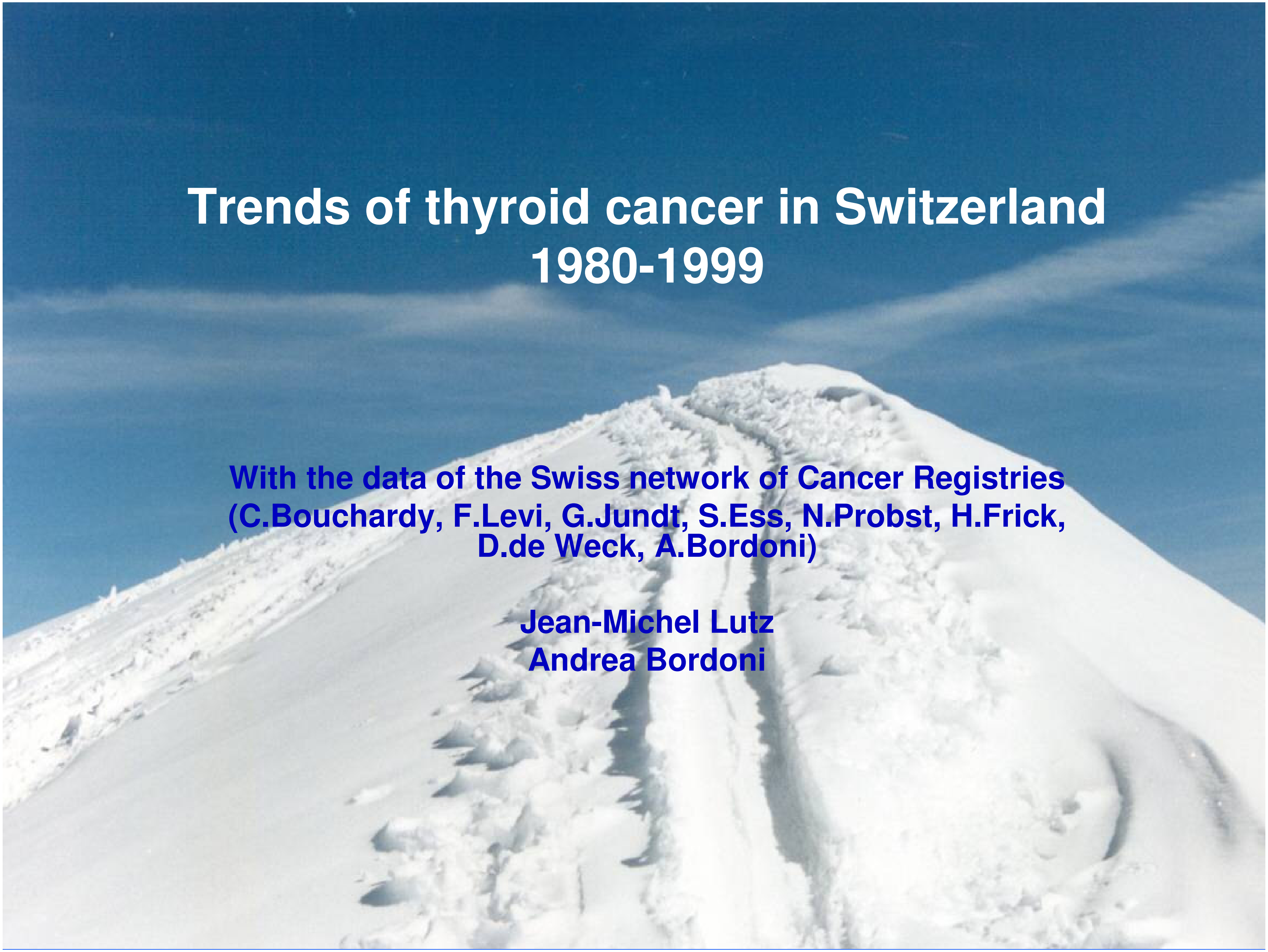
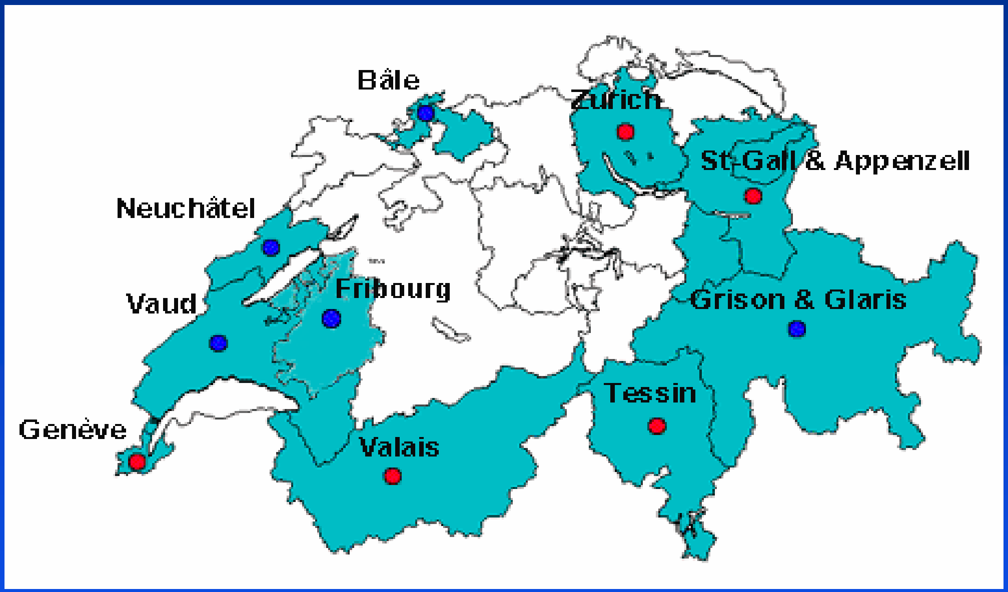


