

Melanoma tumour thickness in Norway

An analysis of incidence and
survival, 1983–2019



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**Research is what I'm doing when I don't know
what I'm doing.**

Wernher von Braun (1912–1977) |
A German-American physicist |

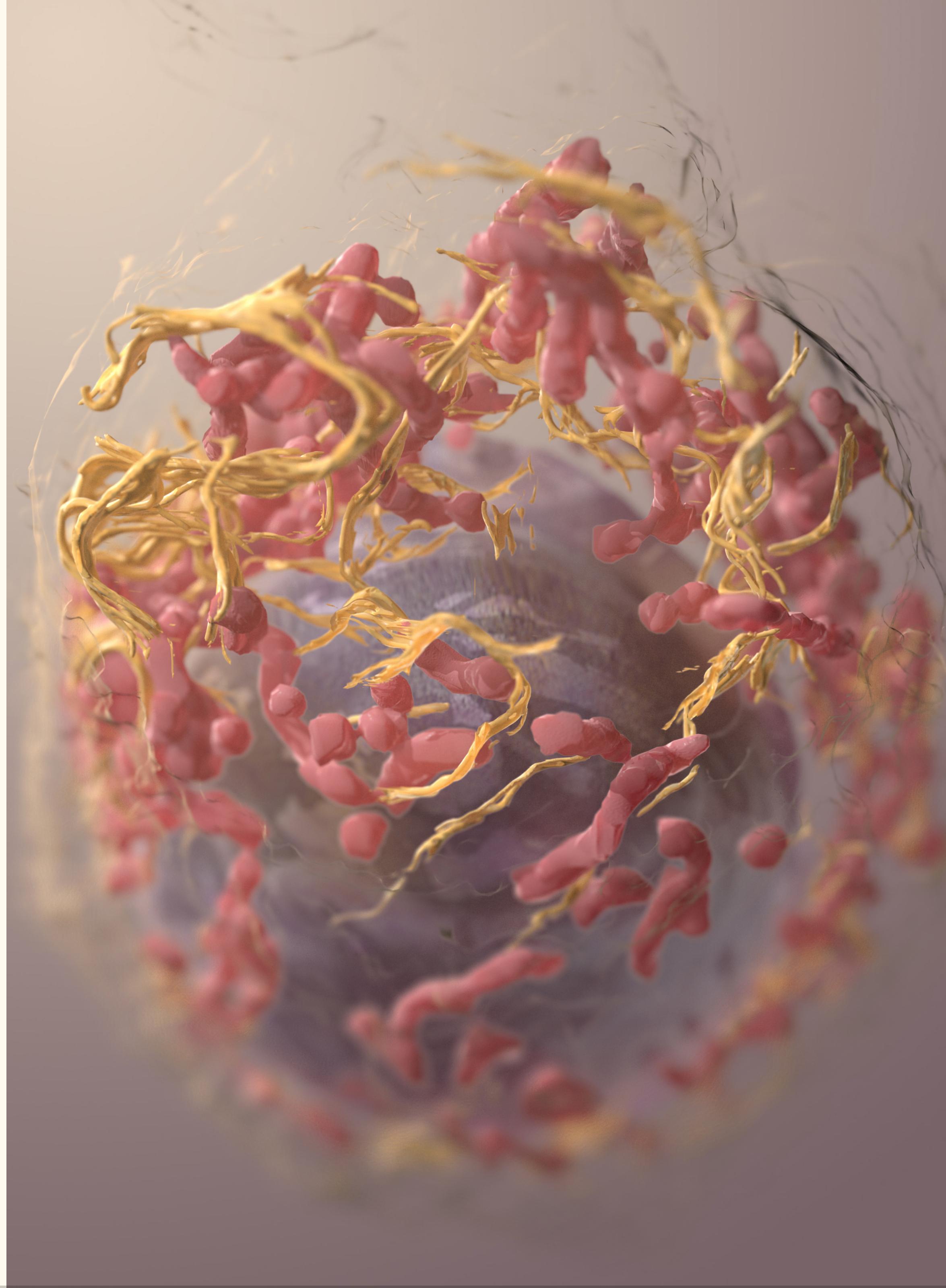
Scientific research is one of the most exciting and rewarding of occupations.

Frederick Sanger (1918–2013) |

An English biochemist with two Nobel Prize in Chemistry |

What am I doing and why?

- Cutaneous melanoma (CM) is the most aggressive and lethal form of skin cancer.
- Increasing dramatically in fair skinned population.
- Norway is ranked fifth in incidence and third in mortality worldwide.
- It's highly curable if caught early.
- Tumour thickness plays an important role



Outline

- Background
- Data and Methods
- Incidence rate and trend
- Perspectives



Research Objective

To study **melanoma incidence** and their **trend** by tumour thickness, overall and in important subgroups such as *sex*, *age* and *anatomic sites*, in a unique nationwide case series over a 35-year time period.

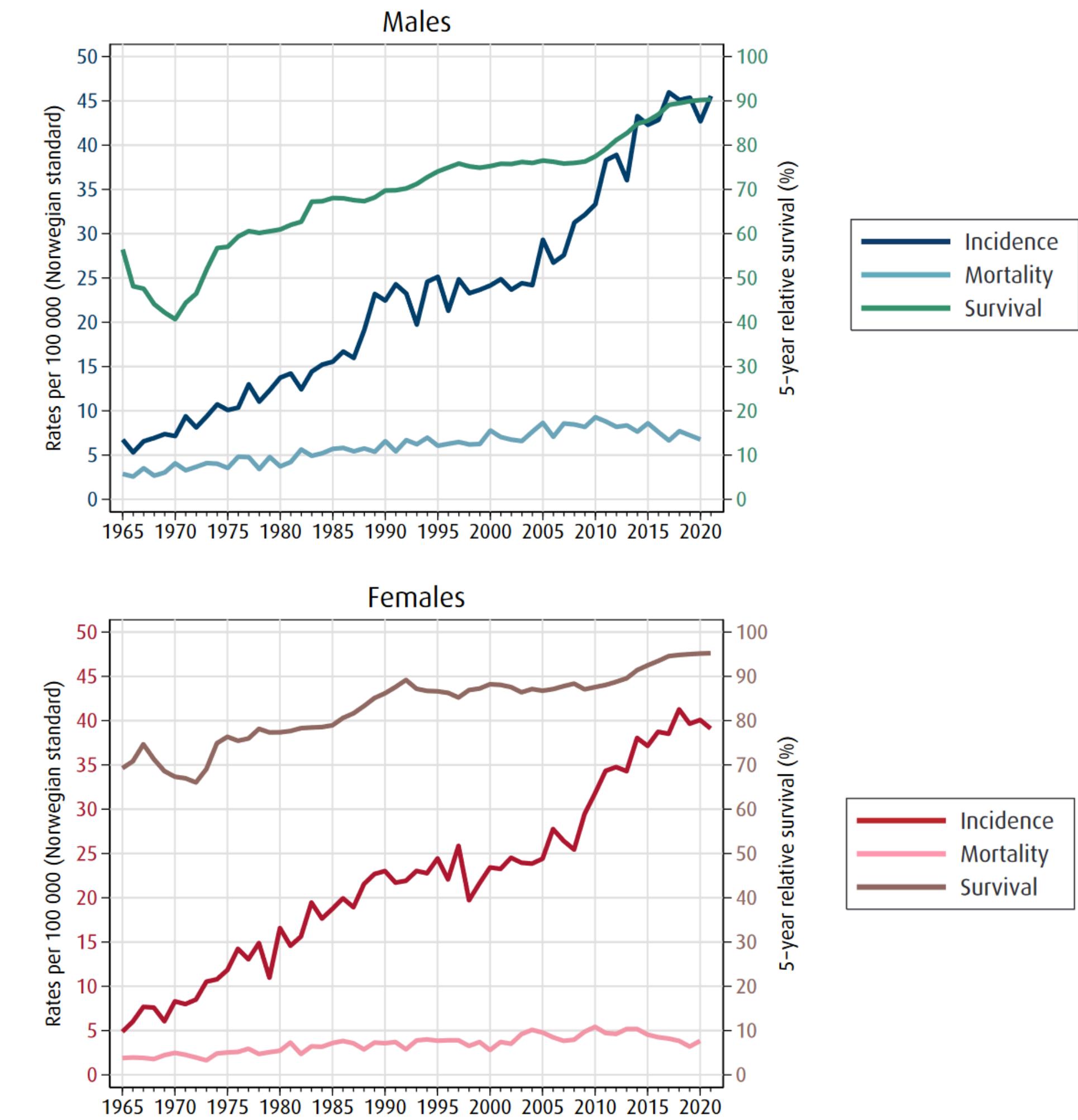
Background

Overall incidence and mortality in Norway

Incidence rates

- The rates of melanoma of the skin increased by 10.3% in men and 8.5% in women.

Figure 9.1-K: Melanoma of the skin (ICD-10 C43)



Source: Cancer in Norway, 2021

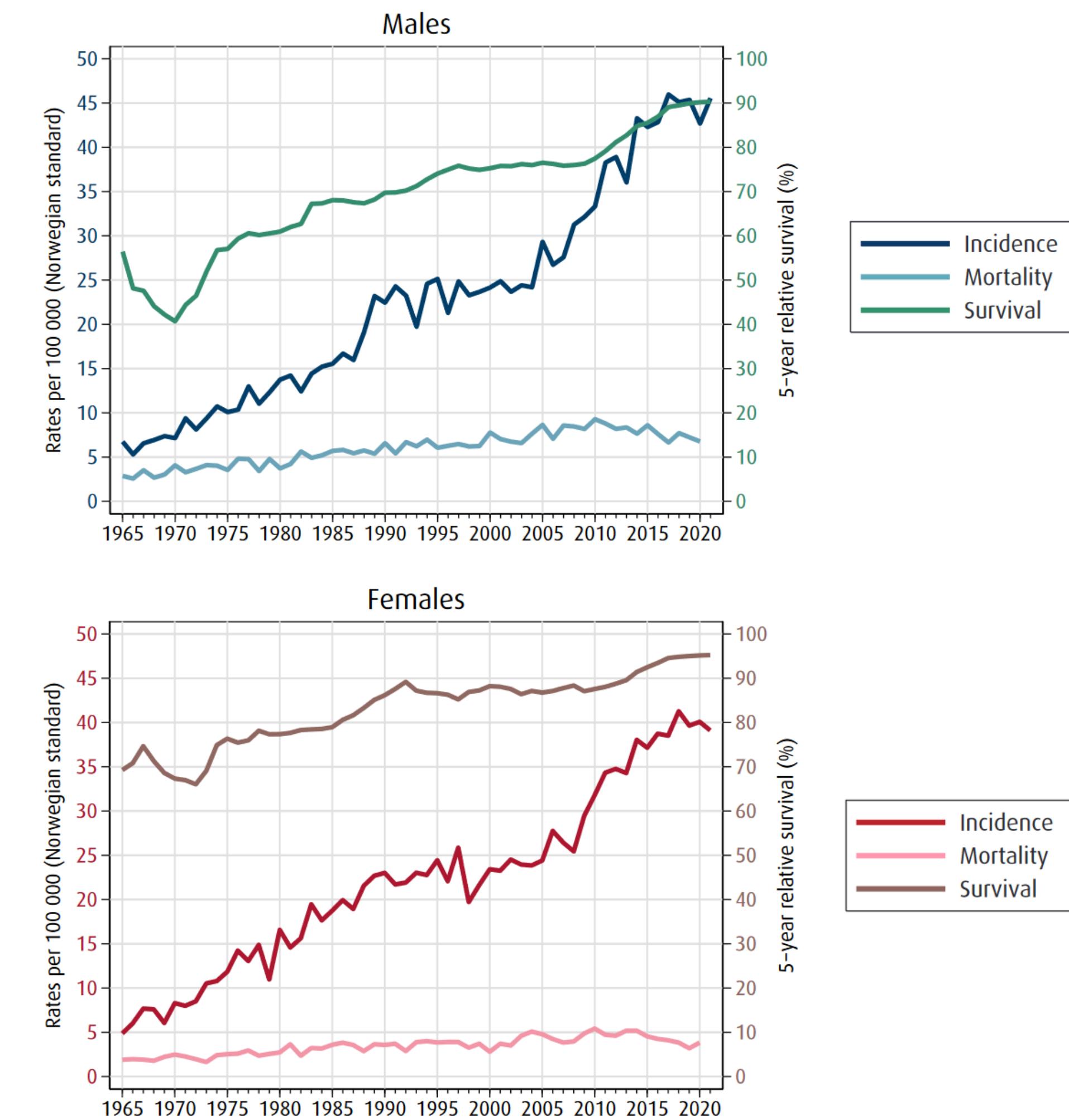
Overall incidence and mortality in Norway

Incidence rates

- The rates of melanoma of the skin increased by 10.3% in men and 8.5% in women.

A remarkable increase in incidence rates has been seen during the last decades for melanoma of the skin in both sexes (Figure 9.1-K). The steep rise is suggested to result from sun exposure habits. However, we cannot exclude the possibility that increased awareness, both in the general population and among general practitioners, and sliding of the diagnostic criteria, may also have contributed to the increase. The moderate but steady increase in melanoma mortality until 2010 indicates that some of the increase in incidence is indeed caused by a higher risk of the disease.

Figure 9.1-K: Melanoma of the skin (ICD-10 C43)

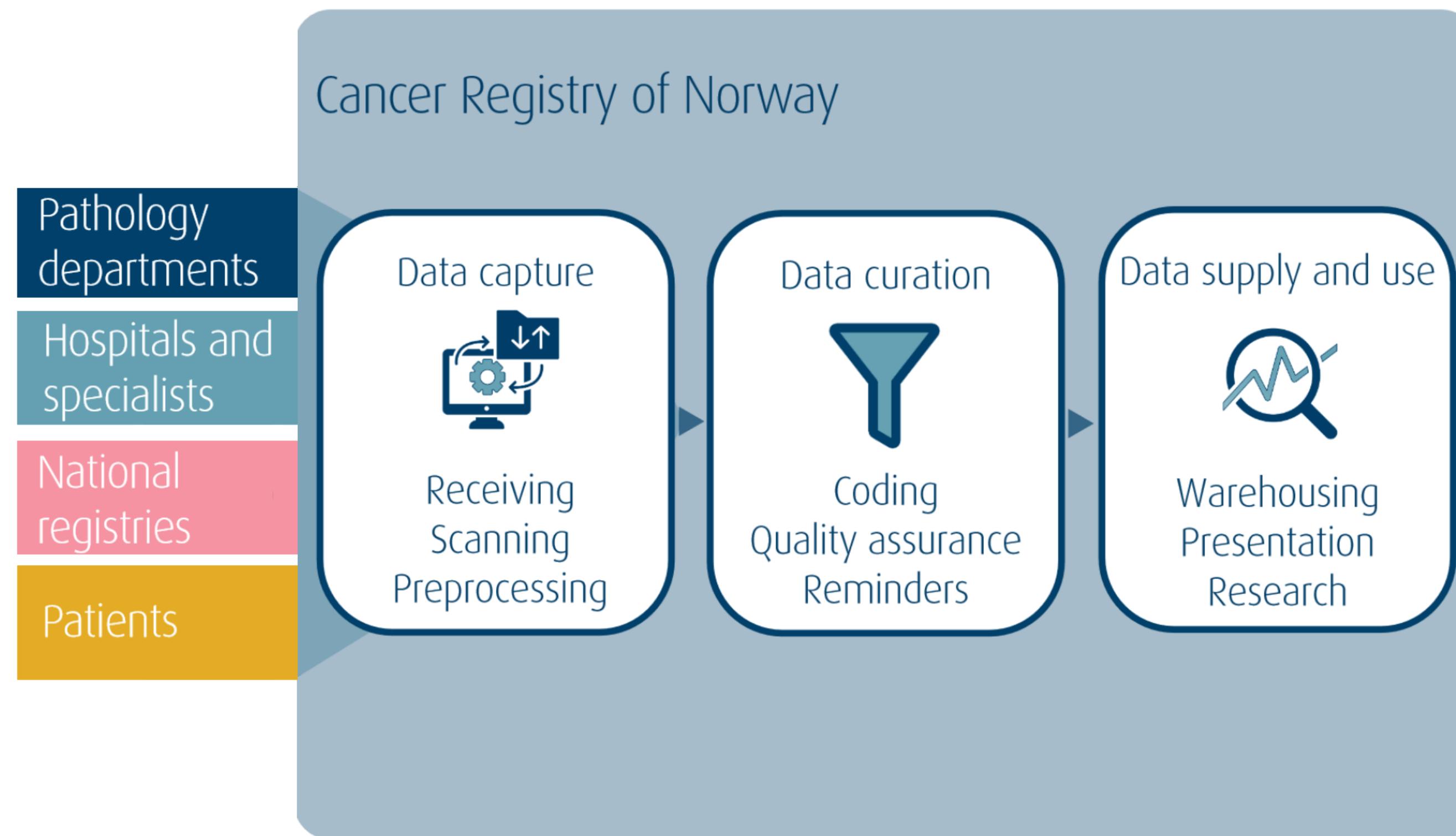


Source: Cancer in Norway, 2021

Data from Cancer Registry of Norway (CRN)

