Time-to-Cure (TTC) in differentiated thyroid carcinoma, by covariate level combinations: age group and distant metastasis

Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
<i>Differentiated thyroid carcinoma</i>						
<45	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	5,336	99	10.29 (0.01, 20.05)
45-54	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	3,449	169	10.16 (0.04, 20.05)
55-64	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	2,922	343	9.37 (0.02, 20.05)
65-74	M0/MX	0 (0,0)	1.0 (1.0, 1.0)	1,809	467	7.84 (0, 20.05)
<45	M1	14.1 (0, 16.0)	NE*	30	3	6.61 (0.20, 20.05)
45-54	M1	16.2 (0, 17.1)	0.59 (0.35, 0.98)	20	6	7.23 (1.34, 18.80)
55-64	M1	17.2 (14.6, 17.7)	0.29 (0.16, 0.54)	45	28	5.58 (0.07, 19.83)
65-74	M1	17.7 (15.6, 18.1)	0.11 (0.04, 0.29)	91	67	3.36 (0.01; 15.47]

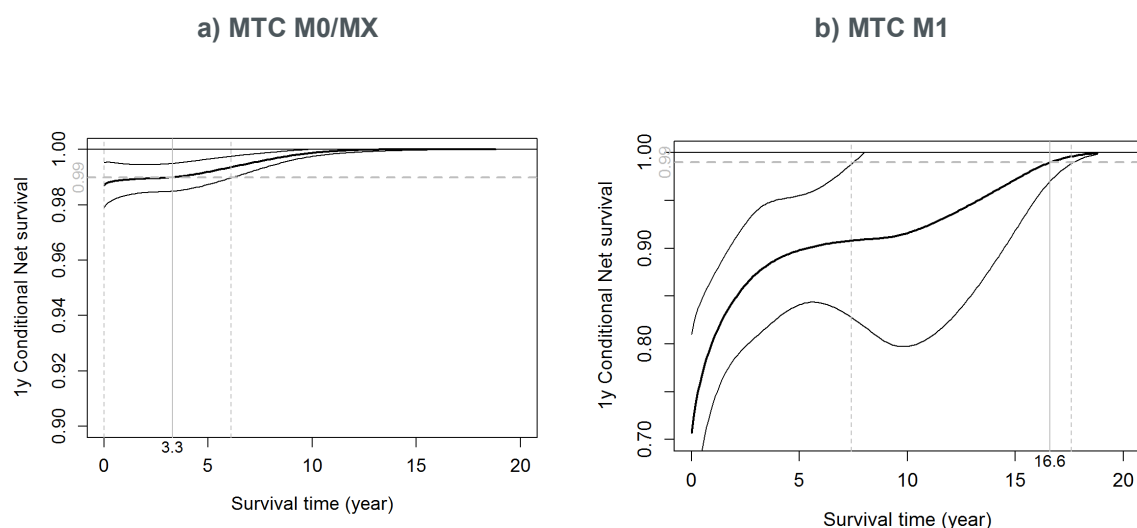
*Not estimable due to very small sample size

Table 32 – Predicted marginal 1-year Conditional Net Survival in medullary thyroid carcinoma with and without distant metastasis, by time since diagnosis

Time after diagnosis (Years)	MTC M0/MX		MTC M1	
	1-yCNS	95%CI	1-yCNS	95%CI
0	0.987	[0.979, 0.995]	0.707	[0.604, 0.81]
1	0.989	[0.983, 0.995]	0.804	[0.738, 0.871]
2	0.989	[0.984, 0.995]	0.847	[0.785, 0.909]
3	0.990	[0.985, 0.995]	0.873	[0.808, 0.939]
4	0.991	[0.986, 0.996]	0.889	[0.827, 0.951]
5	0.992	[0.987, 0.997]	0.898	[0.841, 0.955]
6	0.994	[0.99, 0.997]	0.904	[0.843, 0.964]
7	0.995	[0.992, 0.998]	0.907	[0.833, 0.98]
8	0.997	[0.994, 0.999]	0.909	[0.818, 1]
9	0.998	[0.996, 1]	0.911	[0.802, 1]
10	0.999	[0.998, 1]	0.916	[0.797, 1]
11	0.999	[0.998, 1]	0.924	[0.806, 1]
12	1.000	[0.999, 1]	0.935	[0.826, 1]
13	1.000	[0.999, 1]	0.947	[0.853, 1]

14	1.000	[1, 1]	0.959	[0.884, 1]
15	1.000	[1, 1]	0.972	[0.919, 1]
16	1.000	[1, 1]	0.984	[0.954, 1]
17	1.000	[1, 1]	0.993	[0.979, 1]
18	1.000	[1, 1]	0.998	[0.993, 1]
19	NA	[NA, NA]	NA	[NA, NA]

Figure 38 – Predicted marginal 1-year Conditional Net Survival: medullary thyroid carcinoma, stratified by distant metastasis



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

Table 33 – Predicted Time-to-Cure (TTC) in medullary thyroid carcinoma, by covariate level combinations: age group and distant metastasis

Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
Medullary thyroid carcinoma						
<45	M0/MX	0 (0, 0.35)	0.96 (0.93, 0.99)	134	8	11.67 (0.25, 20.05)
45-54	M0/MX	4.2 (0, 6.9)	0.91 (0.86, 0.97)	121	16	9.45 (0.91, 20.05)
55-64	M0/MX	3.4 (0, 6.6)	0.92 (0.87, 0.97)	148	27	9.02 (0.11, 20.05)
65-74	M0/MX	6.0 (0, 7.9)	0.88 (0.81, 0.96)	122	52	7.95 (0.11, 20.05)
<45	M1	15.9 (2.4, 17.3)	0.40 (0.18, 0.91)	11	4	3.01 (0.11, 18.0)
45-54	M1	17.0 (6.4, 18.0)	0.11 (0.02, 0.81)	10	8	2.35 (0.13, 5.84)
55-64	M1	16.9 (6.9, 18.0)	0.14 (0.03, 0.72)	11	8	1.81 (0.06, 12.59)
65-74	M1	17.3 (6.9, 18.2)	0.05 (0.0, 0.64)	19	16	1.60 (0.02, 5.44)

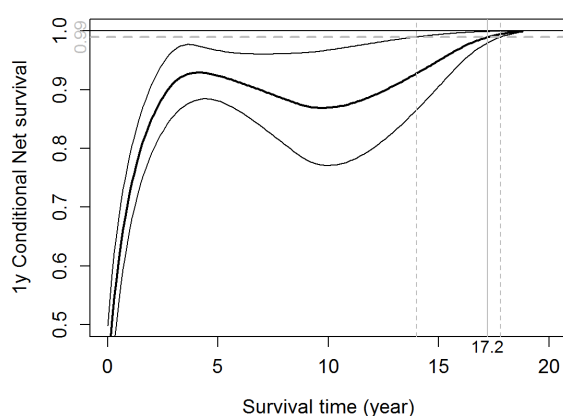


Table 34 – Predicted marginal 1-year Conditional Net Survival in anaplastic thyroid carcinoma with and without clinically confirmed distant metastasis, by time since diagnosis