Trends of thyroid cancer in Switzerland 1980-1999

With the data of the Swiss network of Cancer Registries (C.Bouchardy, F.Levi, G.Jundt, S.Ess, N.Probst, H.Frick, D.de Weck, A.Bordoni)

Jean-Michel Lutz
Andrea Bordoni

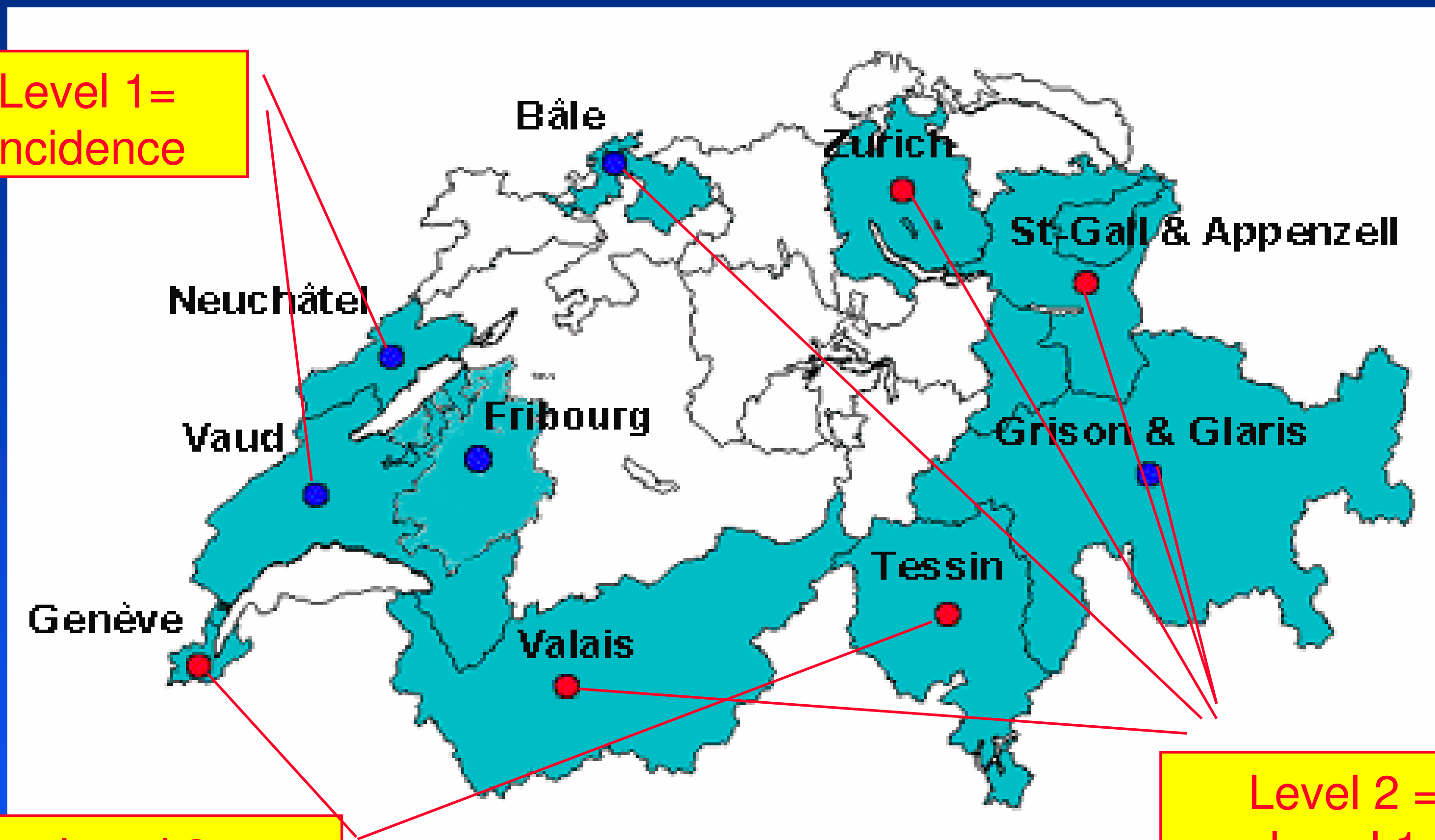
Population based cancer registries in Switzerland