- *Histologically verified data*
- *Tumour thickness recorded since 1980 are now digitized*
- *Melanoma registry established in 2008*
- Here we will use data from 1983 to 2019

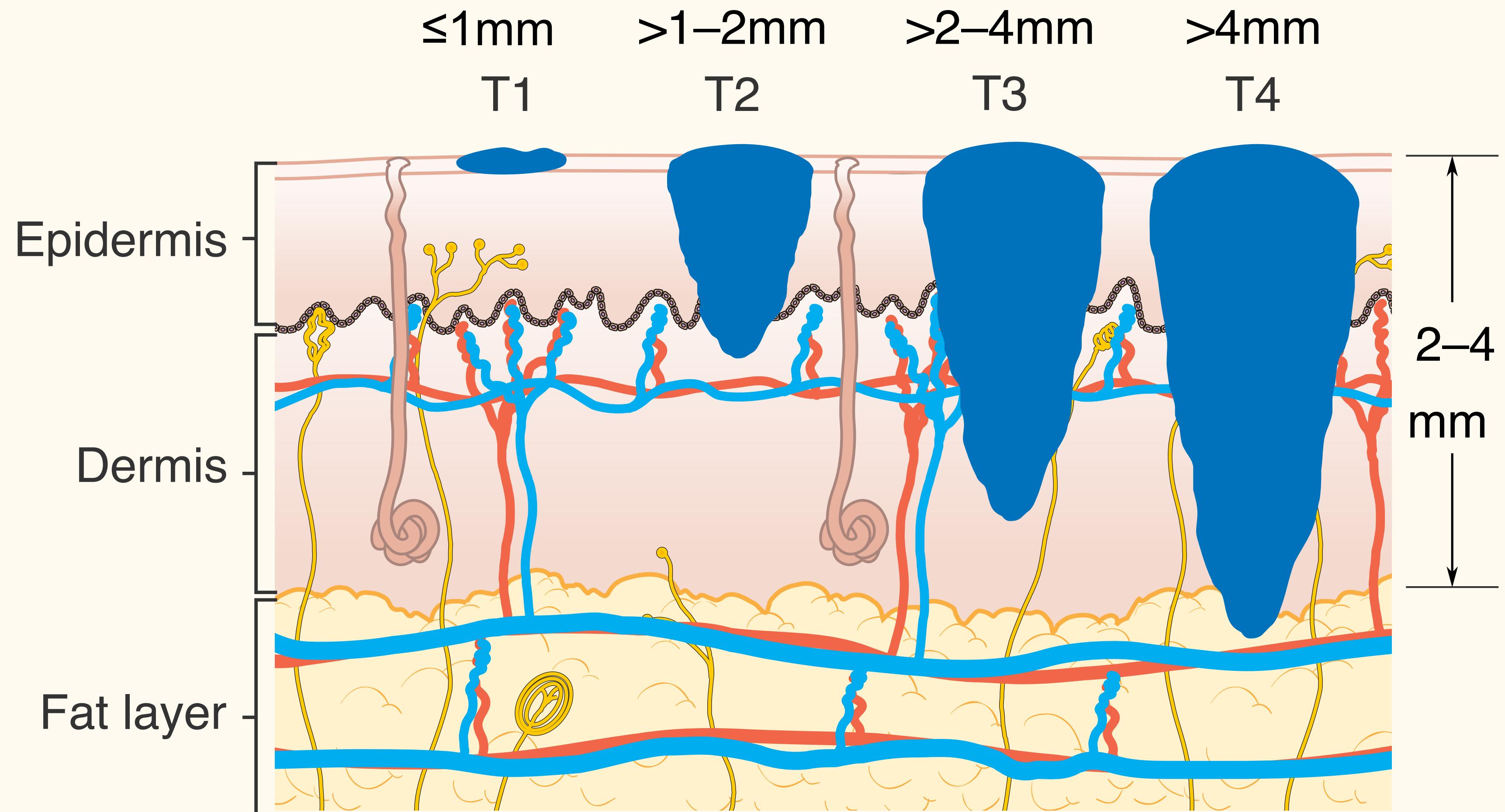
Figure 3.1: Sources of information and the process of cancer registration at the Cancer Registry of Norway