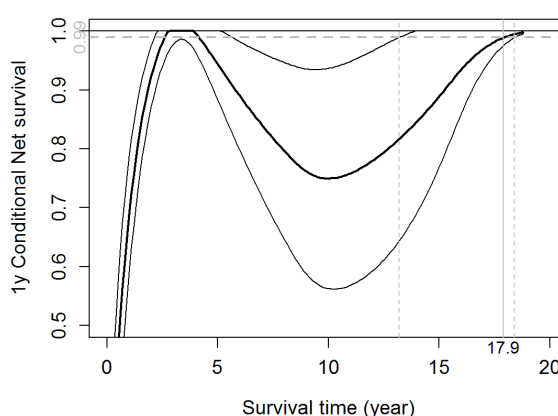
Time after diagnosis (Years)	ATC M0/MX		ATC M1	
	1-yCNS	95%CI	1-yCNS	95%CI
0	0.423	[0.347, 0.499]	0.176	[0.109, 0.244]
1	0.725	[0.662, 0.788]	0.689	[0.591, 0.787]
2	0.851	[0.792, 0.909]	0.924	[0.872, 0.976]
3	0.912	[0.856, 0.968]	1.000	[0.978, 1]
4	0.929	[0.882, 0.976]	0.997	[0.964, 1]
5	0.924	[0.881, 0.967]	0.944	[0.883, 1]
6	0.912	[0.863, 0.962]	0.890	[0.797, 0.982]
7	0.898	[0.836, 0.961]	0.841	[0.718, 0.963]
8	0.884	[0.808, 0.961]	0.797	[0.647, 0.947]
9	0.872	[0.781, 0.963]	0.762	[0.587, 0.936]
10	0.869	[0.771, 0.968]	0.750	[0.563, 0.937]
11	0.876	[0.779, 0.973]	0.759	[0.568, 0.949]
12	0.890	[0.8, 0.979]	0.780	[0.593, 0.967]
13	0.908	[0.83, 0.985]	0.810	[0.634, 0.986]
14	0.928	[0.866, 0.99]	0.847	[0.692, 1]
15	0.950	[0.906, 0.994]	0.889	[0.769, 1]
16	0.971	[0.946, 0.997]	0.935	[0.86, 1]
17	0.987	[0.975, 0.999]	0.970	[0.934, 1]
18	0.996	[0.992, 1]	0.990	[0.979, 1]
19	NA	[NA, NA]	NA	[NA, NA]

Figure 39 – Predicted marginal 1-year Conditional Net Survival: anaplastic thyroid carcinoma, stratified by distant metastasis

a) ATC M0/MX



b) ATC M1



Predicted marginal 1y conditional net survival obtained with the non-mixture flexible parametric cure model, thinner lines represent the 95% CI

Table 35 – Predicted Time-to-Cure (TTC) in anaplastic thyroid carcinoma, by covariate level combinations: 4 age groups and distant metastasis

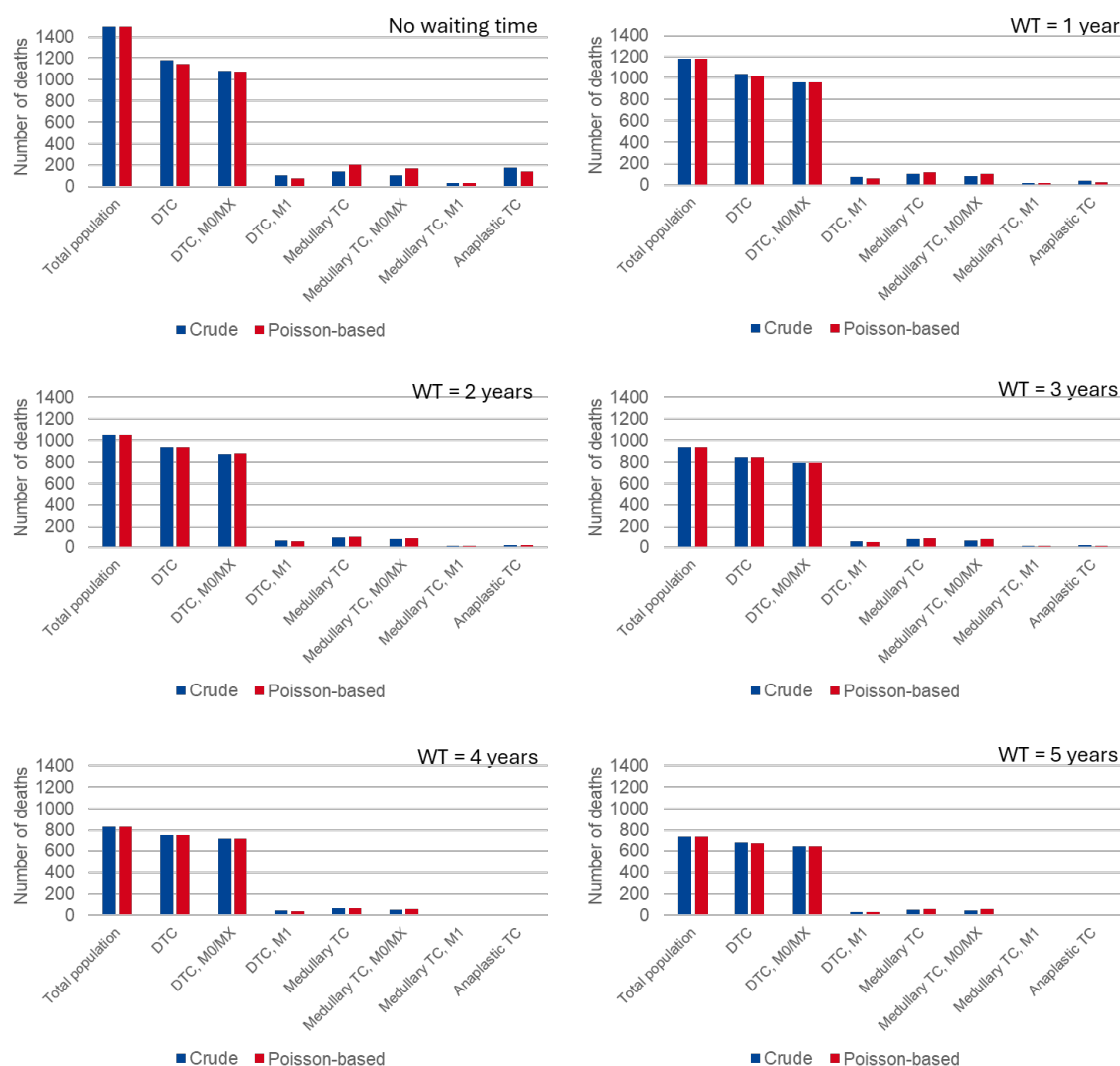
Age group	M0/MX/M1	TTC (95%CI)	Cure fraction (95%CI)	N at risk	N of deaths	Median follow-up (min, max)
<i>Anaplastic thyroid carcinoma</i>						
<45	M0/MX	16.6 (0, 17.6)	NE*	3	2	7.71 (0.47, 10.73)
45-54	M0/MX	16.7 (7.5, 17.6)	0.30 (0.14, 0.66)	16	8	5.29 (0.65, 16.95)
55-64	M0/MX	17.7 (11.6, 18.3)	0.03 (0.01, 0.20)	33	31	0.59 (0.01, 16.08)
65-74	M0/MX	17.9 (12.1, 18.4)	0.02 (0.0, 0.14)	72	64	0.50 (0.01, 13.05)
<45	M1	17.9 (0.3, 18.5)	NE*	2	1	1.80 (0.63, 2.97)
45-54	M1	17.9 (1.8, 18.5)	0.08 (0.01, 0.83)	8	6	0.31 (0.02, 7.27)
55-64	M1	18.5 (13.1, NA)	0.0 (0.0, 0.20)	27	26	0.31 (0.02, 7.27)
65-74	M1	18.6 (13.7, NA)	0.0 (0.0, 0.13)	41	39	0.12 (0.01, 8.63)

*Not estimatable due to very small sample size

Appendix 4.3. Standard mortality ratios

Appendix 4.3.1. Observed and predicted death counts in the thyroid cancer cohort

Figure 40 – Crude death counts in the thyroid cancer cohort and deaths expected from Poisson-modelled mortality rates, by subgroup and waiting time



WT: waiting time, DTC: differentiated thyroid cancer, M0/MX: no clinically confirmed distant metastasis, M1: presence of clinically confirmed distant metastasis.