Geneva (1970)
Neuchatel (1974)
Vaud (1974)
St-Gall & Appenzell (1980)
Zurich (1980)
Bale City & Countryside (1981)
Valais (1989)
Graubünden & Glarus (1989)
Tessin (1996)

Fribourg (2006)

Contracts for data quality



Level 1= incidence

Level 2 = Level 1 + staging + active FU

Level 3 = Level 2 + SES + Treatment

Descriptive analysis and geographical comparison

Pooled time trend analysis

Age period cohort modelling

Thyroid cancer in Swiss Cancer Registries - Men

Registry	Nb	EASR * Papill.	EASR * Not pap.	EASR * All	IRR	95% CI
GG (1989-99)	17	0.58	0.74	1.32	1.00	(Ref.)
NE (1980-99)	32	0.90	0.97	1.86	1.41	0.79-2.51
GE (1980-99)	73	1.23	0.73	1.96	1.48	0.92-2.40
TI (1996-99)	15	1.65	0.57	2.22	1.68	0.80-3.54
VD (1980-99)	132	1.27	0.98	2.25	1.70	1.11-2.60
VS (1989-98)	32	1.53	0.99	2.51	1.90	1.06-3.40
GA (1980-99)	127	1.01	1.58	2.59	1.95	1.29-2.96
BA (1981-99)	124	1.16	1.60	2.76	2.08	1.29-4.14
ZH (1980-96)	304	1.74	1.29	3.03	2.29	1.61-3.25
All (1980-99)	**856**	**1.33**	**1.19**	**2.52**		

** European Age-standardized annual rates per 100,000, related to the period covered by each registry, age classes 0-85+*