Sources: Cancer Registry of Norway

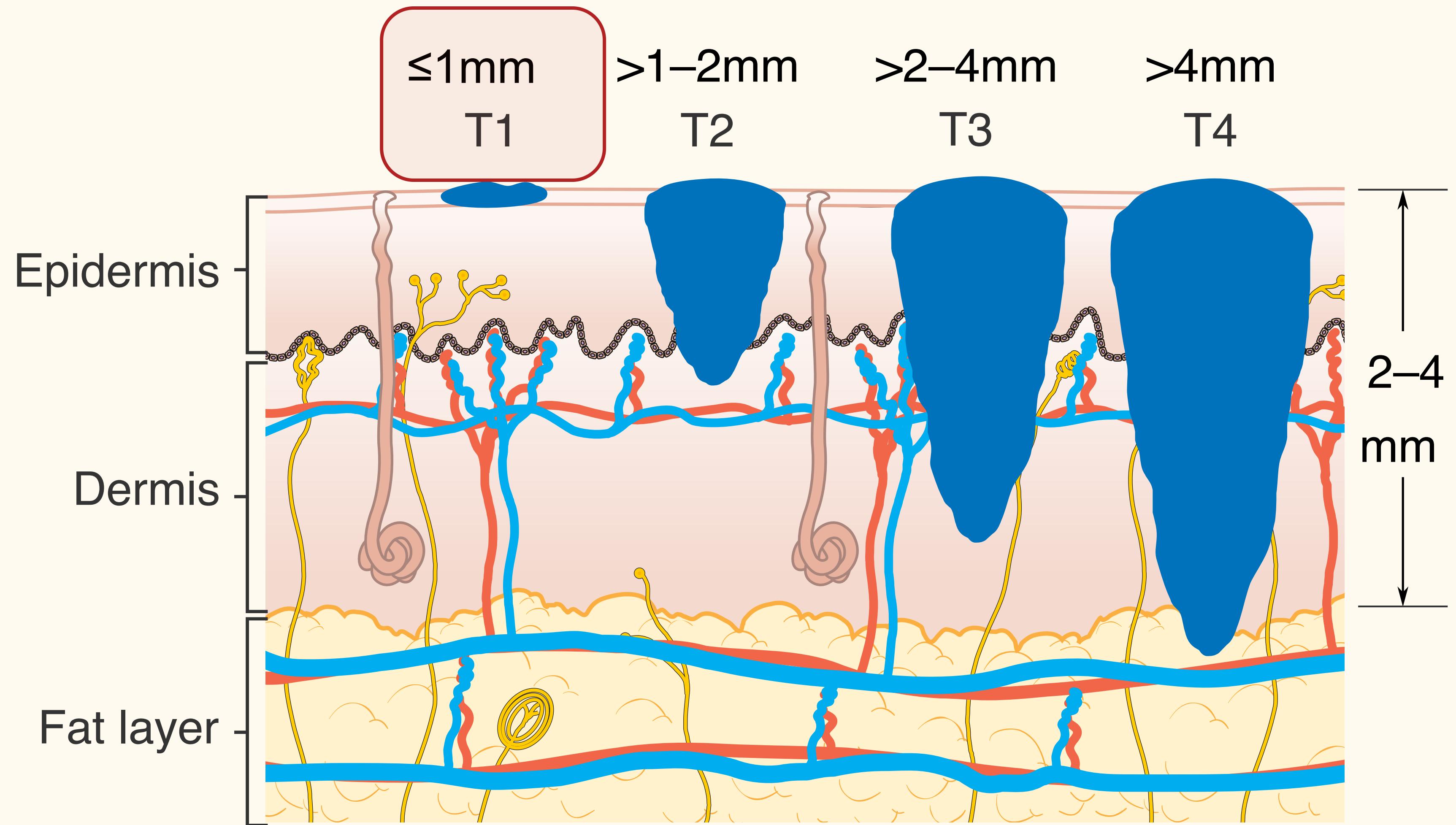
Melanoma and tumour thickness

T-categories



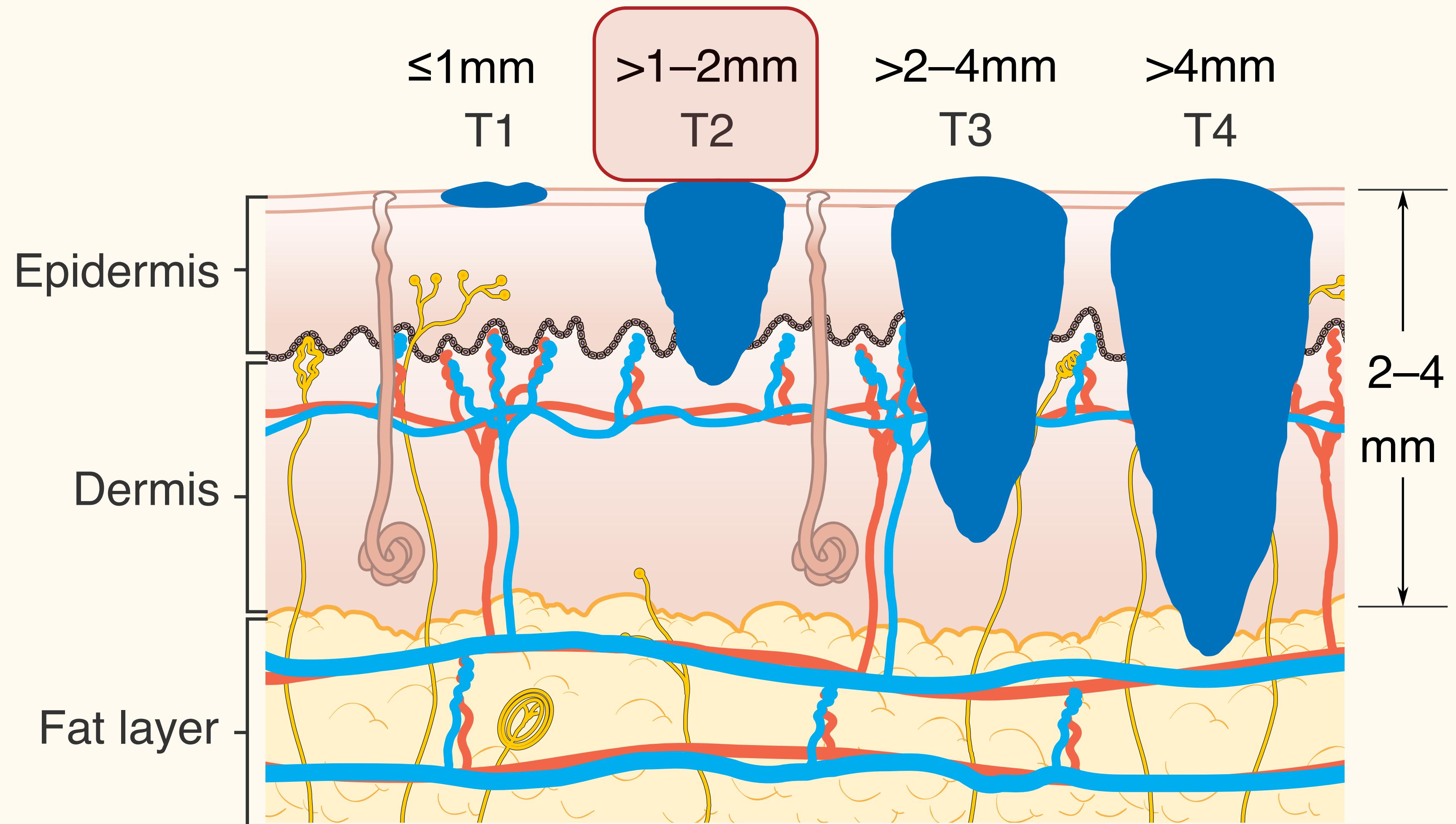
Melanoma and tumour thickness

T-categories



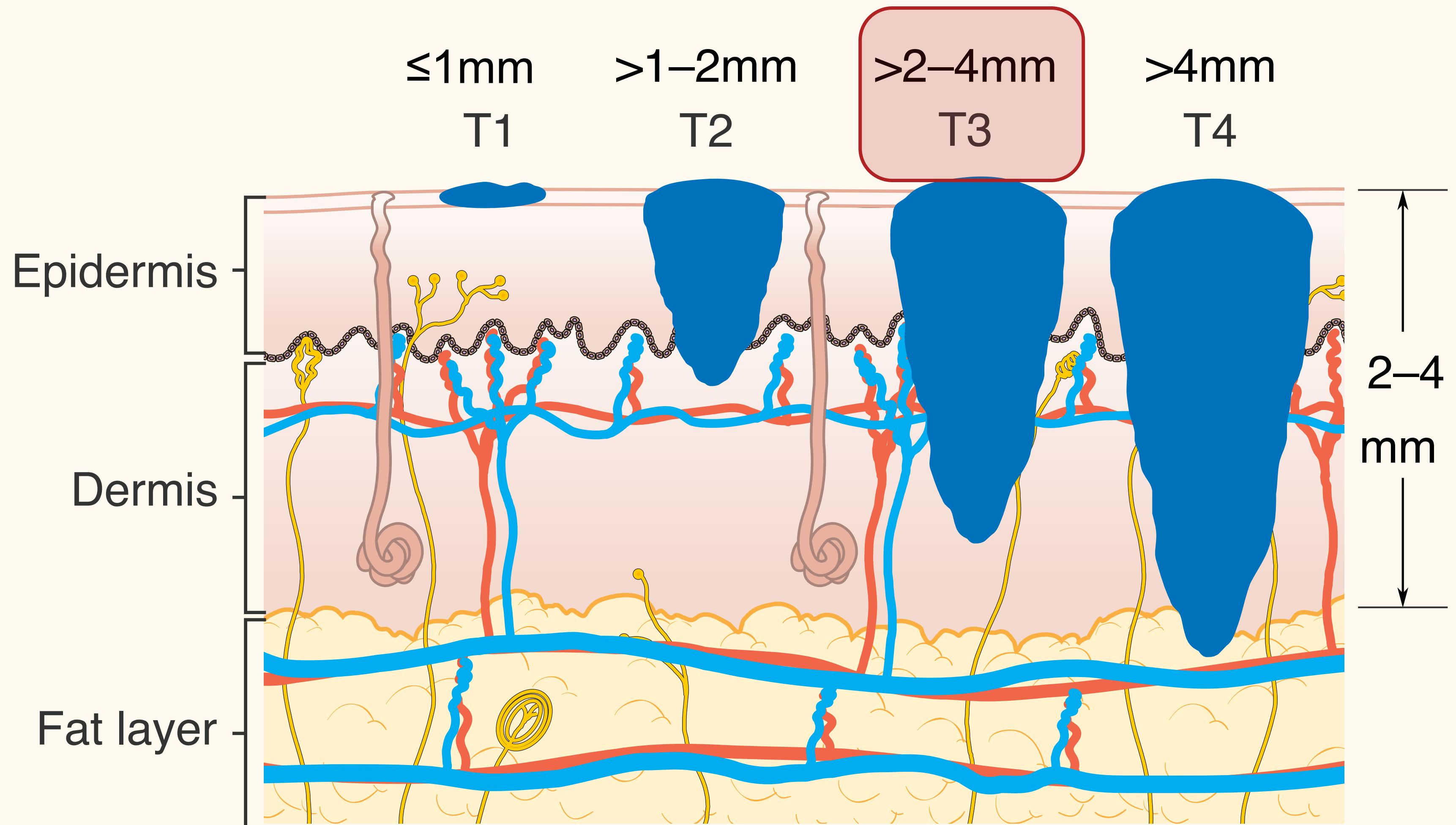
Melanoma and tumour thickness

T-categories



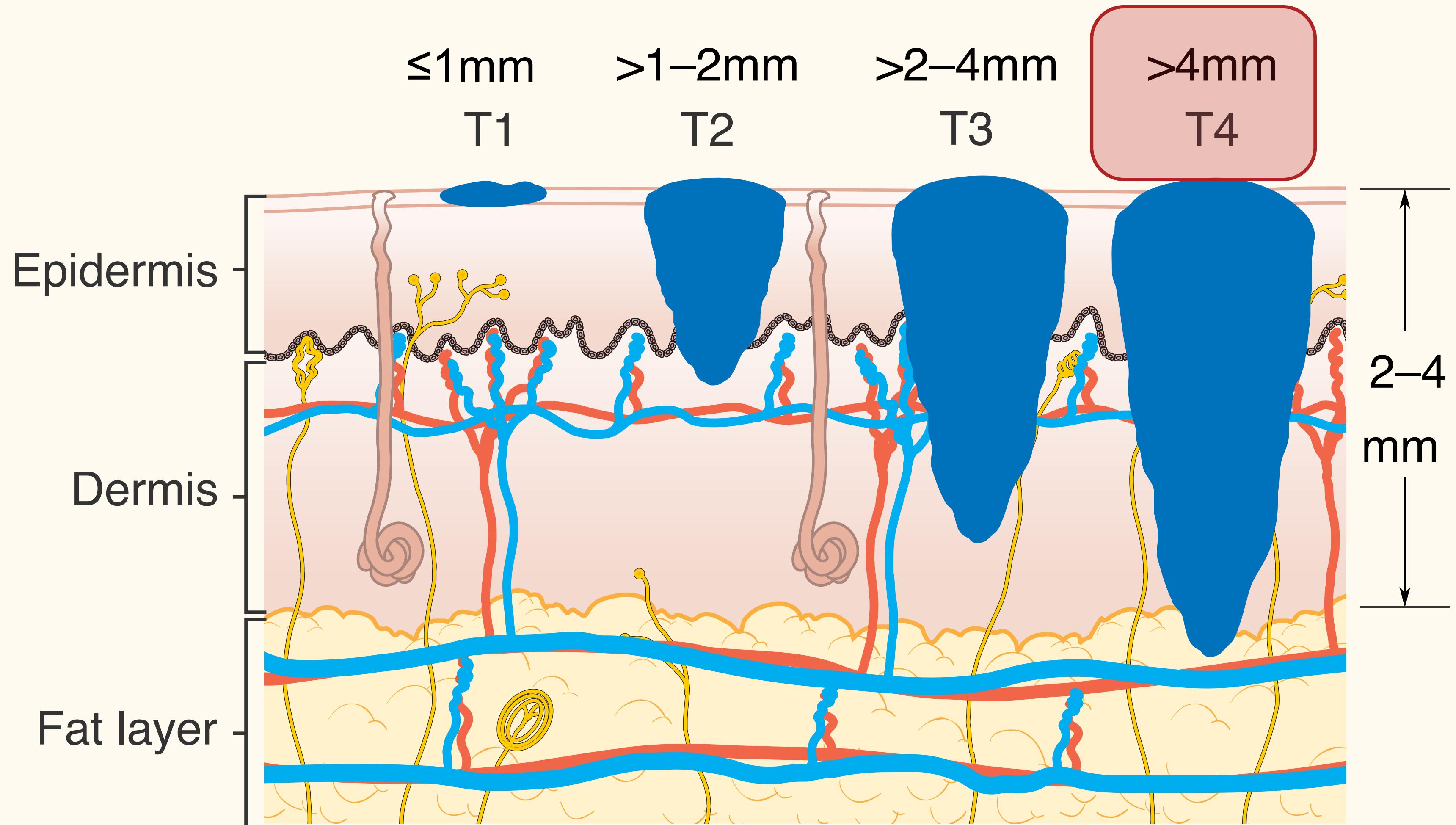
Melanoma and tumour thickness

T-categories

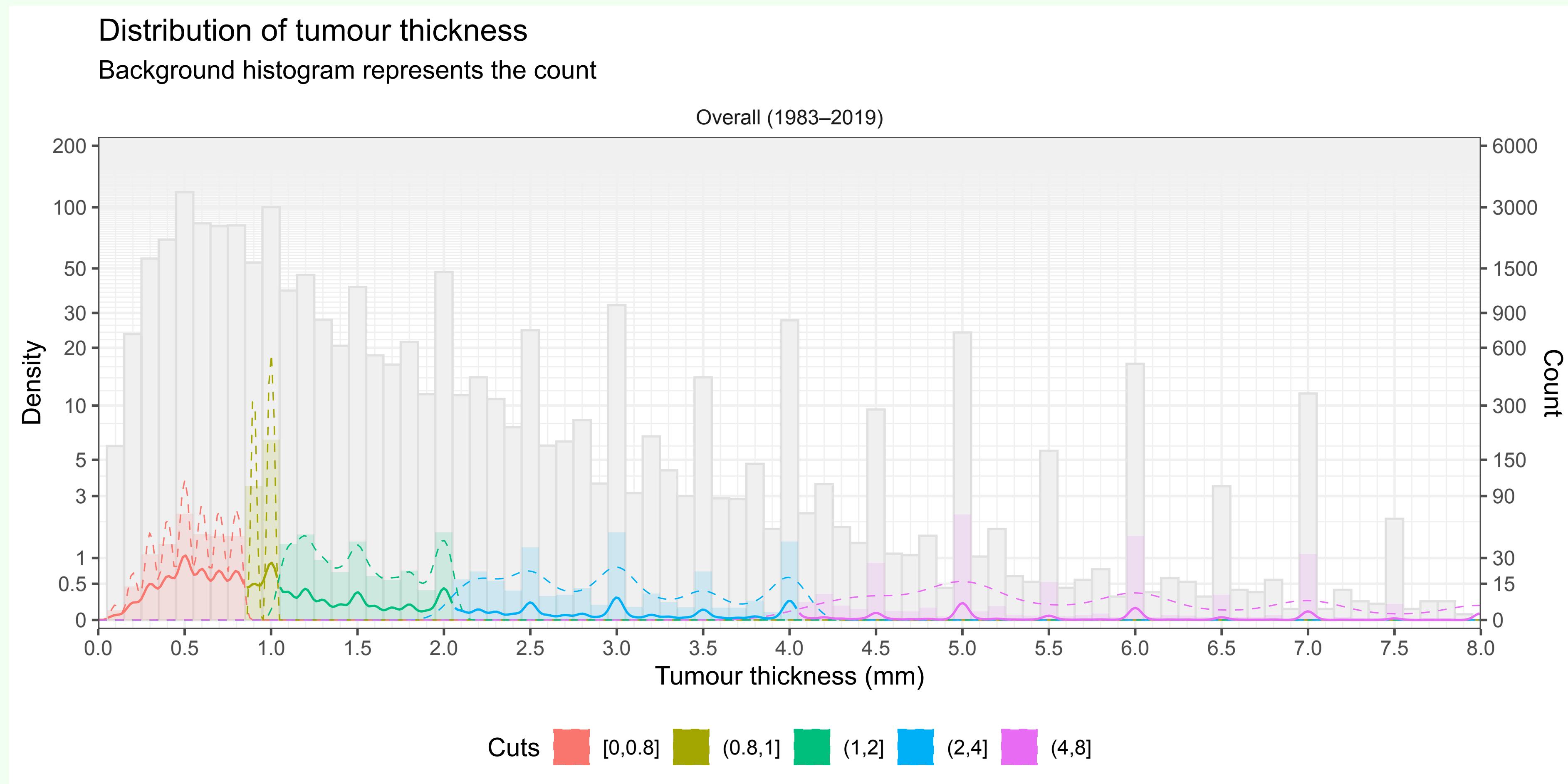


Melanoma and tumour thickness

T-categories



Diagnosis, thickness pattern, and T categories



Terminal digit preference, in diagnosis process. Cut-points can change the course of prognosis and follow-up. Need more exploration.

Data & Methods

Basic characteristics of data

Age at diagnosis

Age at diagnosis has increased in the recent period than earlier.

Characteristic	Sex	1983–1999	2000–2007	2008–2019	Overall
Number of cases, n (%)	Women	7,720 (54%)	4,632 (53%)	11,267 (50%)	23,619 (52%)
	Men	6,578 (46%)	4,150 (47%)	11,465 (50%)	22,193 (48%)
Age at diagnosis (years), median (IQR)	Women	56 (42 – 71)	60 (46 – 75)	63 (50 – 75)	61 (46 – 73)
	Men	59 (46 – 71)	63 (52 – 75)	67 (56 – 76)	64 (52 – 74)
Tumour thickness (mm), median (IQR)	Women	1.0 (0.6 – 2.0)	1.0 (0.6 – 2.0)	0.9 (0.5 – 1.8)	1.0 (0.6 – 2.0)
	Men	1.3 (0.7 – 2.8)	1.3 (0.7 – 3.0)	1.0 (0.6 – 2.3)	1.1 (0.7 – 2.5)

IQR: interquartile range

Basic characteristics of data

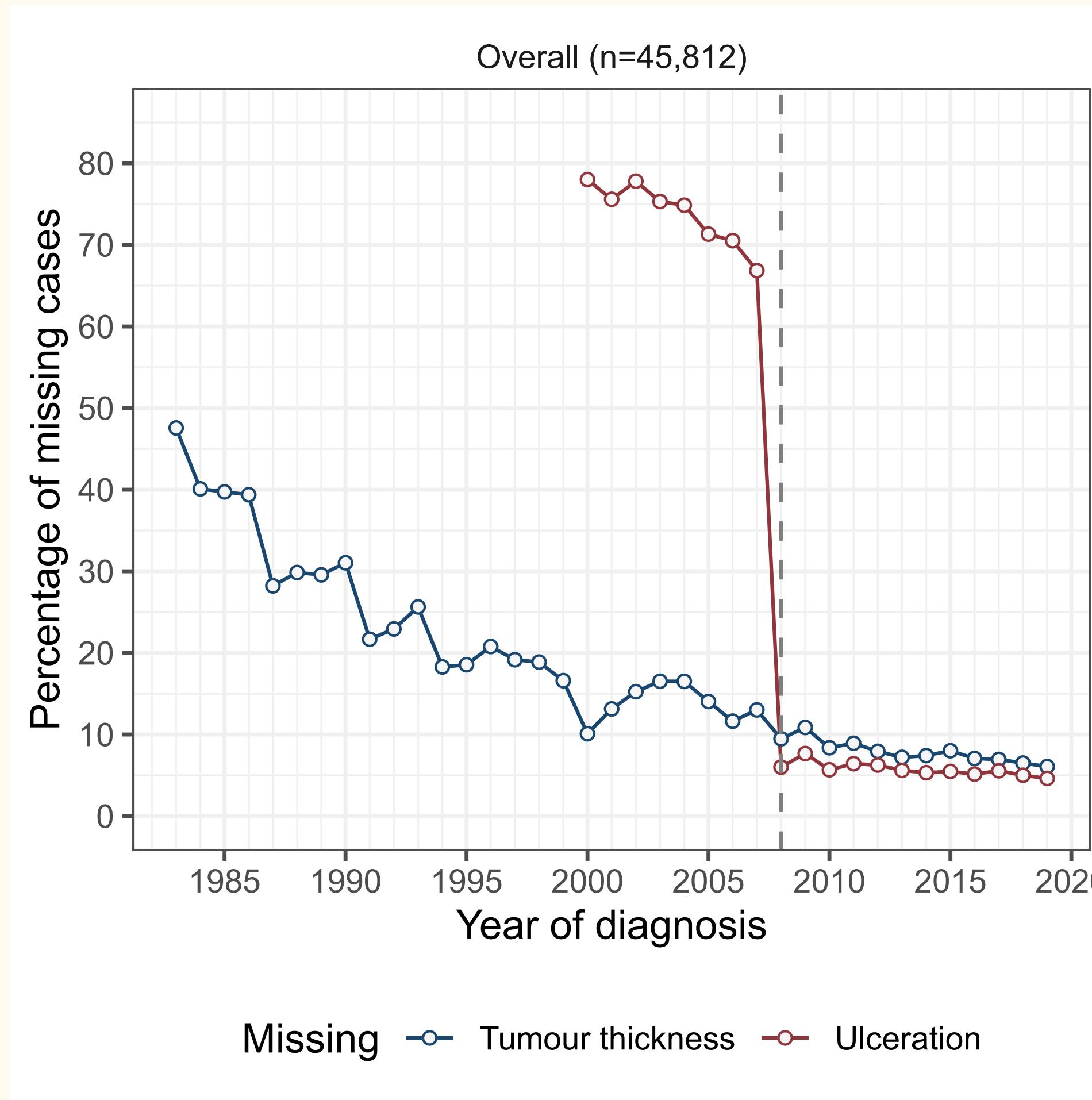
Tumour thickness

The thickness of tumour at diagnosis has decreased in the recent period than earlier.