Appendix 4.3.2. SMRs derived from predicted death counts in the thyroid cancer cohort

Table 36 – Standardized mortality ratios by waiting time in the cohort excluding anaplastic histology (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Differentiated and medullary TC					
0	14 278	149 199	1 392.3	1055.9	1.32 [1.23;1.41]
1	13 921	133 777	1 155.1	978.8	1.18 [1.10;1.26]
2	13 197	119 222	1 035.8	908.3	1.14 [1.06;1.22]
3	12 251	105 276	924.8	833.1	1.11 [1.03;1.19]
4	11 279	92 364	824.9	759.9	1.09 [1.01;1.17]
5	10 456	80 495	733.3	689.9	1.06 [0.98;1.15]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 37 – Standardized mortality ratios by waiting time in differentiated thyroid cancer (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Differentiated Thyroid Carcinoma					
0	13 702	143 528	1 156.3	995.6	1.16 [1.09;1.24]
1	13 395	128 796	1 013.2	924.3	1.10 [1.03;1.17]
2	12 710	114 803	918.8	857.8	1.07 [1.00;1.15]
3	11 795	101 360	825.5	786.5	1.05 [0.98;1.13]
4	10 864	88 932	740.5	717.5	1.03 [0.96;1.11]
5	10 083	77 486	659.2	650.9	1.01 [0.94;1.09]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 38 – Standardized mortality ratio by waiting time in differentiated thyroid cancer, stratified by distant metastasis (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Differentiated Thyroid Carcinoma without clinically confirmed distant metastasis					
0	13 516	142 319	1 056.3	982.0	1.08 [1.01;1.15]
1	13 240	127 799	943.5	912.9	1.03 [0.97;1.10]
2	12 569	113 992	861.0	848.6	1.01 [0.95;1.08]
3	11 675	100 692	776.4	778.8	1.00 [0.93;1.07]
4	10 767	88 385	699.0	711.0	0.98 [0.92;1.06]
5	10 005	77 038	628.2	645.5	0.97 [0.90;1.05]
Differentiated Thyroid Carcinoma with clinically confirmed distant metastasis					
0	186	1 209	100.0	13.6	7.33 [2.48;21.70]
1	155	997	69.8	11.4	6.13 [1.80;20.81]
2	141	811	57.7	9.2	6.27 [1.55;25.41]
3	120	668	49.1	7.8	6.32 [1.34;29.72]
4	97	547	41.5	6.5	6.37 [1.14;35.52]
5	78	448	31.0	5.4	5.70 [0.92;35.31]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 39 – Standardized mortality ratios in differentiated thyroid cancer without clinically confirmed distant metastasis at diagnosis, by age: <55 vs 55-74 years (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Diagnosis before age 55 years					
0	9 126	96 391	281.9	247.8	1.14 [1.01;1.29]
1	8 676	87 287	254.4	234.7	1.08 [0.95;1.23]
2	7 971	78 331	231.2	220.6	1.05 [0.92;1.19]
3	7 190	69 713	208.8	205.5	1.02 [0.89;1.16]
4	6 440	61 698	189.6	190.3	1.00 [0.87;1.14]
5	5 748	54 210	167.7	175.5	0.96 [0.83;1.10]
Diagnosed between 55 and 74 years of age					
0	4 390	45 928	774.4	734.1	1.05 [0.98;1.13]
1	4 564	40 512	689.1	678.2	1.02 [0.94;1.09]
2	4 598	35 661	629.9	628.0	1.00 [0.93;1.08]
3	4 485	30 979	567.6	573.3	0.99 [0.92;1.07]
4	4 327	26 687	509.4	520.6	0.98 [0.90;1.06]
5	4 257	22 828	460.5	469.9	0.98 [0.90;1.07]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 40 – Standardized mortality ratios by waiting time in medullary thyroid cancer (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Medullary Thyroid Carcinoma					
0	576	5 671	236.0	60.3	3.91 [2.78;5.51]
1	526	4 981	141.9	54.5	2.60 [1.88;3.61]
2	487	4 419	117.0	50.5	2.32 [1.67;3.21]
3	456	3 916	99.2	46.5	2.13 [1.54;2.96]
4	415	3 432	84.4	42.4	1.99 [1.42;2.78]
5	373	3 009	74.1	39.0	1.90 [1.34;2.69]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 41 – Standardized mortality ratios by waiting time in medullary thyroid cancer, stratified by distant metastasis (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Medullary Thyroid Carcinoma without clinically confirmed distant metastasis					
0	525	5 468	197.6	58.5	3.38 [2.42;4.71]
1	493	4 833	123.7	53.2	2.33 [1.71;3.17]
2	461	4 304	103.8	49.4	2.10 [1.54;2.86]
3	435	3 827	89.4	45.8	1.95 [1.43;2.67]
4	399	3 364	77.3	41.9	1.85 [1.34;2.54]
5	364	2 957	69.5	38.6	1.80 [1.28;2.52]
Medullary Thyroid Carcinoma with clinically confirmed distant metastasis					
0	51	203	38.4	1.8	21.40 [1.16;395.1]
1	33	148	18.1	1.3	13.52 [0.84;217.1]
2	26	115	13.2	1.0	12.98 [0.64;264.1]
3	21	89	9.8	0.8	13.04 [0.46;370.5]
4	16	68	7.1	0.5	13.32 [0.30;594.1]
5	9	52	4.6	0.4	11.87 [0.21;674.0]



WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation. Number in light grey are results for which the hypothesis of Poisson modelling are not met (Expected deaths ≤ 5).

Table 42 – Standardized mortality ratios by waiting time in medullary thyroid cancer without clinically confirmed distant metastasis, by age: <55 vs 55-74 (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Diagnosis before age 55 years					
0	268	2 798	31.0	8.3	3.73 [2.19;6.33]
1	246	2 516	19.7	7.8	2.53 [1.63;3.92]
2	227	2 270	16.5	7.3	2.26 [1.48;3.45]
3	212	2 034	14.1	6.8	2.06 [1.36;3.13]
4	184	1 807	12.3	6.4	1.93 [1.27;2.93]
5	157	1 595	10.7	5.9	1.81 [1.19;2.77]
Diagnosed between 55 and 74 years of age					
0	257	2 670	166.6	50.2	3.32 [2.38;4.64]
1	247	2 317	104.1	45.4	2.29 [1.68;3.12]
2	234	2 034	87.3	42.1	2.07 [1.52;2.83]
3	223	1 793	75.3	38.9	1.93 [1.41;2.65]
4	215	1 557	65.0	35.5	1.83 [1.33;2.53]
5	207	1 362	58.9	32.8	1.80 [1.28;2.53]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation.