Incidence Rate Ratios (IRRs) for all morphologies combined

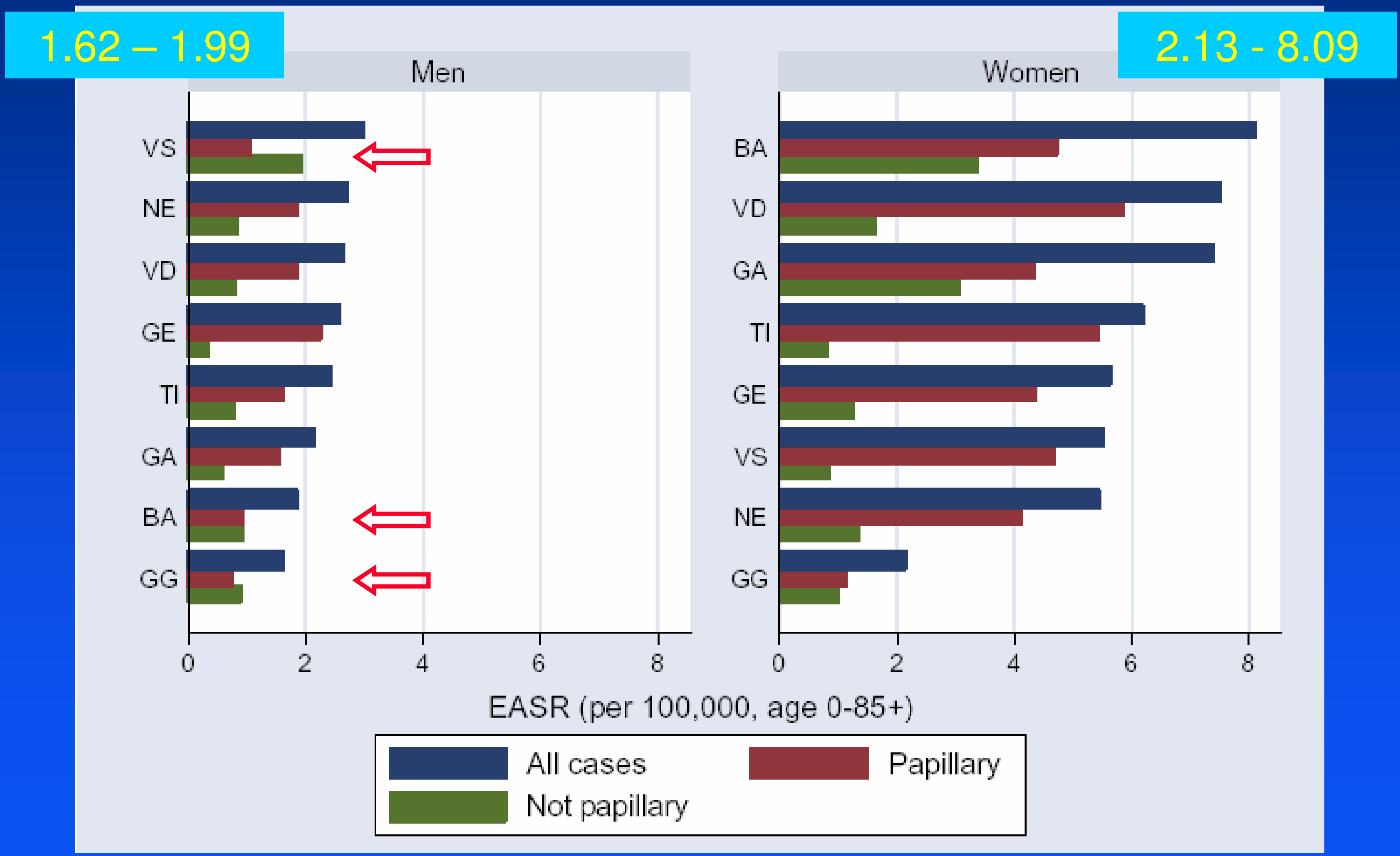
Thyroid cancer in Swiss Cancer Registries - Women

Registry	Nb	EASR * Papill.	EASR * Not pap.	EASR * All	IRR	95% CI
GG (1989-99)	52	2.22	1.38	3.60	1.00	(Ref.)
NE (1980-99)	88	2.32	2.16	4.48	1.24	0.88-1.77
TI (1996-99)	43	4.41	0.79	5.21	1.45	0.93-2.26
GE (1980-99)	236	3.69	1.54	5.24	1.45	1.10-1.93
VS (1989-98)	81	4.10	1.36	5.46	1.51	1.06-2.17
VD (1980-99)	382	3.90	1.68	5.58	1.55	1.19-2.01
BA (1981-99)	320	3.25	2.67	5.92	1.64	1.26-2.14
ZH (1980-96)	724	3.87	2.06	5.94	1.65	1.30-2.09
GA (1980-99)	333	3.13	2.82	5.95	1.65	1.27-2.14
All (1980-99)	**2'259**	**3.55**	**2.05**	**5.60**		