Characteristic	Sex	1983–1999	2000–2007	2008–2019	Overall
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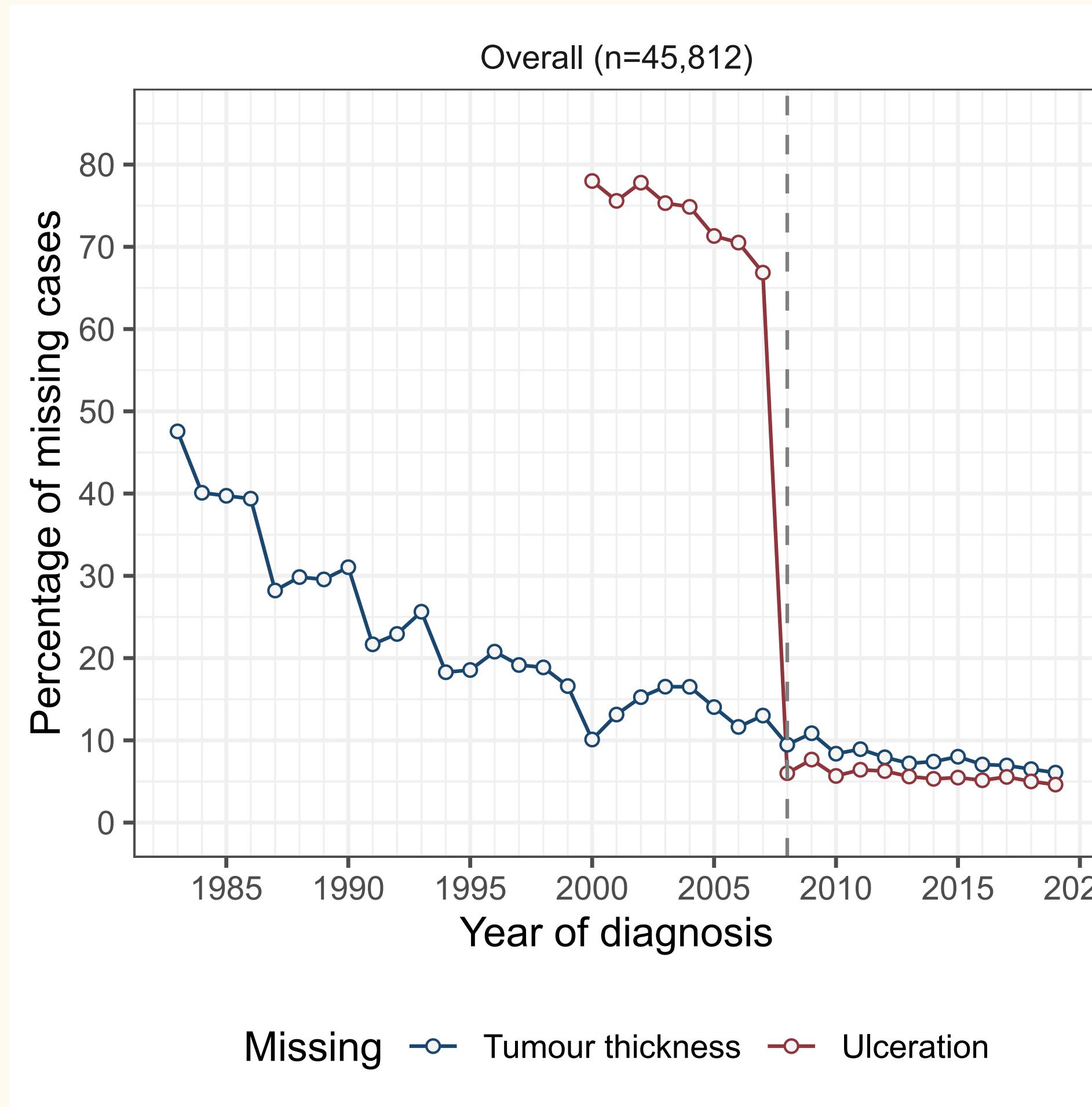
IQR: interquartile range

Missing thickness and imputation



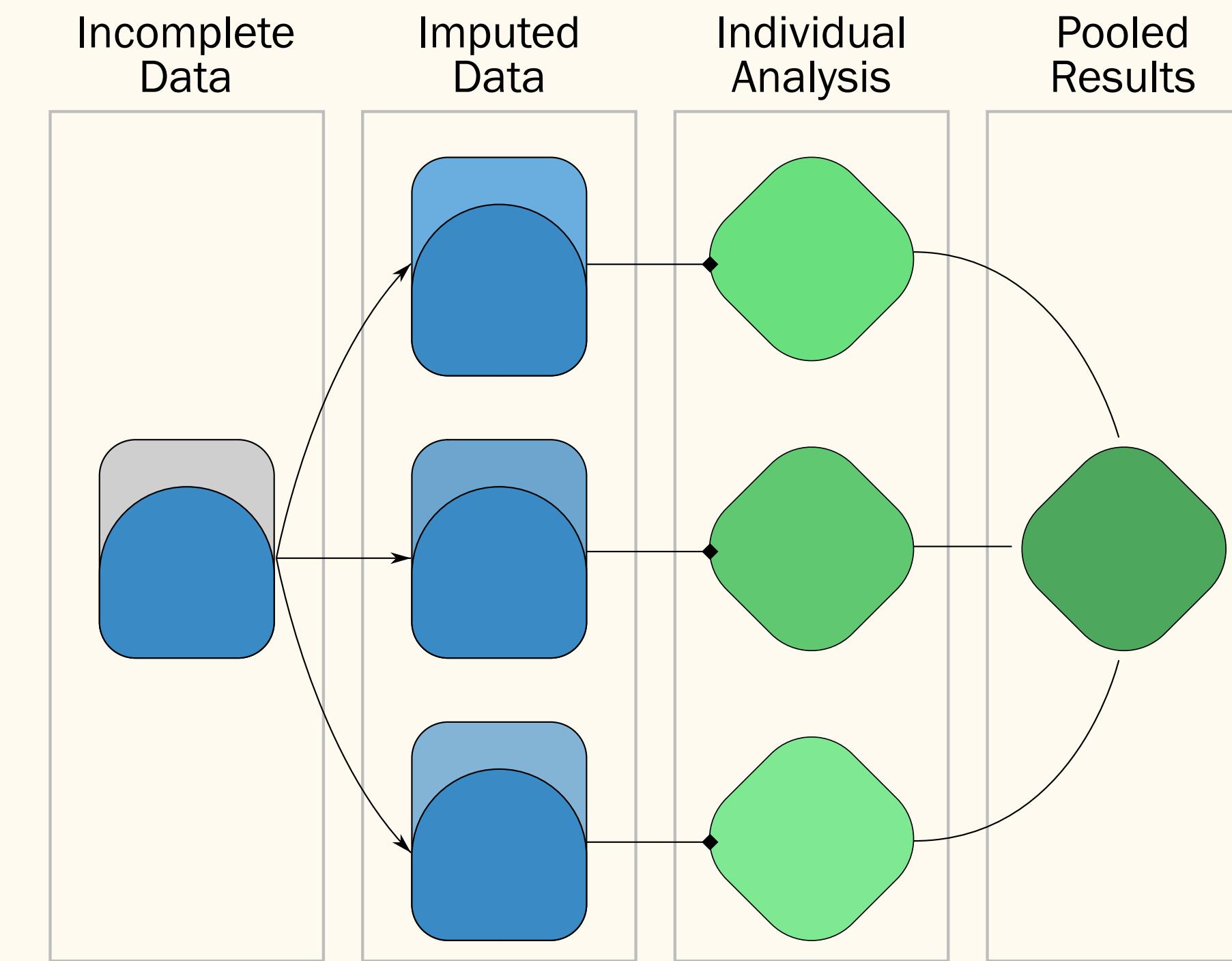
Proportion of cases with missing thickness

Missing thickness and imputation



Proportion of cases with missing thickness

Multiple Imputation Process



- 30 imputations
- Predictors: log-thickness, anatomic site, melanoma sub-type, age, sex, etc

Incidence rate, adjustment, and segmented regression

Incidence Rate

Age-adjustment

Segmented Regression

$$r = \frac{\text{\# melanoma patients}}{\text{\# people at risk}}$$

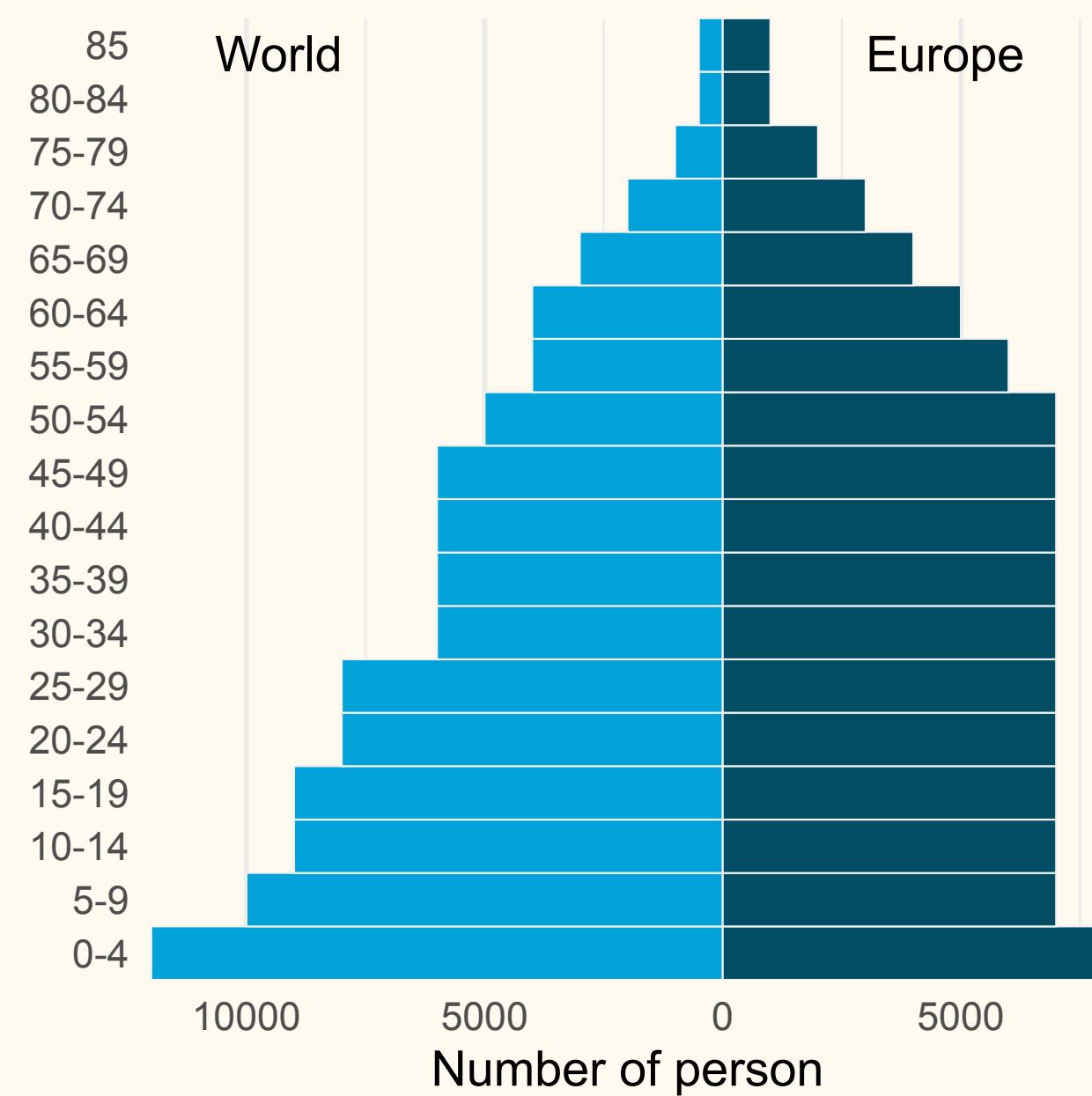
Rate for each year of diagnosis,
age-group and other strata are
computed for further analysis.