Table 43 – Standardized mortality ratios by waiting time in anaplastic thyroid carcinoma (entire follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort*	Number of deaths expected	SMR (95%CI)
Anaplastic TC					
0	202	477	105.7	6.0	17.65 [1.67;186.8]
1	62	270	23.9	3.6	6.56 [1.80;23.86]
2	41	193	15.2	2.7	5.60 [1.58;19.80]
3	33	152	11.2	2.2	5.08 [1.42;18.23]
4	21	118	8.1	1.7	4.70 [1.26;17.55]
5	18	93	4.7	1.4	3.42 [1.22;9.62]

WT: waiting time, SMR: standard mortality ratio, CI: confidence interval, TC: thyroid cancer. *Cohort death counts were smoothed using a Poisson generalized linear model before SMR calculation. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Appendix 4.3.3. SMRs derived from observed death counts in thyroid cancer cohort (follow-up: up to 5, 10 and 15 years)

Table 44 – Standardized mortality ratios by waiting time in the full thyroid cancer cohort (up to 15, 10 and 5 years follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
≤15 years of follow-up					
0	14 480	142 357	1 380.0	960.9	1.44 [1.36;1.51]
1	13 983	129 137	1 091.0	914.4	1.19 [1.12;1.26]
2	13 238	116 429	993.0	868.8	1.14 [1.07;1.21]
3	12 284	103 853	908.0	812.5	1.12 [1.04;1.19]
4	11 300	91 834	819.0	752.1	1.09 [1.01;1.16]
5	10 474	80 460	730.0	689.5	1.06 [0.98;1.14]
≤10 years of follow-up					
0	14 480	119 794	1 059.0	718.4	1.47 [1.39;1.56]
1	13 983	110 206	809.0	697.2	1.16 [1.08;1.24]
2	13 238	100 783	745.0	678.6	1.10 [1.02;1.18]
3	12 284	91 298	706.0	652.6	1.08 [1.00;1.16]
4	11 300	82 119	662.0	622.7	1.06 [0.98;1.14]
5	10 474	73 321	619.0	591.5	1.05 [0.96;1.13]
≤5 years of follow-up					
0	14 480	77 289	663.0	398.8	1.66 [1.54;1.79]
1	13 983	72 199	440.0	394.0	1.12 [1.01;1.22]
2	13 238	67 084	395.0	390.8	1.01 [0.91;1.11]
3	12 284	61 752	376.0	382.8	0.98 [0.88;1.08]
4	11 300	56 565	361.0	372.7	0.97 [0.87;1.07]
5	10 474	51 485	332.0	361.8	0.92 [0.82;1.02]

WT: waiting time, SMR: standard mortality ratio, TC: thyroid cancer, CI: confidence interval.

Table 45 – Standardized mortality ratios by waiting time in the full cohort excluding anaplastic thyroid cancer (up to 15, 10 and 5 years follow-up)

WT (year)	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
≤15 years of follow-up					
0	14 278	141 882	1 205	955.0	1.26 [1.19;1.33]
1	13 921	128 867	1 055	910.7	1.16 [1.09;1.23]
2	13 197	116 236	971	866.1	1.12 [1.05;1.19]
3	12 251	103 701	891	810.3	1.10 [1.03;1.17]
4	11 279	91 716	809	750.4	1.08 [1.00;1.15]
5	10 456	80 367	720	688.1	1.05 [0.97;1.12]
≤10 years of follow-up					
0	14 278	119 342	887	712.9	1.24 [1.16;1.33]
1	13 921	109 956	774	693.9	1.12 [1.04;1.19]
2	13 197	100 601	725	676.0	1.07 [0.99;1.15]
3	12 251	91 153	690	650.4	1.06 [0.98;1.14]
4	11 279	82 005	653	621.0	1.05 [0.97;1.13]
5	10 456	73 229	610	590.1	1.03 [0.95;1.12]
≤5 years of follow-up					
0	14 278	76 901	498	394.3	1.26 [1.15;1.37]
1	13 921	72 000	412	391.6	1.05 [0.95;1.15]
2	13 197	66 937	382	388.9	0.98 [0.88;1.08]
3	12 251	61 634	366	381.2	0.96 [0.86;1.06]
4	11 279	56 472	357	371.4	0.96 [0.86;1.06]
5	10 456	51 411	326	360.7	0.90 [0.81;1.00]

WT: waiting time, SMR: standard mortality ratio, TC: thyroid cancer, CI: confidence interval.



Table 46 – Standardized mortality ratios after diagnosis (no waiting time), by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 0 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	14 480	142 357	1 380	960.9	1.44 [1.36;1.51]
<i>DTC (all)</i>	13 702	136 498	1 069	900.4	1.19 [1.12;1.26]
<i>M0/MX</i>	13 516	135 304	965	886.9	1.09 [1.02;1.16]
<i>M1</i>	186	1 194	104	13.5	7.70 [6.22;9.18]
<i>M0/MX <55y</i>	9 126	91 004	234	216.0	1.08 [0.94;1.22]
<i>M1 <55y</i>	53	406	9	0.9	10.00 [3.47;16.53]
<i>M0/MX 55-74y</i>	4 390	44 300	731	670.9	1.09 [1.01;1.17]
<i>M1 55-74y</i>	133	788	95	12.6	7.54 [6.02;9.06]
<i>Medullary (all)</i>	576	5 384	136	54.6	2.49 [2.07;2.91]
<i>M0/MX</i>	525	5 185	100	52.8	1.89 [1.52;2.27]
<i>M1</i>	51	199	36	1.8	20.00 [13.47;26.53]
<i>M0/MX <55y</i>	268	2 660	24	7.5	3.20 [1.92;4.48]
<i>M1 <55y</i>	22	99	12	0.2	60.00 [26.05;93.95]
<i>M0/MX 55-74y</i>	257	2 525	76	45.3	1.68 [1.30;2.05]
<i>M1 55-74y</i>	29	100	24	1.6	15.00 [9.00;21.00]
<i>Anaplastic (all)</i>	202	475	175	5.9	29.66 [25.27;34.06]
<i>M0/MX</i>	124	354	103	4.5	22.89 [18.47;27.31]
<i>M1</i>	78	121	72	1.4	51.43 [39.55;63.31]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 47 – Standardized mortality ratios after diagnosis (no waiting time), by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 0 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	14 480	119 794	1059	718.4	1.47 [1.39;1.56]
<i>DTC (all)</i>	13 702	114 862	771	673.2	1.15 [1.06;1.23]
<i>M0/MX</i>	13 516	113 772	682	661.4	1.03 [0.95;1.11]
<i>M1</i>	186	1 090	89	11.9	7.48 [5.93;9.03]
<i>M0/MX <55y</i>	9 126	75 644	161	154.7	1.04 [0.88;1.20]
<i>M1 <55y</i>	53	363	9	0.8	11.25 [3.90;18.60]
<i>M0/MX 55-74y</i>	4 390	38 128	521	506.6	1.03 [0.94;1.12]
<i>M1 55-74y</i>	133	727	80	11.1	7.21 [5.63;8.79]
<i>Medullary (all)</i>	576	4 480	116	39.6	2.93 [2.40;3.46]
<i>M0/MX</i>	525	4 294	81	37.9	2.14 [1.67;2.60]
<i>M1</i>	51	186	35	1.7	20.59 [13.77;27.41]
<i>M0/MX <55y</i>	268	2 178	20	5.3	3.77 [2.12;5.43]
<i>M1 <55y</i>	22	89	12	0.2	60.00 [26.05;93.95]
<i>M0/MX 55-74y</i>	257	2 116	61	32.6	1.87 [1.40;2.34]
<i>M1 55-74y</i>	29	97	23	1.5	15.33 [9.07;21.6]
<i>Anaplastic (all)</i>	202	452	172	5.6	30.71 [26.12;35.3]
<i>M0/MX</i>	124	331	100	4.2	23.81 [19.14;28.48]
<i>M1</i>	78	121	72	1.4	51.43 [39.55;63.31]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected

Table 48 – Standardized mortality ratios after diagnosis (no waiting time), by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 0 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	14 480	77 289	663	398.8	1.66 [1.54;1.79]
<i>DTC (all)</i>	13 702	73 962	414	372.0	1.11 [1.01;1.22]
<i>M0/MX</i>	13 516	73 147	347	363.6	0.95 [0.85;1.05]
<i>M1</i>	186	815	67	8.4	7.98 [6.07;9.89]
<i>M0/MX <55y</i>	9 126	47 996	82	82.1	1.00 [0.78;1.21]
<i>M1 <55y</i>	53	254	6	0.5	12.00 [2.40;21.60]
<i>M0/MX 55-74y</i>	4 390	25 151	265	281.5	0.94 [0.83;1.05]
<i>M1 55-74y</i>	133	561	61	7.9	7.72 [5.78;9.66]
<i>Medullary (all)</i>	576	2 939	84	22.2	3.78 [2.97;4.59]
<i>M0/MX</i>	525	2 779	51	20.7	2.46 [1.79;3.14]
<i>M1</i>	51	160	33	1.5	22.00 [14.49;29.51]
<i>M0/MX <55y</i>	268	1 387	12	2.9	4.14 [1.80;6.48]
<i>M1 <55y</i>	22	73	12	0.1	120.00 [52.1;187.9]
<i>M0/MX 55-74y</i>	257	1 392	39	17.9	2.18 [1.49;2.86]
<i>M1 55-74y</i>	29	87	21	1.4	15.00 [8.58;21.42]
<i>Anaplastic (all)</i>	202	388	165	4.5	36.67 [31.07;42.26]
<i>M0/MX</i>	124	275	96	3.2	30.00 [24.00;36.00]
<i>M1</i>	78	113	69	1.3	53.08 [40.55;65.6]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 49 – Standardized mortality ratios after a waiting time of 1 year, by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 1 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	13 983	129 137	1091	914.4	1.19 [1.12;1.26]
<i>DTC (all)</i>	13 395	124 078	952	860.3	1.11 [1.04;1.18]
<i>M0/MX</i>	13 240	123 092	876	849.0	1.03 [0.96;1.10]
<i>M1</i>	155	986	76	11.3	6.73 [5.21;8.24]
<i>M0/MX <55y</i>	8 676	83 600	218	211.9	1.03 [0.89;1.17]
<i>M1 <55y</i>	49	360	8	0.9	8.89 [2.73;15.05]
<i>M0/MX 55-74y</i>	4 564	39 492	658	637.2	1.03 [0.95;1.11]
<i>M1 55-74y</i>	106	626	68	10.4	6.54 [4.98;8.09]
<i>Medullary (all)</i>	526	4 789	103	50.4	2.04 [1.65;2.44]
<i>M0/MX</i>	493	4 643	84	49.1	1.71 [1.34;2.08]
<i>M1</i>	33	146	19	1.3	14.62 [8.04;21.19]
<i>M0/MX <55y</i>	246	2 431	21	7.2	2.92 [1.67;4.16]
<i>M1 <55y</i>	14	76	6	0.2	30.00 [6.00;54.00]
<i>M0/MX 55-74y</i>	247	2 212	63	41.9	1.50 [1.13;1.87]
<i>M1 55-74y</i>	19	70	13	1.1	11.82 [5.39;18.24]
<i>Anaplastic (all)</i>	62	270	36	3.6	10.00 [6.73;13.27]
<i>M0/MX</i>	51	232	30	3.1	9.68 [6.21;13.14]
<i>M1</i>	11	38	6	0.5	12.00 [2.40;21.60]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).



Table 50 – Standardized mortality ratios after a waiting time of 1 year, by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 1 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	13 983	110 206	809	697.2	1.16 [1.08;1.24]
<i>DTC (all)</i>	13 395	105 933	688	656.4	1.05 [0.97;1.13]
<i>M0/MX</i>	13 240	105 019	625	646.2	0.97 [0.89;1.04]
<i>M1</i>	155	914	63	10.2	6.18 [4.65;7.70]
<i>M0/MX <55y</i>	8 676	70 527	149	155.0	0.96 [0.81;1.12]
<i>M1 <55y</i>	49	326	8	0.7	11.43 [3.51;19.35]
<i>M0/MX 55-74y</i>	4 564	34 492	476	491.2	0.97 [0.88;1.06]
<i>M1 55-74y</i>	106	588	55	9.5	5.79 [4.26;7.32]
<i>Medullary (all)</i>	526	4 023	86	37.4	2.30 [1.81;2.79]
<i>M0/MX</i>	493	3 888	68	36.1	1.88 [1.44;2.33]
<i>M1</i>	33	135	18	1.3	13.85 [7.45;20.24]
<i>M0/MX <55y</i>	246	2 022	19	5.3	3.58 [1.97;5.20]
<i>M1 <55y</i>	14	66	6	0.1	60.00 [11.99;108.0]
<i>M0/MX 55-74y</i>	247	1 866	49	30.9	1.59 [1.14;2.03]
<i>M1 55-74y</i>	19	69	12	1.1	10.91 [4.74;17.08]
<i>Anaplastic (all)</i>	62	250	35	3.3	10.61 [7.09;14.12]
<i>M0/MX</i>	51	212	29	2.8	10.36 [6.59;14.13]
<i>M1</i>	11	38	6	0.5	12.00 [2.40;21.60]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 51 – Standardized mortality ratios after a waiting time of 1 year, by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 1 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	13 983	72 199	440	394.0	1.12 [1.01;1.22]
<i>DTC (all)</i>	13 395	69 360	355	370.6	0.96 [0.86;1.06]
<i>M0/MX</i>	13 240	68 678	310	363.4	0.85 [0.76;0.95]
<i>M1</i>	155	682	45	7.2	6.25 [4.42;8.08]
<i>M0/MX <55y</i>	8 676	45 475	72	83.7	0.86 [0.66;1.06]
<i>M1 <55y</i>	49	231	6	0.5	12.00 [2.40;21.60]
<i>M0/MX 55-74y</i>	4 564	23 203	238	279.7	0.85 [0.74;0.96]
<i>M1 55-74y</i>	106	451	39	6.7	5.82 [3.99;7.65]
<i>Medullary (all)</i>	526	2 640	57	21.0	2.71 [2.01;3.42]
<i>M0/MX</i>	493	2 529	39	19.9	1.96 [1.34;2.57]
<i>M1</i>	33	111	18	1.1	16.36 [8.8;23.92]
<i>M0/MX <55y</i>	246	1 289	11	2.8	3.93 [1.61;6.25]
<i>M1 <55y</i>	14	52	6	0.1	60.00 [11.99;108.0]
<i>M0/MX 55-74y</i>	247	1 240	28	17.1	1.64 [1.03;2.24]
<i>M1 55-74y</i>	19	59	12	1.0	12.00 [5.21;18.79]
<i>Anaplastic (all)</i>	62	199	28	2.4	11.67 [7.35;15.99]
<i>M0/MX</i>	51	165	24	2.0	12.00 [7.20;16.80]
<i>M1</i>	11	34	4	0.5	8.00 [0.16;15.84]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 52 – Standardized mortality ratios after a waiting time of 2 years, by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 2 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	13 238	116 429	993	868.8	1.14 [1.07;1.21]
<i>DTC (all)</i>	12 710	111 927	883	818.2	1.08 [1.01;1.15]
<i>M0/MX</i>	12 569	111 123	818	809.1	1.01 [0.94;1.08]
<i>M1</i>	141	804	65	9.1	7.14 [5.41;8.88]
<i>M0/MX <55y</i>	7 971	76 050	202	205.9	0.98 [0.85;1.12]
<i>M1 <55y</i>	42	314	6	0.8	7.50 [1.50;13.50]
<i>M0/MX 55-74y</i>	4 598	35 073	616	603.2	1.02 [0.94;1.10]
<i>M1 55-74y</i>	99	490	59	8.3	7.11 [5.29;8.92]
<i>Medullary (all)</i>	487	4 309	88	47.9	1.84 [1.45;2.22]
<i>M0/MX</i>	461	4 194	75	46.8	1.60 [1.24;1.97]
<i>M1</i>	26	115	13	1.0	13.00 [5.93;20.07]
<i>M0/MX <55y</i>	227	2 225	19	7.0	2.71 [1.49;3.93]
<i>M1 <55y</i>	12	64	5	0.2	25.00 [3.09;46.91]
<i>M0/MX 55-74y</i>	234	1 969	56	39.8	1.41 [1.04;1.78]
<i>M1 55-74y</i>	14	51	8	0.8	10.00 [3.07;16.93]
<i>Anaplastic (all)</i>	41	193	22	2.7	8.15 [4.74;11.55]
<i>M0/MX</i>	35	166	20	2.3	8.70 [4.88;12.51]
<i>M1</i>	6	27	2	0.4	5.00 [-1.93;11.93]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 53 – Standardized mortality ratios after a waiting time of 2 years, by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 2 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	13 238	100 783	745	678.6	1.10 [1.02;1.18]
<i>DTC (all)</i>	12 710	96 915	650	639.1	1.02 [0.94;1.10]
<i>M0/MX</i>	12 569	96 159	594	630.6	0.94 [0.87;1.02]
<i>M1</i>	141	756	56	8.5	6.59 [4.86;8.31]
<i>M0/MX <55y</i>	7 970	65 084	145	154.0	0.94 [0.79;1.09]
<i>M1 <55y</i>	42	288	6	0.7	8.57 [1.71;15.43]
<i>M0/MX 55-74y</i>	4 599	31 075	449	476.6	0.94 [0.85;1.03]
<i>M1 55-74y</i>	99	468	50	7.8	6.41 [4.63;8.19]
<i>Medullary (all)</i>	487	3 686	75	36.9	2.03 [1.57;2.49]
<i>M0/MX</i>	461	3 581	62	35.9	1.73 [1.30;2.16]
<i>M1</i>	26	105	13	1.0	13.00 [5.93;20.07]
<i>M0/MX <55y</i>	227	1 892	17	5.3	3.21 [1.68;4.73]
<i>M1 <55y</i>	12	54	5	0.1	50.00 [6.17;93.83]
<i>M0/MX 55-74y</i>	234	1 689	45	30.6	1.47 [1.04;1.90]
<i>M1 55-74y</i>	14	51	8	0.8	10.00 [3.07;16.93]
<i>Anaplastic (all)</i>	41	182	20	2.6	7.69 [4.32;11.06]
<i>M0/MX</i>	35	155	18	2.1	8.57 [4.61;12.53]
<i>M1</i>	6	27	2	0.4	5.00 [-1.93;11.93]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).