** European age-standardized annual rates per 100,000, related to the period covered by each registry, age classes 0-85+*

Incidence Rate Ratios (IRRs) for all morphologies combined

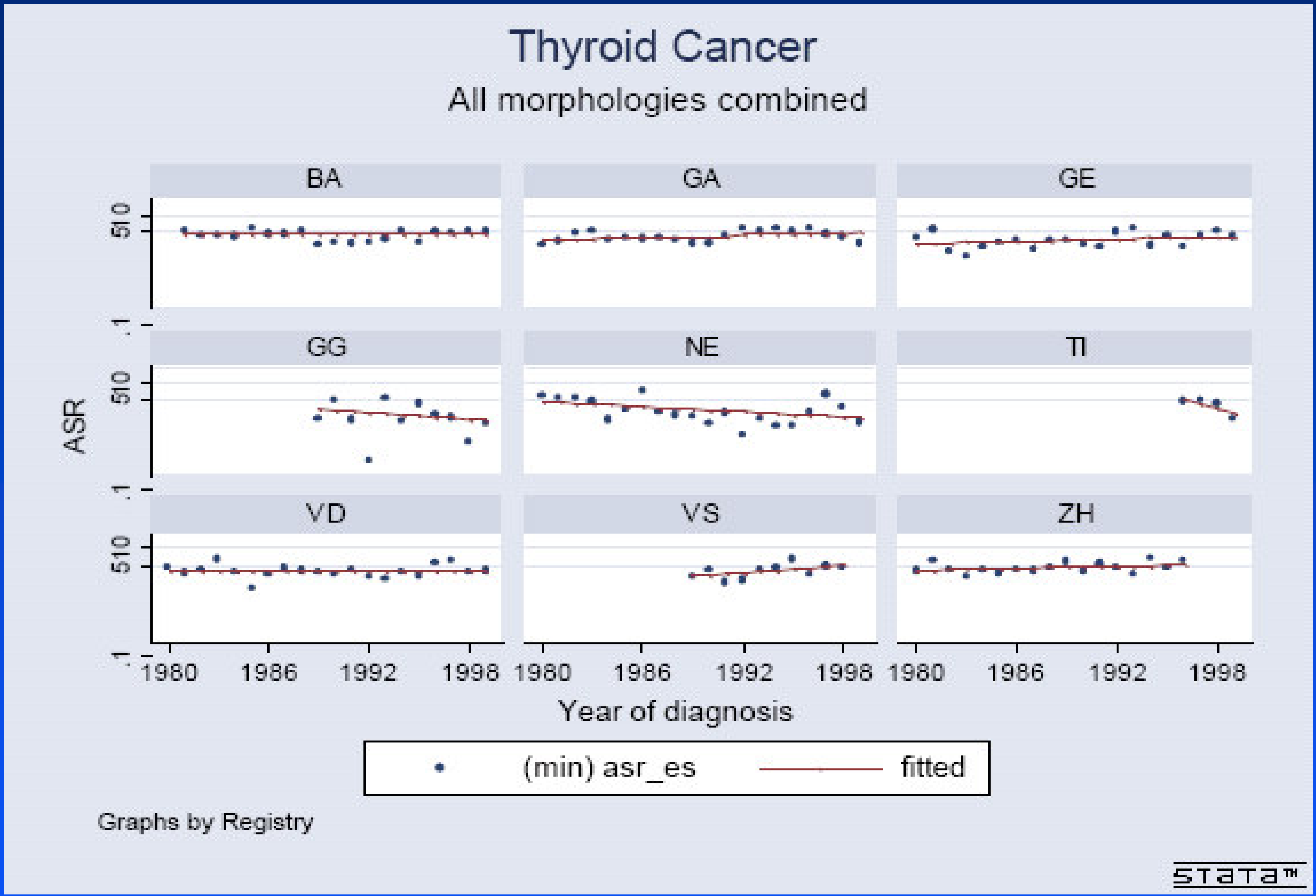
European age-standardised incidence rates (EASR) for thyroid cancer observed by Swiss cancer registries during the period 1996-1998 (rates/100'000 x year)