Incidence rate, adjustment, and segmented regression

Incidence Rate

Age-adjustment

Segmented Regression



$$r_a = \left[\sum_{i=1}^{a_k} (r_i \times a_i^s) \right] \times 100,000$$

where,

r_i = incidence rate of age-group i

a_i^s = prop. of standard population
for age-group i

Incidence rate, adjustment, and segmented regression

Incidence Rate

Age-adjustment

Segmented Regression

$$\log(r_a)_k = f(y_k) + \varepsilon$$

where,

$$y_k = \beta_1 y_k + \beta_2 (y_k - \psi)_+$$

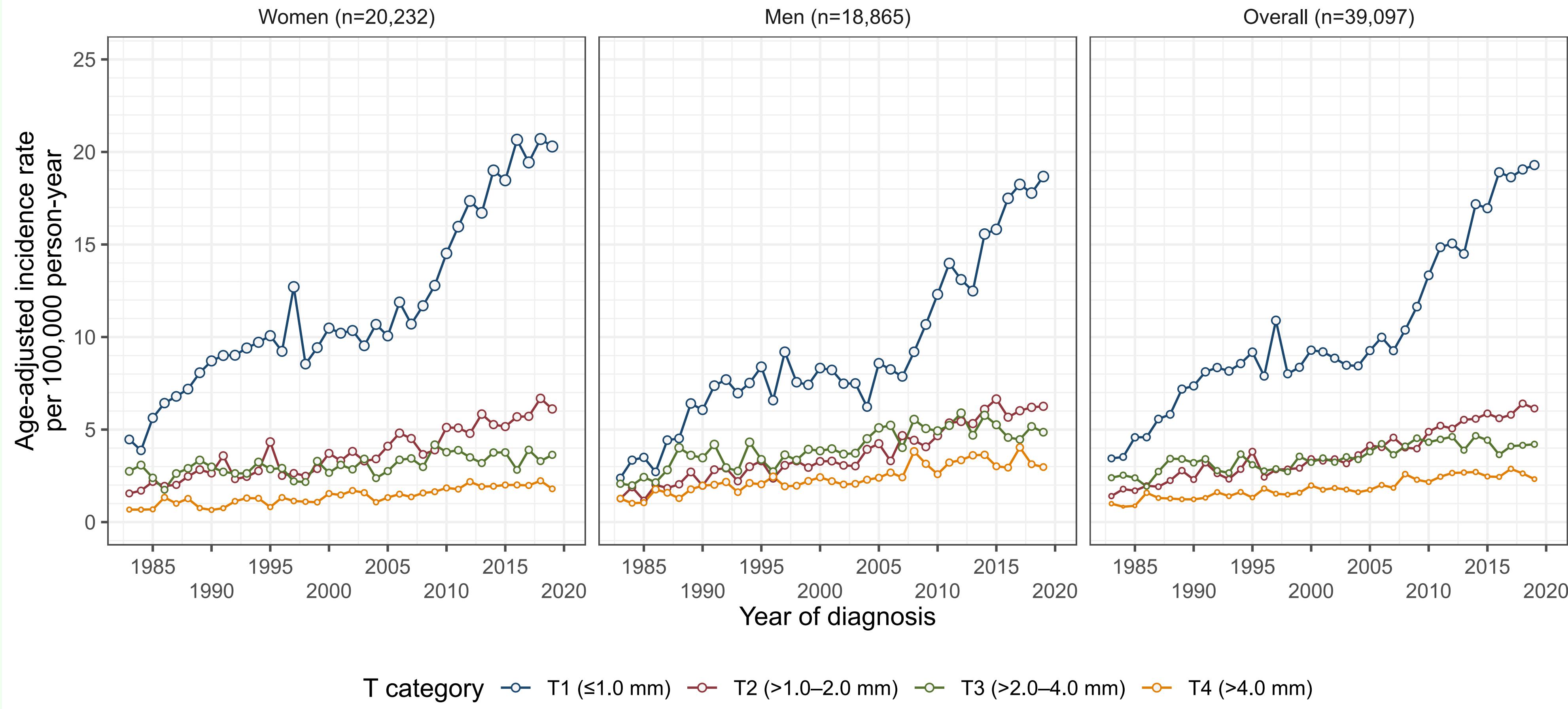
y_k is the year k

- Identify segments
- Annual percentage change

Results

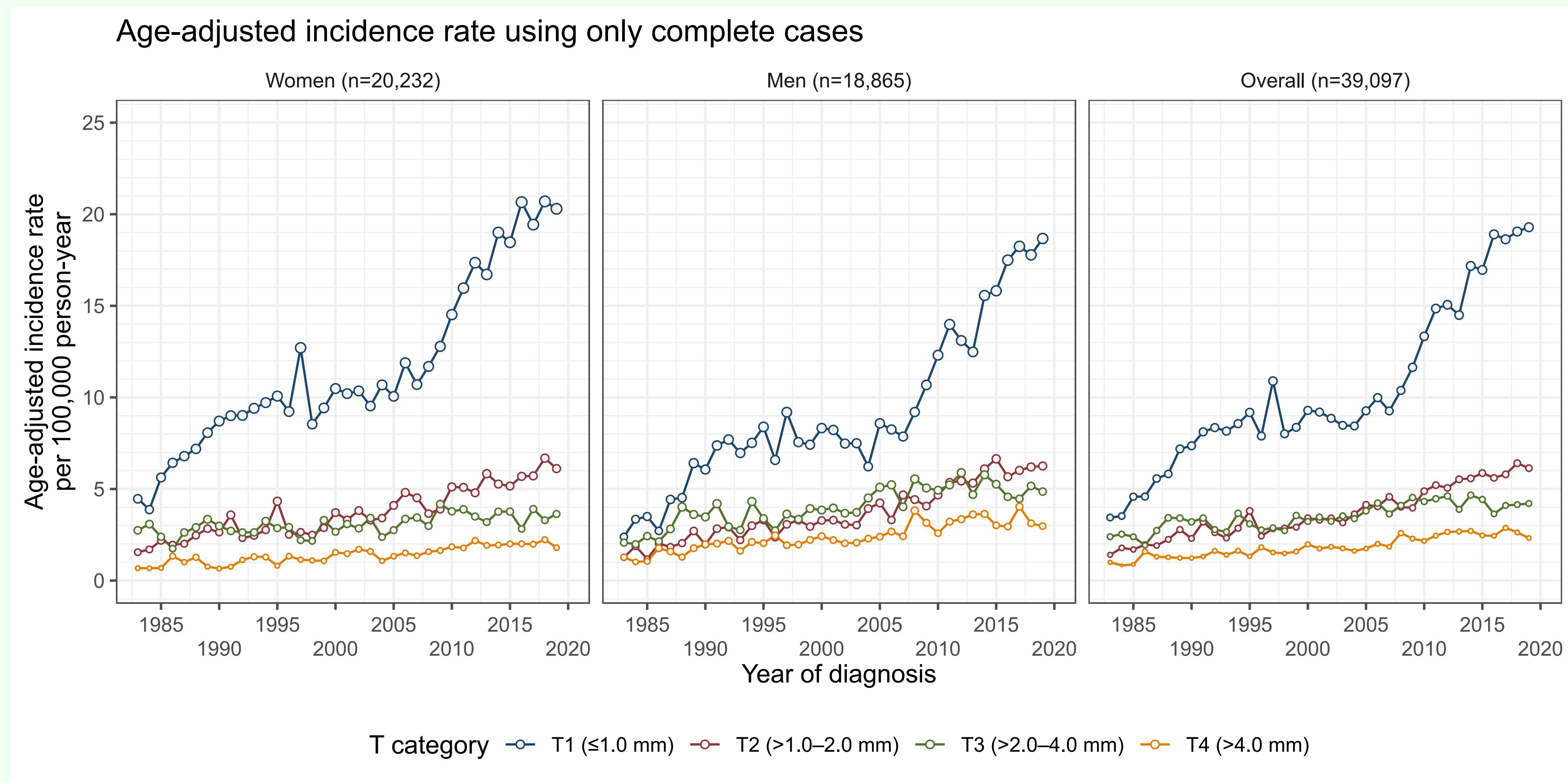
Incidence over time

Age-adjusted incidence rate using only complete cases



Age-adjusted incidence rate by sex and T category

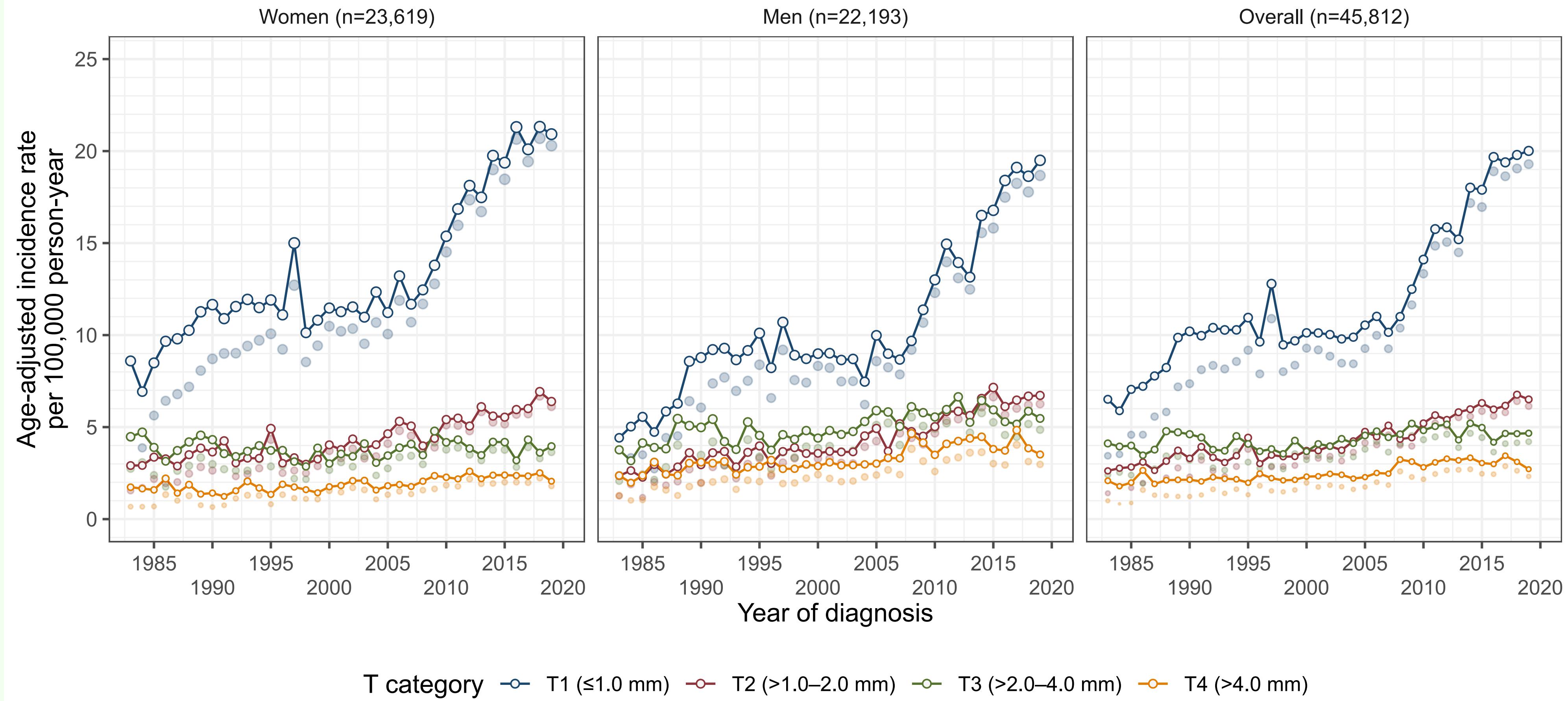
Incidence over time



Complete Cases: only used cases with non-missing thumour thickness

Incidence over time

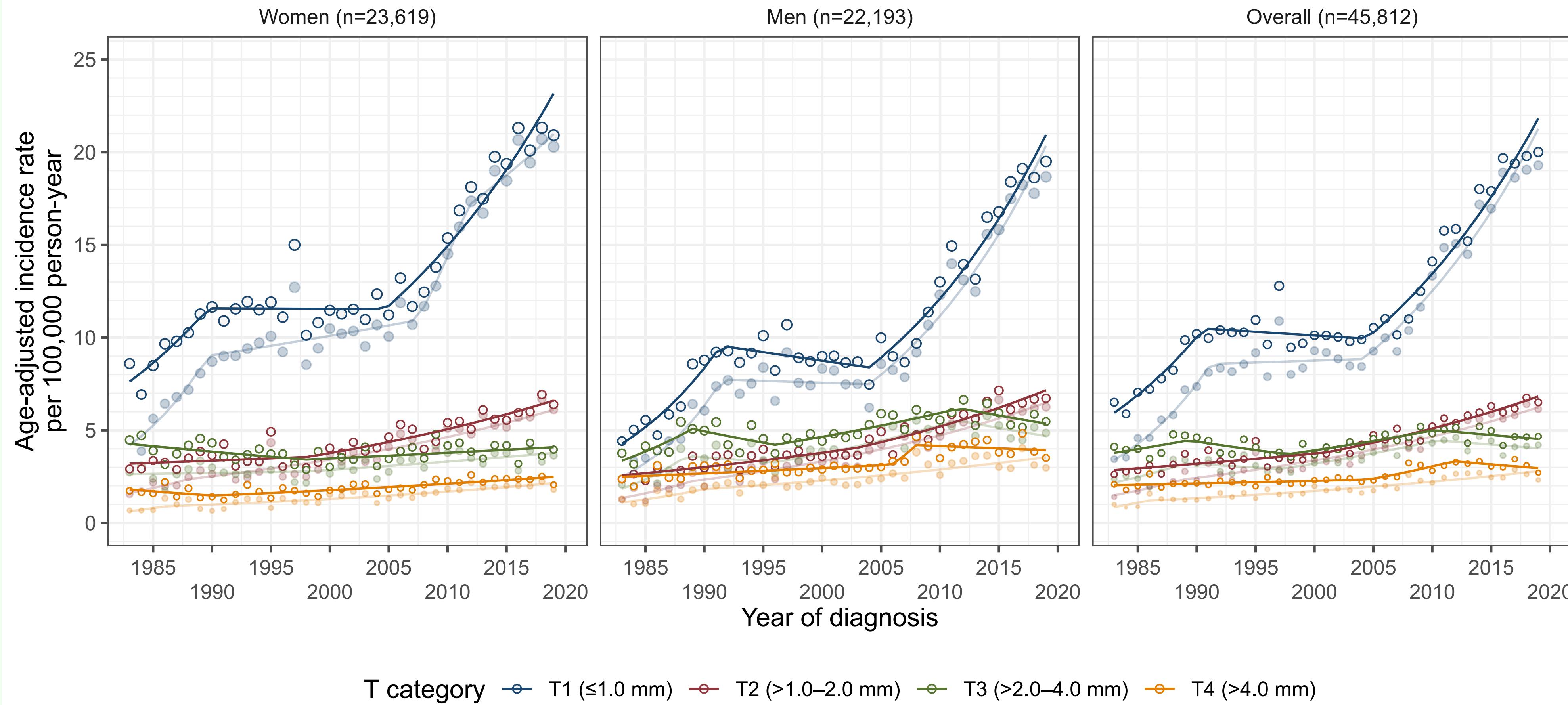
Age-adjusted incidence rate using imputed data



Imputed Data: Earlier periods have more missing cases. More missing leads to more imputation and raise in incidence.

Incidence over time

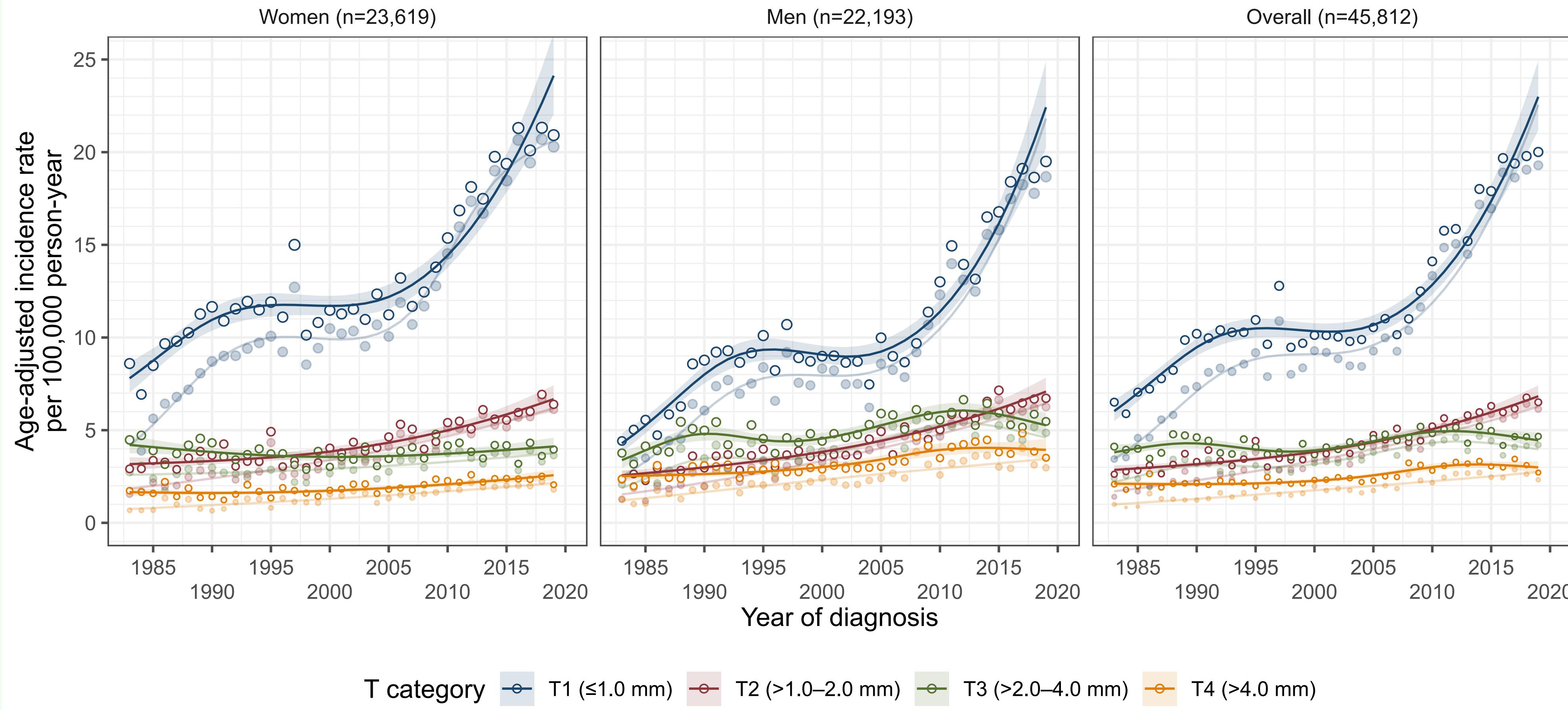
Age-adjusted incidence rate using imputed data with segmented regression



Segmented Regression: Change point mainly in T1 was detected in early 90s and mid 2000s.

Incidence over time

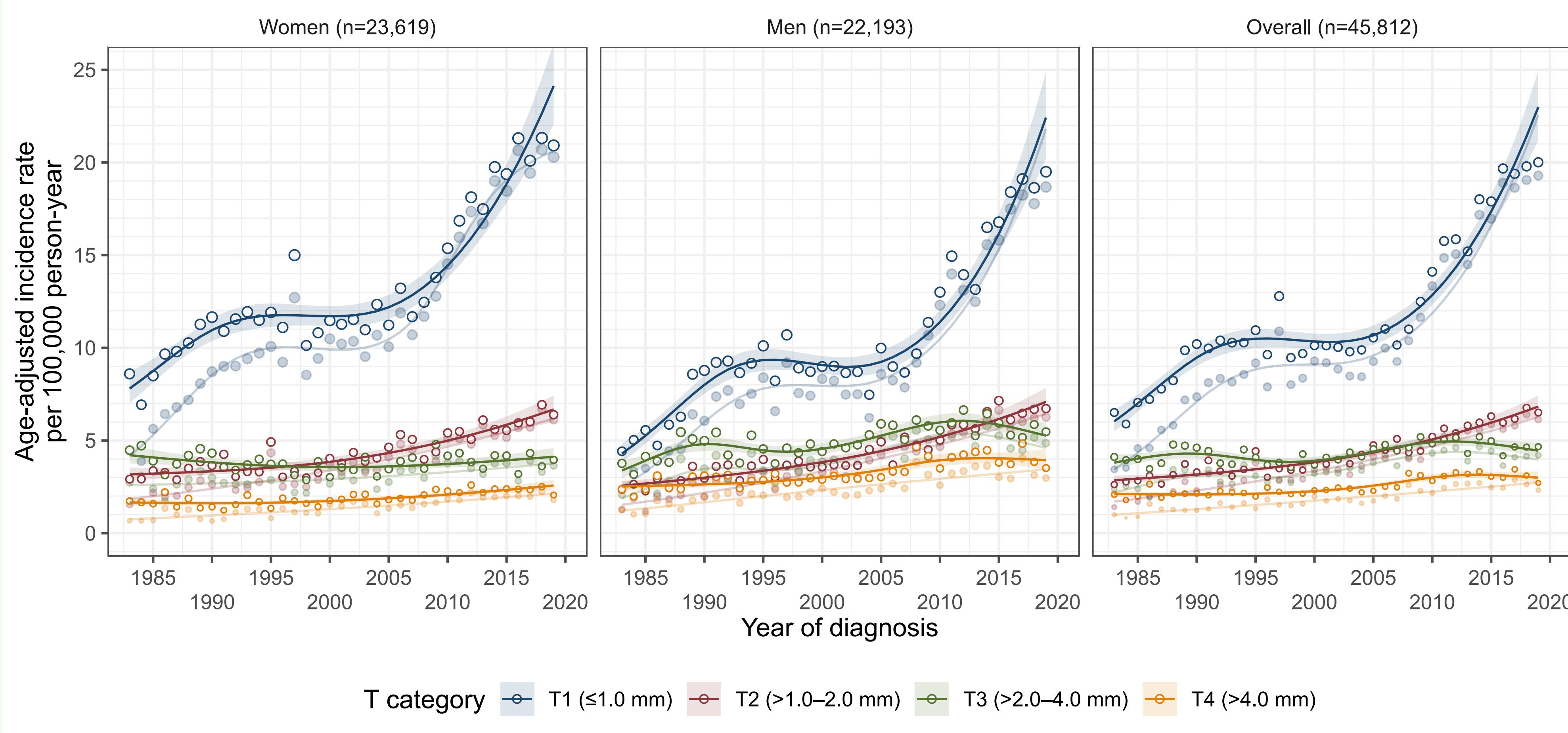
Age-adjusted incidence rate using imputed data with splines



Trend: Added spline shows a clear plateau in T1. Sharp raise in incidence in the recent years mainly in thinner cases (T1 and T2).