Table 54 – Standardized mortality ratios after a waiting time of 2 years, by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 2 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	13 238	67 084	395	390.8	1.01 [0.91;1.11]
DTC (all)	12 710	64 510	332	368.3	0.90 [0.8;1.00]
M0/MX	12 569	63 941	291	362.2	0.80 [0.71;0.90]
M1	141	569	41	6.0	6.83 [4.74;8.93]
M0/MX <55y	7 970	42 644	69	84.8	0.81 [0.62;1.01]
M1 <55y	42	208	4	0.5	8.00 [0.16;15.84]
M0/MX 55-74y	4 599	21 297	222	277.5	0.80 [0.69;0.91]
M1 55-74y	99	361	37	5.6	6.61 [4.48;8.74]
Medullary (all)	487	2 427	50	20.6	2.43 [1.75;3.10]
M0/MX	461	2 343	38	19.8	1.92 [1.31;2.53]
M1	26	84	12	0.8	15.00 [6.51;23.49]
M0/MX <55y	227	1 211	11	2.9	3.79 [1.55;6.03]
M1 <55y	12	42	5	0.1	50.00 [6.17;93.83]
M0/MX 55-74y	234	1 132	27	17.0	1.59 [0.99;2.19]
M1 55-74y	14	42	7	0.7	10.00 [2.59;17.41]
Anaplastic (all)	41	147	13	1.9	6.84 [3.12;10.56]
M0/MX	35	121	13	1.5	8.67 [3.96;13.38]
M1	6	26	0	0.4	0 [0;0]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 55 – Standardized mortality ratios after a waiting time of 3 years, by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 3 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	12 284	103 853	908	812.5	1.12 [1.04;1.19]
DTC (all)	11 795	99 846	819	765.2	1.07 [1.00;1.14]
M0/MX	11 675	99 182	765	757.5	1.01 [0.94;1.08]
M1	120	664	54	7.7	7.01 [5.14;8.88]
M0/MX <55y	7 190	68 492	196	197.4	0.99 [0.85;1.13]
M1 <55y	35	269	4	0.7	5.71 [0.11;11.31]
M0/MX 55-74y	4 485	30 690	569	560.1	1.02 [0.93;1.10]
M1 55-74y	85	395	50	7.0	7.14 [5.16;9.12]
Medullary (all)	456	3 855	72	45.1	1.60 [1.23;1.97]
M0/MX	435	3 766	62	44.3	1.40 [1.05;1.75]
M1	21	89	10	0.8	12.50 [4.75;20.25]
M0/MX <55y	212	2 010	16	6.7	2.39 [1.22;3.56]
M1 <55y	9	52	3	0.1	30.00 [-3.95;63.95]
M0/MX 55-74y	223	1 756	46	37.6	1.22 [0.87;1.58]
M1 55-74y	12	37	7	0.6	11.67 [3.02;20.31]
Anaplastic (all)	33	152	11.4	2.2	5.18 [2.18;8.18]
M0/MX	28	131	4.2	1.9	2.24 [0.09;4.40]
M1	5	21	7.3	0.4	20.71 [5.65;35.76]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 56 – Standardized mortality ratio after a waiting time of 3 years, by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 3 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	12 284	91 298	706	652.6	1.08 [1.00;1.16]
<i>DTC (all)</i>	11 795	87 792	626	614.5	1.02 [0.94;1.10]
<i>M0/MX</i>	11 675	87 162	577	607.3	0.95 [0.87;1.03]
<i>M1</i>	120	630	49	7.3	6.71 [4.83;8.59]
<i>M0/MX <55y</i>	7 190	59 559	143	151.6	0.94 [0.79;1.10]
<i>M1 <55y</i>	35	249	4	0.6	6.67 [0.13;13.2]
<i>M0/MX 55-74y</i>	4 485	27 603	434	455.7	0.95 [0.86;1.04]
<i>M1 55-74y</i>	85	381	45	6.7	6.72 [4.75;8.68]
<i>Medullary (all)</i>	456	3 361	64	35.9	1.78 [1.35;2.22]
<i>M0/MX</i>	435	3 280	54	35.2	1.53 [1.12;1.94]
<i>M1</i>	21	81	10	0.7	14.29 [5.43;23.14]
<i>M0/MX <55y</i>	212	1 753	14	5.3	2.64 [1.26;4.03]
<i>M1 <55y</i>	9	44	3	0.1	30.00 [-3.95;63.95]
<i>M0/MX 55-74y</i>	223	1 527	40	29.9	1.34 [0.92;1.75]
<i>M1 55-74y</i>	12	37	7	0.6	11.67 [3.02;20.31]
<i>Anaplastic (all)</i>	33	145	16	2.1	7.62 [3.89;11.35]
<i>M0/MX</i>	28	124	14	1.8	7.78 [3.70;11.85]
<i>M1</i>	5	21	2	0.4	5.00 [-1.93;11.93]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 57 – Standardized mortality ratios after a waiting time of 3 years, by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 3 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	12 284	61 752	376	382.8	0.98 [0.88;1.08]
<i>DTC (all)</i>	11 795	59 408	326	361.1	0.90 [0.80;1.00]
<i>M0/MX</i>	11 675	58 931	292	355.9	0.82 [0.73;0.91]
<i>M1</i>	120	477	34	5.2	6.54 [4.34;8.74]
<i>M0/MX <55y</i>	7 190	39 680	72	85.2	0.85 [0.65;1.04]
<i>M1 <55y</i>	35	183	2	0.4	5.00 [-1.93;11.93]
<i>M0/MX 55-74y</i>	4 485	19 251	220	270.8	0.81 [0.71;0.92]
<i>M1 55-74y</i>	85	294	32	4.8	6.67 [4.36;8.98]
<i>Medullary (all)</i>	456	2 226	40	20.0	2.00 [1.38;2.62]
<i>M0/MX</i>	435	2 163	31	19.5	1.59 [1.03;2.15]
<i>M1</i>	21	63	9	0.6	15.00 [5.20;24.80]
<i>M0/MX <55y</i>	212	1 132	8	2.9	2.76 [0.85;4.67]
<i>M1 <55y</i>	9	33	3	0.1	30.00 [-3.95;63.95]
<i>M0/MX 55-74y</i>	223	1 031	23	16.6	1.39 [0.82;1.95]
<i>M1 55-74y</i>	12	30	6	0.5	12.00 [2.40;21.60]
<i>Anaplastic (all)</i>	33	118	10	1.6	6.25 [2.38;10.12]
<i>M0/MX</i>	28	97	8	1.3	6.15 [1.89;10.42]
<i>M1</i>	5	21	2	0.4	5.00 [-1.93;11.93]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).