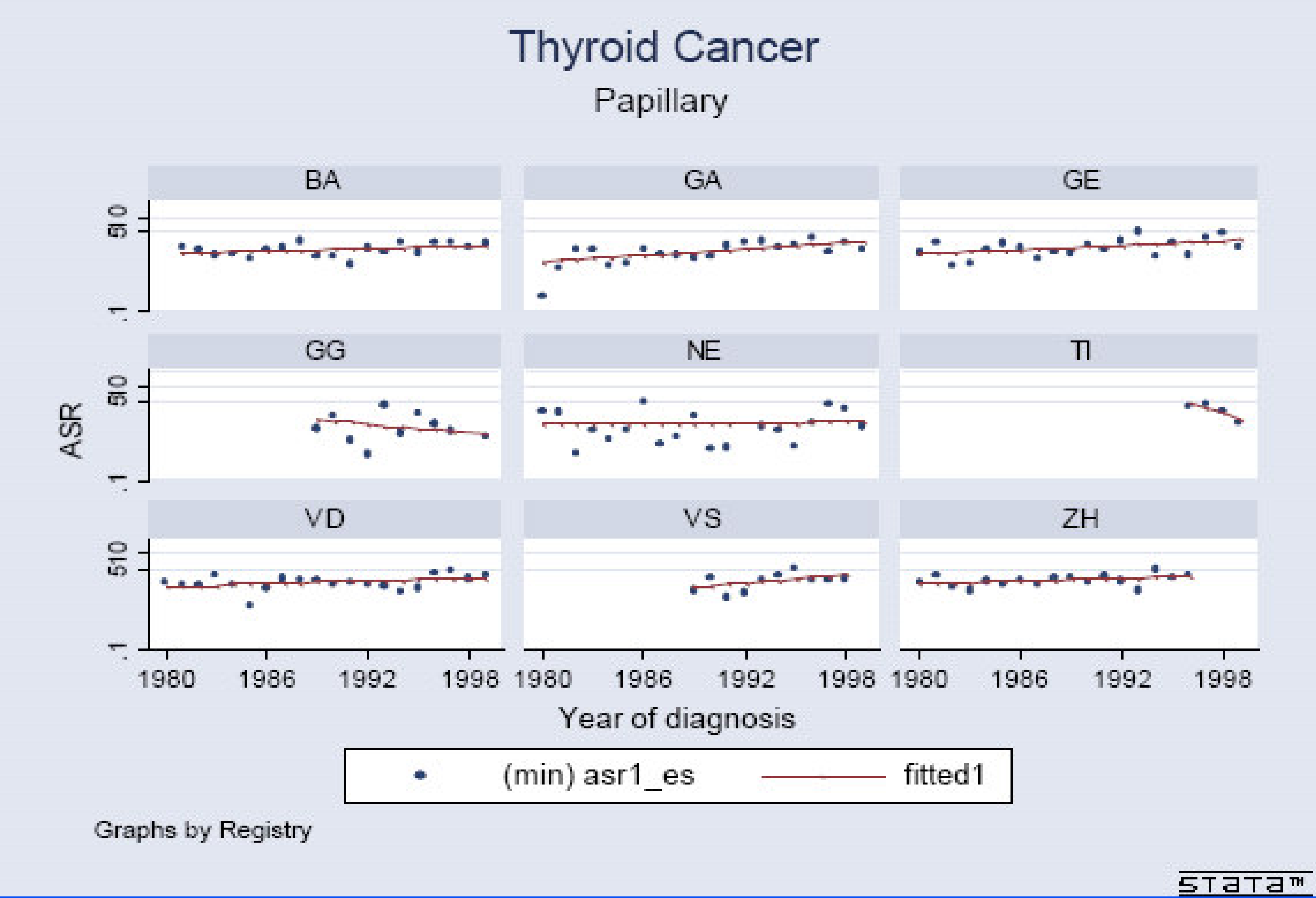
Descriptive analysis and geographical comparison