Incidence over time

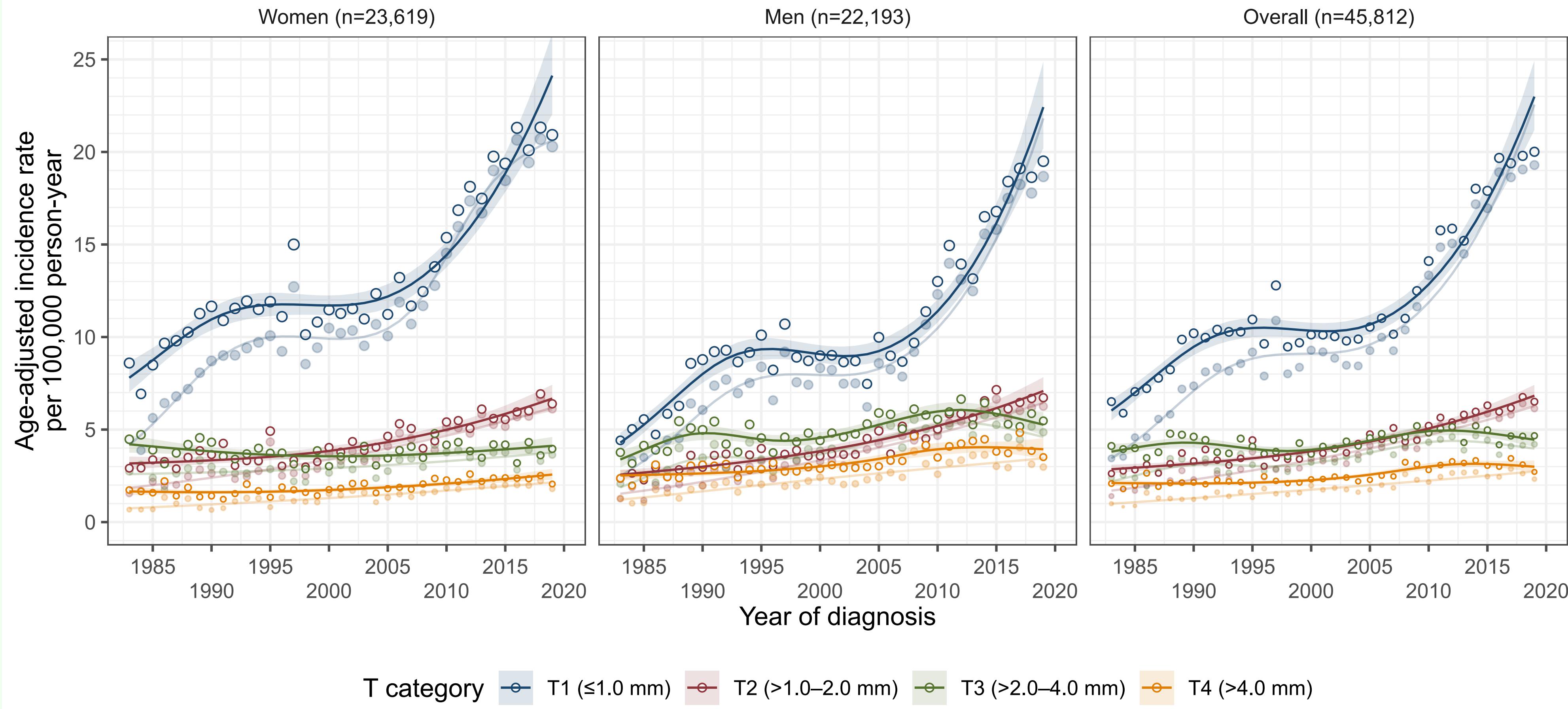
Age-adjusted incidence rate using imputed data with splines



Trend: T1 has largest and sharply incidence of all. (Table in next slide.)

Incidence over time

Age-adjusted incidence rate using imputed data with splines



Trend: Women have higher incidence in thin cases while men have higher incidence in thicker cases.

Changes in melanoma incidence rate

TREND 1

TREND 2

TREND 3

TREND 4

	Trend 1		1983–2019
	APC (95% CI)	Period	AAPC (95% CI)
Women (n=23,619)¹			
T1 (≤ 1.0 mm)	6.4 (3.1, 9.9)	1983–1989	3.1 (2.7, 3.5)
T2 ($>1.0\text{--}2.0$ mm)	0.7 (-0.6, 2.0)	1983–1997	2.0 (1.6, 2.5)
T3 ($>2.0\text{--}4.0$ mm)	-1.5 (-2.8, -0.1)	1983–1997	-0.1 (-0.5, 0.3)
T4 (>4.0 mm)	-2.8 (-6.6, 1.2)	1983–1989	0.9 (0.4, 1.4)
Men (n=22,193)¹			
T1 (≤ 1.0 mm)	10.1 (7.5, 12.7)	1983–1990	4.5 (4.1, 4.9)
T2 ($>1.0\text{--}2.0$ mm)	2.3 (1.5, 3.1)	1983–2002	2.9 (2.5, 3.3)
T3 ($>2.0\text{--}4.0$ mm)	7.1 (3.1, 11.3)	1983–1988	1.3 (0.8, 1.8)
T4 (>4.0 mm)	1.0 (0.3, 1.7)	1983–2005	1.3 (0.9, 1.7)

¹ Average number of cases over 30 imputations

Trend refers to the segments separated by the join-points.

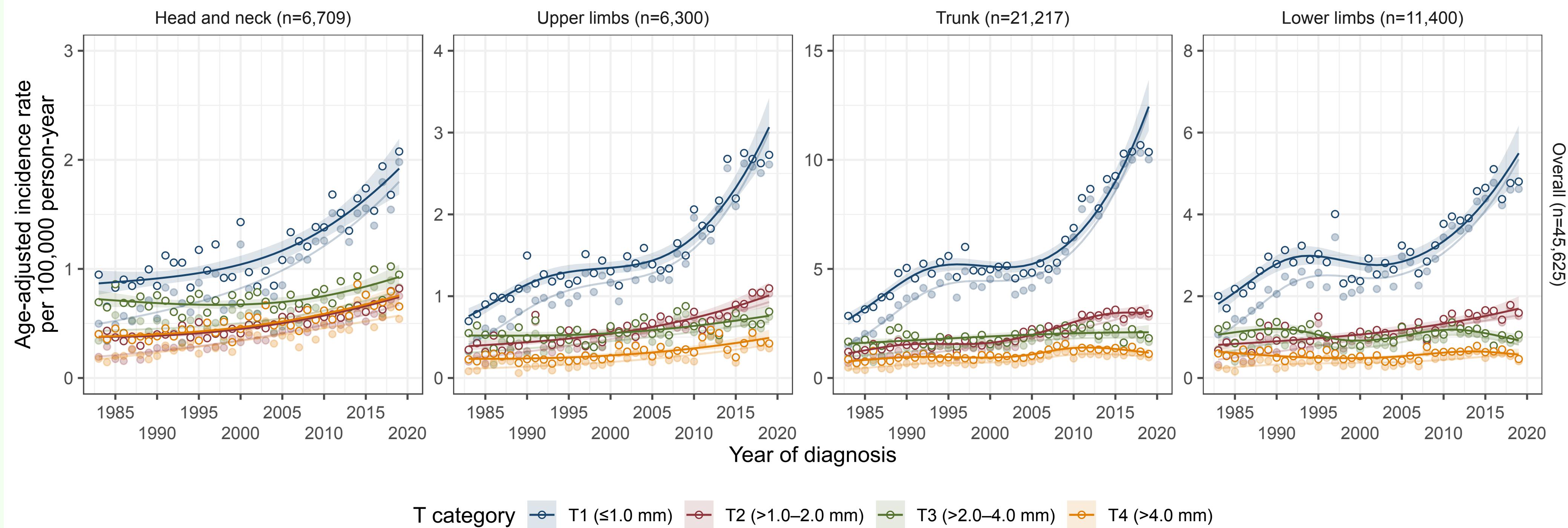
Incidence rate by anatomic site

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and anatomic site



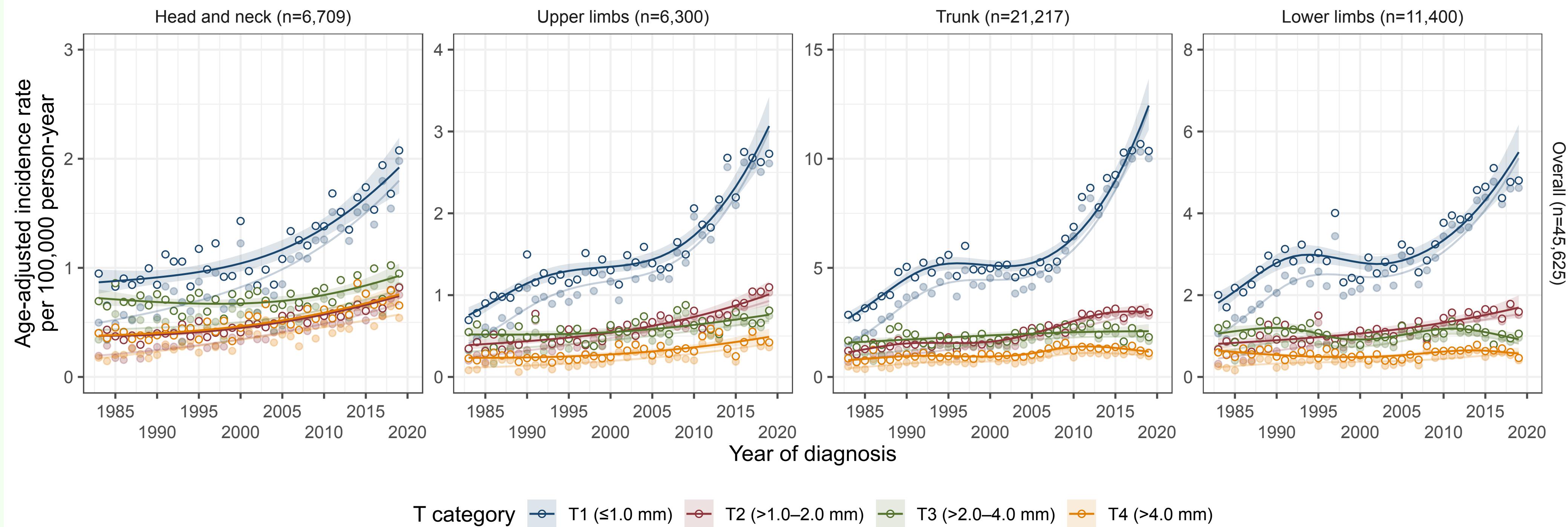
Incidence rate by anatomic site

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and anatomic site



In overall, highest incidence in Trunk (see scale), followed by lower-limbs and upper-limbs.

Incidence rate by anatomic site

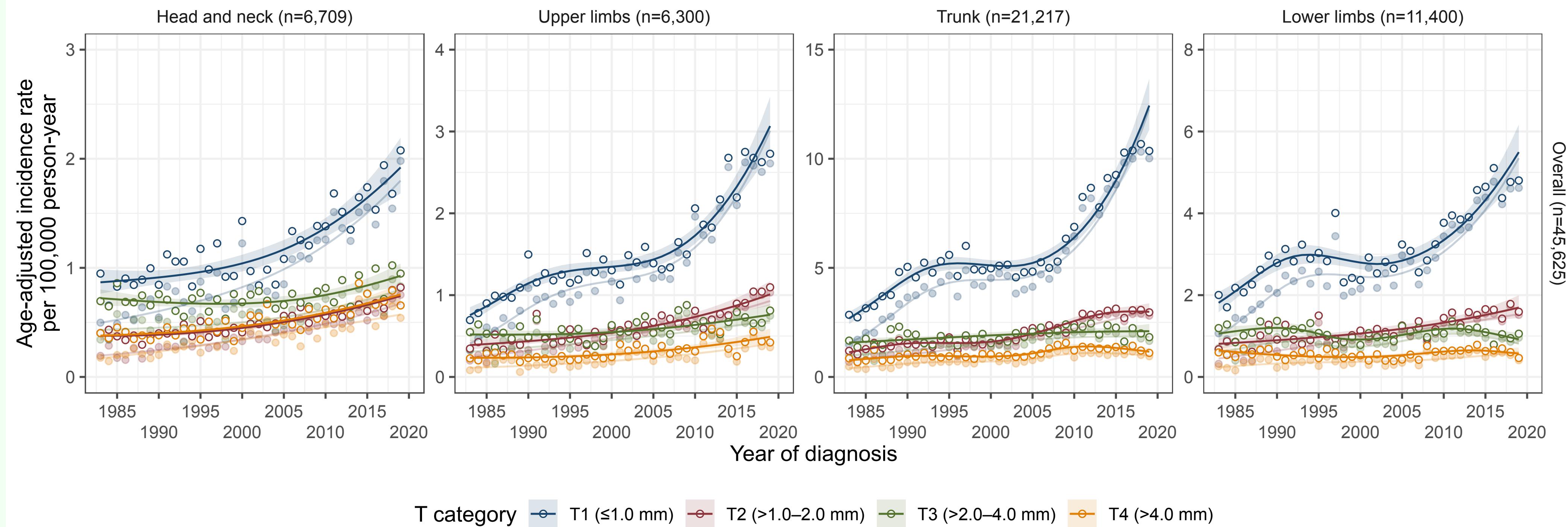
OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum

By T category and anatomic site



In head and neck, thicker cases are also increasing particularly in the recent years.