Table 58 – Standardized mortality ratios after a waiting time of 4 years, by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 4 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	11 300	91 834	819	752.1	1.09 [1.01;1.16]
DTC (all)	10 864	88 316	746	708.7	1.05 [0.98;1.13]
M0/MX	10 767	87 771	702	702.2	1.00 [0.93;1.07]
M1	97	545	44	6.5	6.77 [4.77;8.77]
M0/MX <55y	6 440	61 193	180	186.9	0.96 [0.82;1.10]
M1 <55y	31	230	4	0.7	5.71 [0.11;11.31]
M0/MX 55-74y	4 327	26 578	522	515.3	1.01 [0.93;1.10]
M1 55-74y	66	315	40	5.9	6.78 [4.68;8.88]
Medullary (all)	415	3 400	63	41.7	1.51 [1.14;1.88]
M0/MX	399	3 332	55	41.1	1.34 [0.98;1.69]
M1	16	68	8	0.5	16.00 [4.91;27.09]
M0/MX <55y	184	1 795	14	6.3	2.22 [1.06;3.39]
M1 <55y	7	43	3	0.1	30.00 [-3.95;63.95]
M0/MX 55-74y	215	1 537	41	34.8	1.18 [0.82;1.54]
M1 55-74y	9	25	5	0.4	12.50 [1.54;23.46]
Anaplastic (all)	21	118	10	1.7	5.88 [2.24;9.53]
M0/MX	17	102	8	1.4	5.71 [1.75;9.67]
M1	4	16	2	0.3	6.67 [-2.57;15.91]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 59 – Standardized mortality ratios after a waiting time of 4 years, by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 4 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	11 300	82 119	662	622.7	1.06 [0.98;1.14]
DTC (all)	10 864	78 981	596	586.6	1.02 [0.93;1.10]
M0/MX	10 767	78 457	556	580.3	0.96 [0.88;1.04]
M1	97	524	40	6.3	6.35 [4.38;8.32]
M0/MX <55y	6 440	54 149	140	148.1	0.95 [0.79;1.10]
M1 <55y	31	216	4	0.6	6.67 [0.13;13.2]
M0/MX 55-74y	4 327	24 308	416	432.2	0.96 [0.87;1.06]
M1 55-74y	66	308	36	5.7	6.32 [4.25;8.38]
Medullary (all)	415	3 024	57	34.4	1.66 [1.23;2.09]
M0/MX	399	2 962	49	33.9	1.45 [1.04;1.85]
M1	16	62	8	0.5	16.00 [4.91;27.09]
M0/MX <55y	184	1 604	12	5.2	2.31 [1.00;3.61]
M1 <55y	7	37	3	0.1	30.00 [-3.95;63.95]
M0/MX 55-74y	215	1 358	37	28.7	1.29 [0.87;1.70]
M1 55-74y	9	25	5	0.4	12.50 [1.54;23.46]
Anaplastic (all)	21	114	9	1.7	5.29 [1.84;8.75]
M0/MX	17	98	7	1.4	5.00 [1.30;8.70]
M1	4	16	2	0.3	6.67 [-2.57;15.91]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 60 – Standardized mortality ratios after a waiting time of 4 years, by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 4 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	11 300	56 565	361	372.7	0.97 [0.87;1.07]
<i>DTC (all)</i>	10 864	54 448	323	352.0	0.92 [0.82;1.02]
<i>M0/MX</i>	10 767	54 050	293	347.5	0.84 [0.75;0.94]
<i>M1</i>	97	398	30	4.5	6.67 [4.28;9.05]
<i>M0/MX <55y</i>	6 440	36 774	69	85.1	0.81 [0.62;1.00]
<i>M1 <55y</i>	31	161	4	0.4	10.00 [0.20;19.8]
<i>M0/MX 55-74y</i>	4 327	17 276	224	262.4	0.85 [0.74;0.97]
<i>M1 55-74y</i>	66	237	26	4.1	6.34 [3.90;8.78]
<i>Medullary (all)</i>	415	2 024	34	19.4	1.75 [1.16;2.34]
<i>M0/MX</i>	399	1 977	27	19.0	1.42 [0.89;1.96]
<i>M1</i>	16	47	7	0.4	17.5 [4.54;30.46]
<i>M0/MX <55y</i>	184	1 051	9	2.9	3.10 [1.08;5.13]
<i>M1 <55y</i>	7	27	3	0.1	30.00 [-3.95;63.95]
<i>M0/MX 55-74y</i>	215	926	18	16.1	1.12 [0.60;1.63]
<i>M1 55-74y</i>	9	20	4	0.3	13.33 [0.27;26.4]
<i>Anaplastic (all)</i>	21	93	4	1.3	3.08 [0.06;6.09]
<i>M0/MX</i>	17	77	2	1.1	1.82 [-0.70;4.34]
<i>M1</i>	4	16	2	0.3	6.67 [-2.57;15.91]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 61 – Standardized mortality ratios after a waiting time of 5 years, by clinical subgroup, distant metastasis, and age category (up to 15 years follow-up)

WT = 5 year, FUP = 15 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
<i>Total cohort</i>	10 474	80 460	730	689.5	1.06 [0.98;1.14]
<i>DTC (all)</i>	10 083	77 367	669	649.4	1.03 [0.95;1.11]
<i>M0/MX</i>	10 005	76 920	636	644.0	0.99 [0.91;1.06]
<i>M1</i>	78	447	33	5.4	6.11 [4.03;8.20]
<i>M0/MX <55y</i>	5 748	54 108	162	174.9	0.93 [0.78;1.07]
<i>M1 <55y</i>	26	195	3	0.6	5.00 [-0.66;10.66]
<i>M0/MX 55-74y</i>	4 257	22 812	474	469.1	1.01 [0.92;1.10]
<i>M1 55-74y</i>	52	252	30	4.8	6.25 [4.01;8.49]
<i>Medullary (all)</i>	373	3 000	51	38.7	1.32 [0.96;1.68]
<i>M0/MX</i>	364	2 948	48	38.3	1.25 [0.90;1.61]
<i>M1</i>	9	52	3	0.4	7.50 [-0.99;15.99]
<i>M0/MX <55y</i>	157	1 593	11	5.9	1.86 [0.76;2.97]
<i>M1 <55y</i>	5	35	0	0.1	0 [0;0]
<i>M0/MX 55-74y</i>	207	1 355	37	32.4	1.14 [0.77;1.51]
<i>M1 55-74y</i>	4	17	3	0.3	10.00 [-1.32;21.32]
<i>Anaplastic (all)</i>	18	93	10	1.4	7.14 [2.72;11.57]
<i>M0/MX</i>	15	85	8	1.3	6.15 [1.89;10.42]
<i>M1</i>	3	8	2	0.1	20.00 [-7.72;47.72]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).



Table 62 – Standardized mortality ratios after a waiting time of 5 years, by clinical subgroup, distant metastasis, and age category (up to 10 years follow-up)

WT = 5 year, FUP = 10 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	10 474	73 321	619	591.5	1.05 [0.96;1.13]
DTC (all)	10 083	70 508	562	556.9	1.01 [0.93;1.09]
M0/MX	10 005	70 076	529	551.6	0.96 [0.88;1.04]
M1	78	432	33	5.3	6.23 [4.10;8.35]
M0/MX <55y	5 748	48 830	132	143.8	0.92 [0.76;1.07]
M1 <55y	26	184	3	0.5	6.00 [-0.79;12.79]
M0/MX 55-74y	4 257	21 246	397	407.8	0.97 [0.88;1.07]
M1 55-74y	52	248	30	4.8	6.25 [4.01;8.49]
Medullary (all)	373	2 721	48	33.2	1.45 [1.04;1.85]
M0/MX	364	2 673	45	32.8	1.37 [0.97;1.77]
M1	9	48	3	0.4	7.50 [-0.99;15.99]
M0/MX <55y	157	1 455	11	5.0	2.20 [0.90;3.50]
M1 <55y	5	31	0	0.1	0 [0;0]
M0/MX 55-74y	207	1 218	34	27.8	1.22 [0.81;1.63]
M1 55-74y	4	17	3	0.3	10.00 [-1.32;21.32]
Anaplastic (all)	18	92	9	1.4	6.43 [2.23;10.63]
M0/MX	15	84	7	1.2	5.83 [1.51;10.15]
M1	3	8	2	0.1	20.00 [-7.72;47.72]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).

Table 63 – Standardized mortality ratios after a waiting time of 5 years, by clinical subgroup, distant metastasis, and age category (up to 5 years follow-up)

WT = 5 year, FUP = 5 years	Number of TC patients	Number of patient-years	Number of deaths in the TC cohort	Number of deaths expected	SMR (95%CI)
Total cohort	10 474	51 485	332	361.8	0.92 [0.82;1.02]
DTC (all)	10 083	49 566	297	341.5	0.87 [0.77;0.97]
M0/MX	10 005	49 230	277	337.6	0.82 [0.72;0.92]
M1	78	336	20	3.9	5.13 [2.88;7.38]
M0/MX <55y	5 748	33 820	66	84.5	0.78 [0.59;0.97]
M1 <55y	26	141	3	0.4	7.50 [-0.99;15.99]
M0/MX 55-74y	4 257	15 410	211	253.2	0.83 [0.72;0.95]
M1 55-74y	52	195	17	3.6	4.72 [2.48;6.97]
Medullary (all)	373	1 845	29	19.2	1.51 [0.96;2.06]
M0/MX	364	1 810	27	18.9	1.43 [0.89;1.97]
M1	9	35	2	0.3	6.67 [-2.57;15.91]
M0/MX <55y	157	973	7	2.9	2.41 [0.63;4.20]
M1 <55y	5	21	0	0.0	-
M0/MX 55-74y	207	837	20	16.0	1.25 [0.70;1.80]
M1 55-74y	4	14	2	0.2	10.00 [-3.86;23.86]
Anaplastic (all)	18	74	6	1.1	5.45 [1.09;9.82]
M0/MX	15	66	4	1.0	4.00 [0.08;7.92]
M1	3	8	2	0.1	20.00 [-7.72;47.72]

WT: waiting time, FUP: follow-up, D: differentiated, TC: thyroid cancer, SMR: standard mortality ratio, CI: confidence interval, M0: no distance metastasis, M1: presence of distance metastasis. Numbers in light grey indicate results for which the assumptions of the Poisson distribution are not met (expected deaths ≤ 5).



APPENDIX 5. STAKEHOLDER CONSULTATION ON WAITING PERIOD SCENARIOS FOR RIGHT-TO-BE-FORGOTTEN IN THYROID CANCER

PURPOSE OF THIS CONSULTATION

You are invited to contribute to the KCE stakeholder consultation on waiting period scenarios for individuals with a history of thyroid cancer applying for outstanding balance insurance in Belgium. Your input will inform the policy recommendations that will accompany the forthcoming KCE report.

WHY YOUR INPUT MATTERS

Decisions on waiting periods are not determined by statistical evidence alone. They also involve clinical practice, actuarial considerations, and broader ethical and equity aspects.

Because these dimensions cannot be fully addressed from a single viewpoint, perspectives from all three stakeholder groups are required:

- patients and consumers
- insurers
- clinicians.

Your perspective will be synthesized and presented at a joint stakeholder meeting.

BACKGROUND

In this KCE study, the waiting period is determined by the *Time to statistical cure (TTC)*, - the time after diagnosis when the survival of the cancer cohort becomes (nearly) indistinguishable from that of the general population. In practice, this point is typically reached once early deaths in subgroups with poor prognosis have occurred.

TTC was estimated for the entire thyroid cancer cohort and predefined subgroups. These subgroups were defined based on a rigorous methodological assessment combining:

- the constraints and granularity of available data in the Belgian Cancer Registry, and
- the clinical relevance of subgroup distinctions.

The statistical analysis demonstrates that segmentation choices have a major impact on the estimated TTC:

- Pooling all subgroups produces an estimate dominated by the largest subgroup (differentiated thyroid carcinoma).
- Separating smaller subgroups (e.g. medullary thyroid cancer, metastatic differentiated thyroid carcinoma) reveals their distinctly different prognosis, but results in a more complex policy structure.

The four scenarios below are the direct outputs of the TTC analysis reflecting different segmentation choices. A stakeholder perspective is needed to judge the clinical, actuarial and ethical/ equity implications of implementing each of these options.

WHAT WE ASK FROM YOU

Please:

Step 1: Rank the four scenarios (1 = most preferred; 4 = least preferred)

Step 2: Explain your ranking

Please use the types of arguments that matter most to you as a stakeholder, for example:



- clinical reasoning (prognosis, risk differences, medical relevance)
- actuarial/logical considerations (actuarial fairness, financial sustainability)
- ethical perspectives (fairness, equity, stigma reduction)
- feasibility (clarity, administrative simplicity, risk of errors)

You may use as many or as few dimensions as you wish.

Name stakeholder:

Scenarios to be ranked

Waiting period scenarios	Rank	Motivation
<i>Scenario 1: Uniform 1-year waiting period for all thyroid cancers</i>		
<i>Scenario 2: Immediate statistical cure (0-year waiting period) for all thyroid cancers except anaplastic Anaplastic histology is not eligible.</i>		
<i>Scenario 3 - Immediate statistical cure (0-year waiting period) for differentiated thyroid carcinoma Anaplastic and medullary histology are not eligible.</i>		
<i>Scenario 4 - Immediate statistical cure (0-year waiting period) for differentiated thyroid carcinoma without distant metastasis at diagnosis Anaplastic and medullary histology as well as differentiated thyroid carcinoma with distant metastasis are not eligible.</i>		

COMMENTS (OPTIONAL):

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