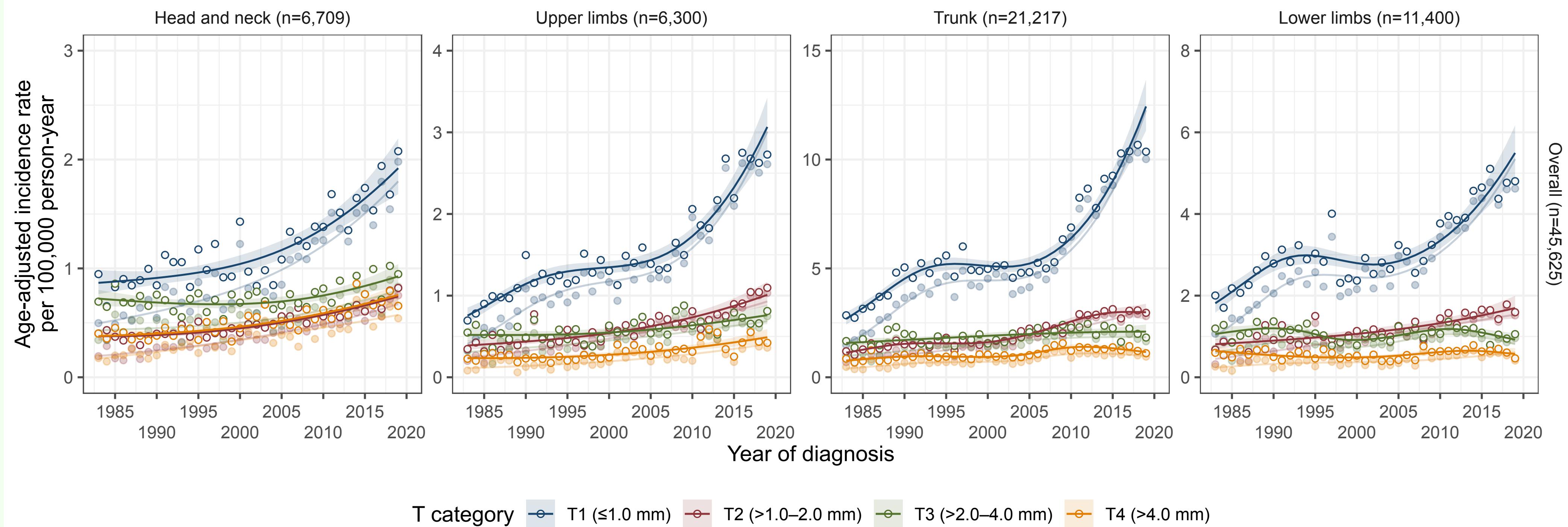
Incidence rate by anatomic site

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and anatomic site



In trunk, men have higher incidence than women. In upper and lower-limbs, women have higher incidence than men.

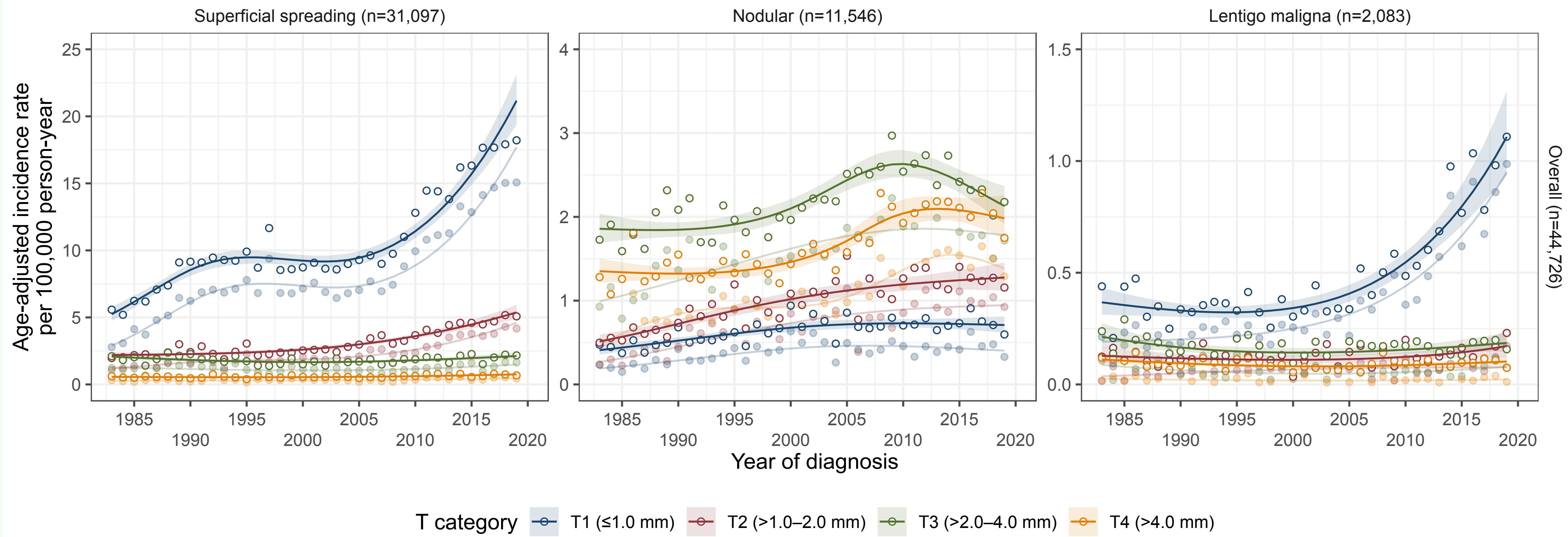
Incidence rate by melanoma sub-type

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and melanoma subtype



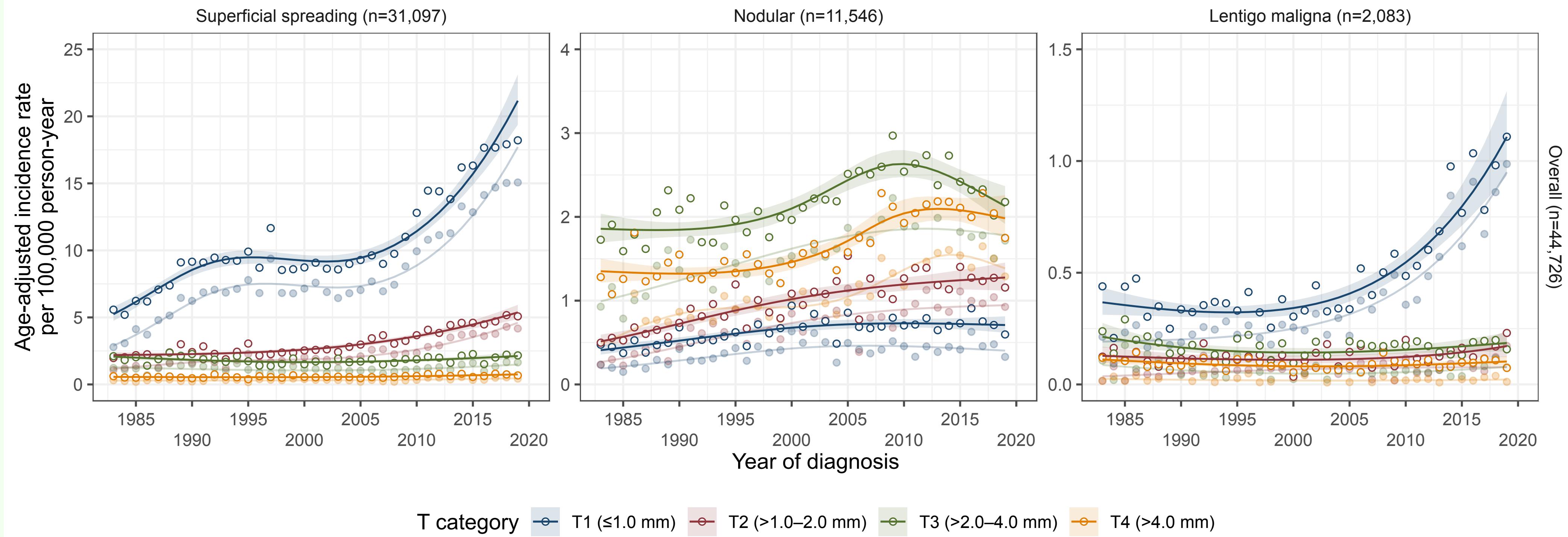
Incidence rate by melanoma sub-type

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and melanoma subtype



In overall, superficial spreading melanoma is most common of all in men, women and overall.

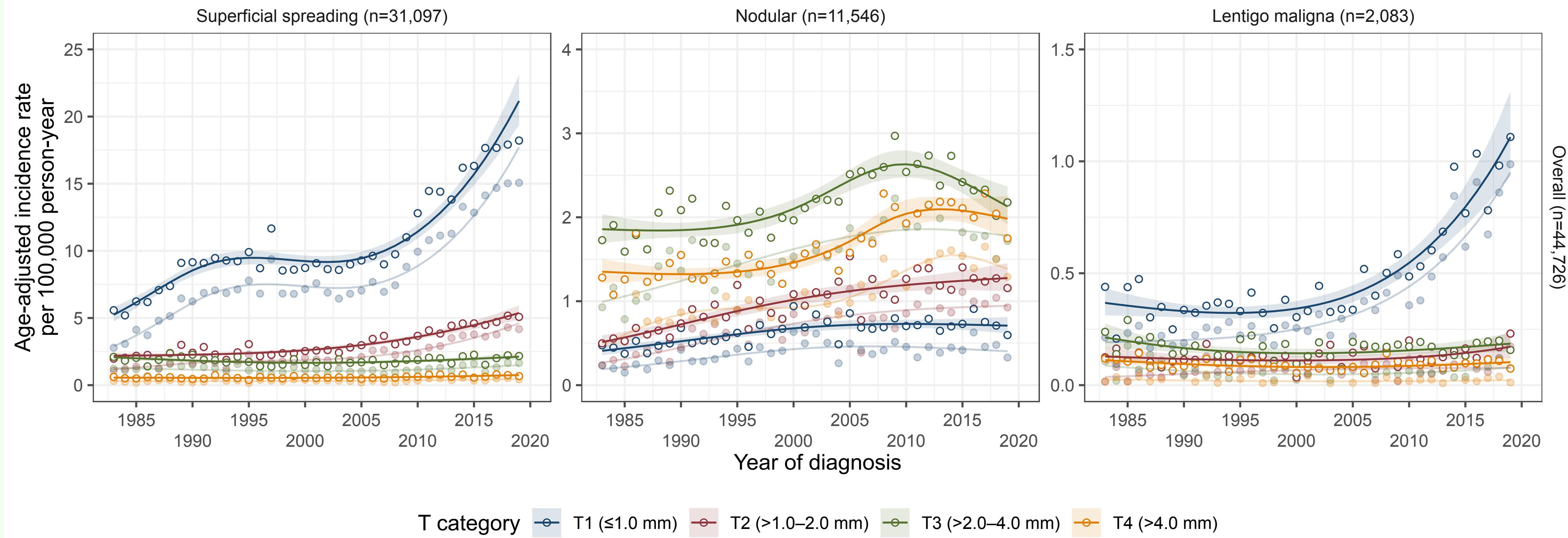
Incidence rate by melanoma sub-type

OVERALL

WOMEN

MEN

Age-adjusted incidence rate in sum
By T category and melanoma subtype



In nodular melanoma, thicker cases have higher incidence than thinner. These are also more fatal.

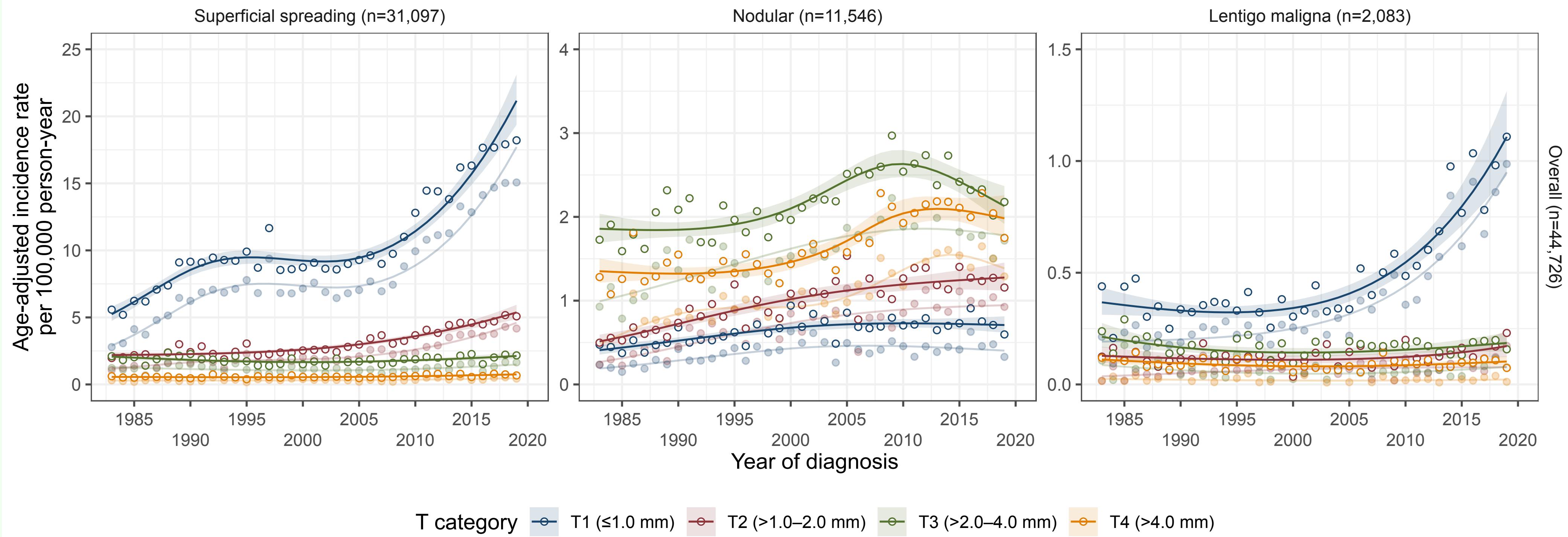
Incidence rate by melanoma sub-type

OVERALL

WOMEN

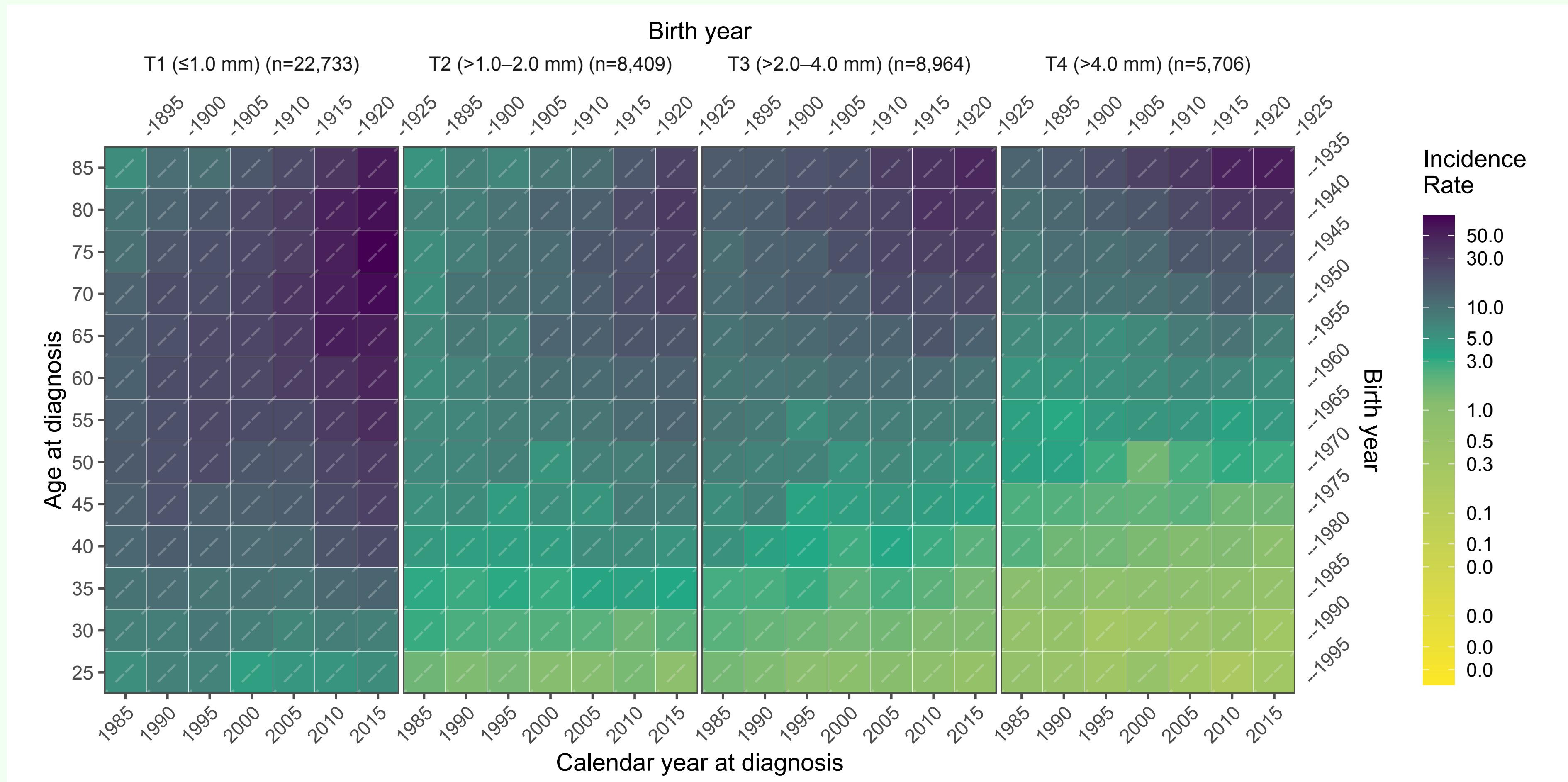
MEN

Age-adjusted incidence rate in sum
By T category and melanoma subtype

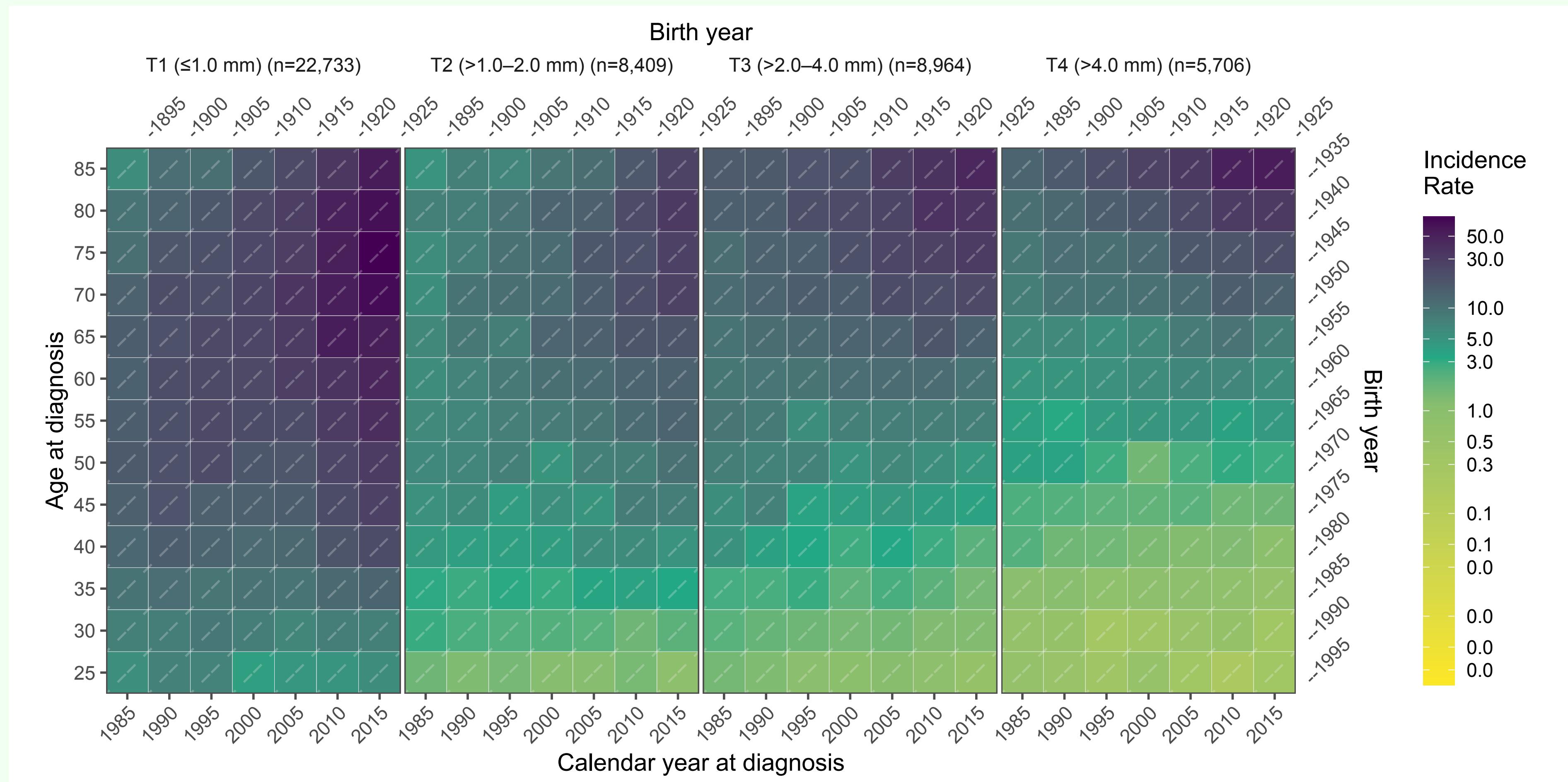


In lentigo maligna melanoma, though less fatal, has sharp raise within thinner cases in the recent year.

Incidence by age, period of diagnosis and cohort

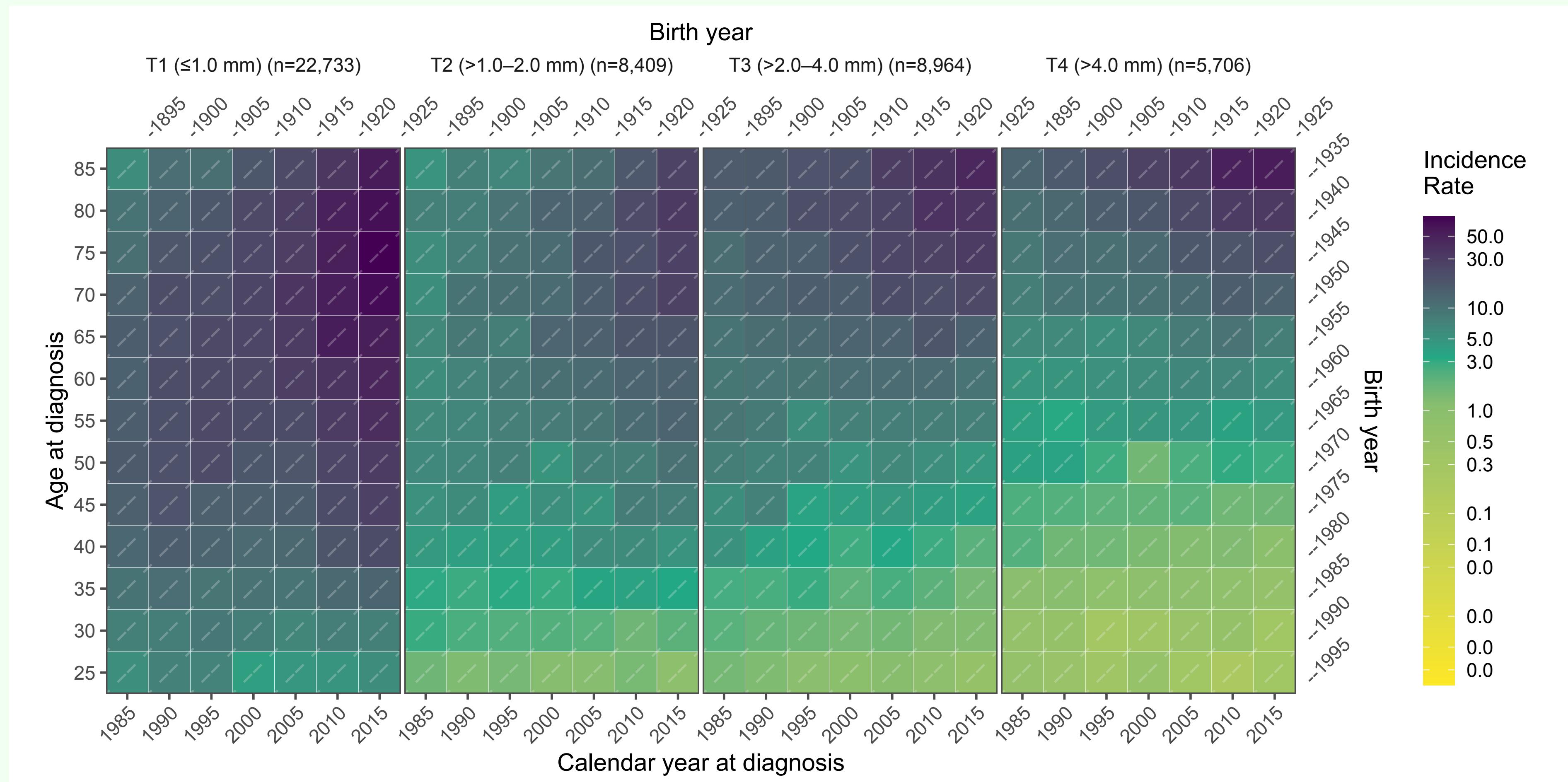


Incidence by age, period of diagnosis and cohort



Dark color represents higher incidence. The high recent raise in incidence of thinner melanoma is found mostly in elderly of age 50 to 80.

Incidence by age, period of diagnosis and cohort



The difference in the incidence of thicker melanoma between young and old is more pronounced in the recent years compared to previous year.

Wrap-up

Further study

Upcoming study

Cut-point analysis

The cut-points are important criteria for risk assessment, diagnosis and follow-up

Survival

Survival by tumour thickness gives more clear explanation on both the increase in incidence and high mortality in Norway due to melanoma

Need more exploration

Plateau

Reason behind the plateau is still unknown and further study is required.



Summary

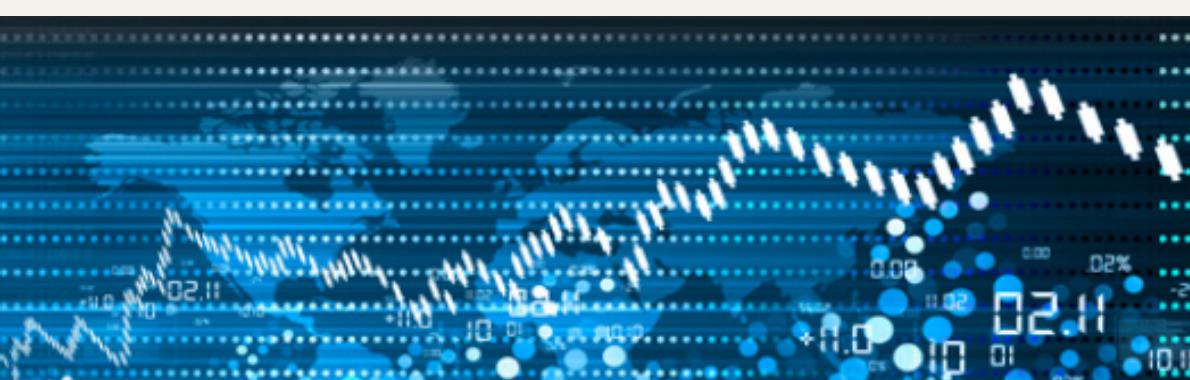
- Awareness may have contributed to the rapid raise in melanoma incidence.
- Overdiagnosis may be considered but unable to explain the increase in thicker cases.
- Awareness focused on *elderly males* may be effective for *early detection*.
- Both *long-term* and *short term* effect may be the reason behind the *plateau*.
- Change in *diagnosis practices, life-style, awareness* may be the reason. More data and simulation studies is required.



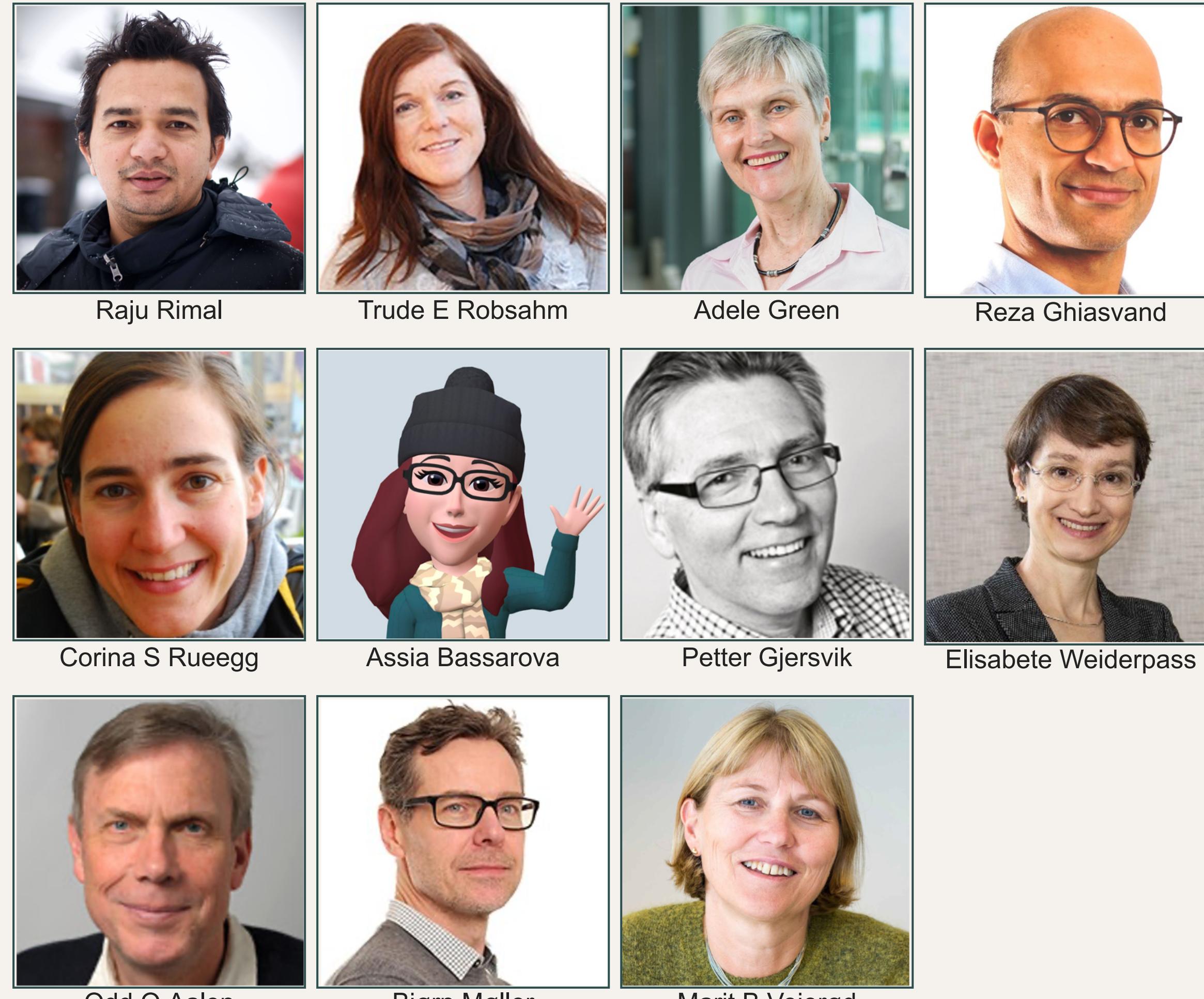
Collaborators



UNIVERSITY
OF OSLO



Coauthors



Funded by: The Research Council of Norway.

Three large central words are written in a bold, hand-drawn style:

- Thank You**
- GRACIAS**
- DANKE**

Surrounding these words are various other languages and their equivalents for "thank you".

Top Row:

- Arabic: لیزج ارکش (Lizj arkš)
- Chinese: 多謝 (Duoxie)
- French: MERCI
- German: DANKE
- Spanish: GRACIAS
- Swedish: TAKK
- Ukrainian: спасибо (spasibo)
- Russian: спасибо (spasibo)
- Polish: dziękuje (dziękuje)
- Portuguese: Obrigado (Obrigado)
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Middle Row:

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