Pooled time trend analysis

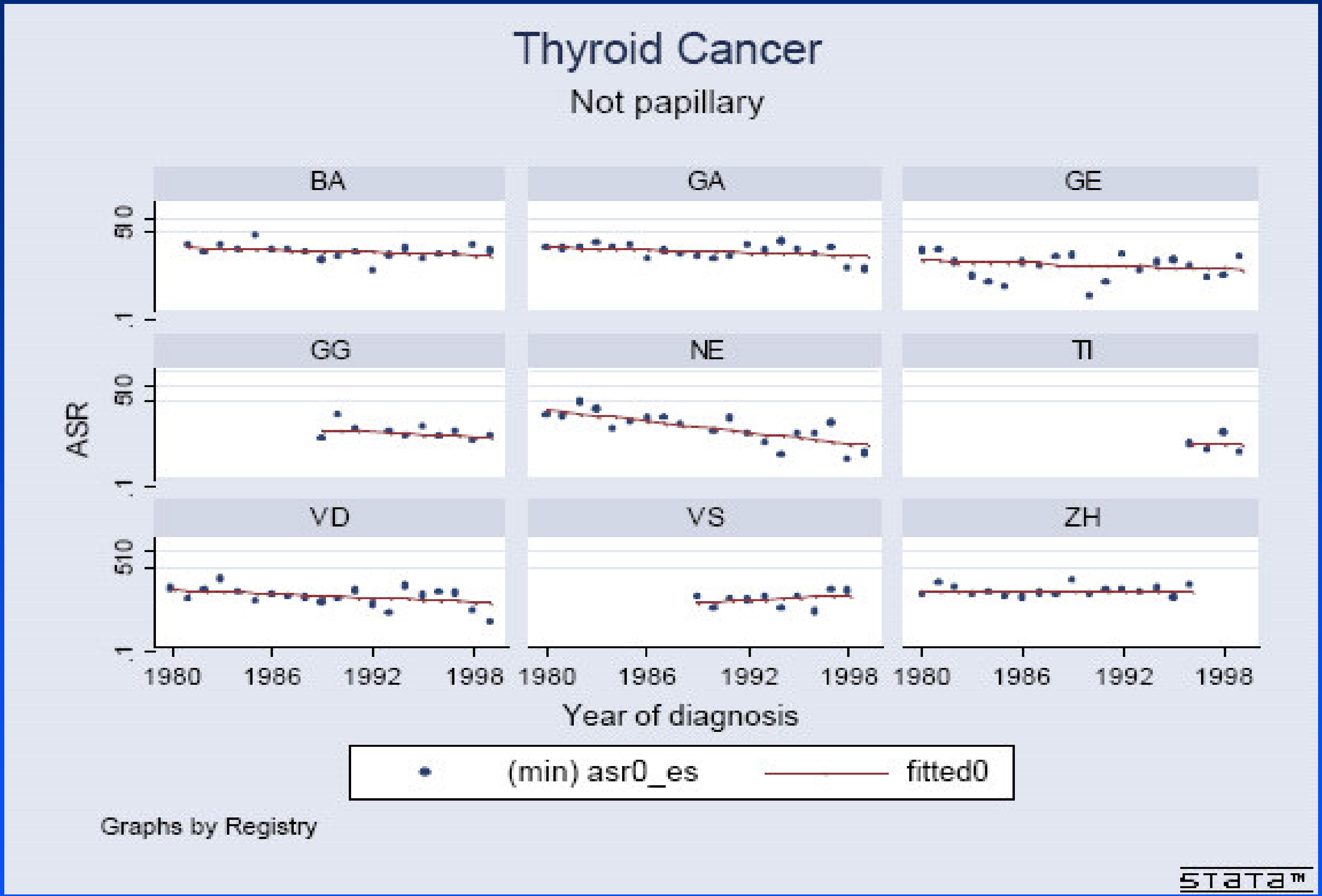
Age period cohort modelling



Thyroid Cancer
All morphologies combined
BA
GA
GE
GG
NE
TI
VD
VS
ZH
ASR
.1
5
10
1980
1986
1992
1998
Year of diagnosis
(min) asr_es
fitted
Graphs by Registry
stata™

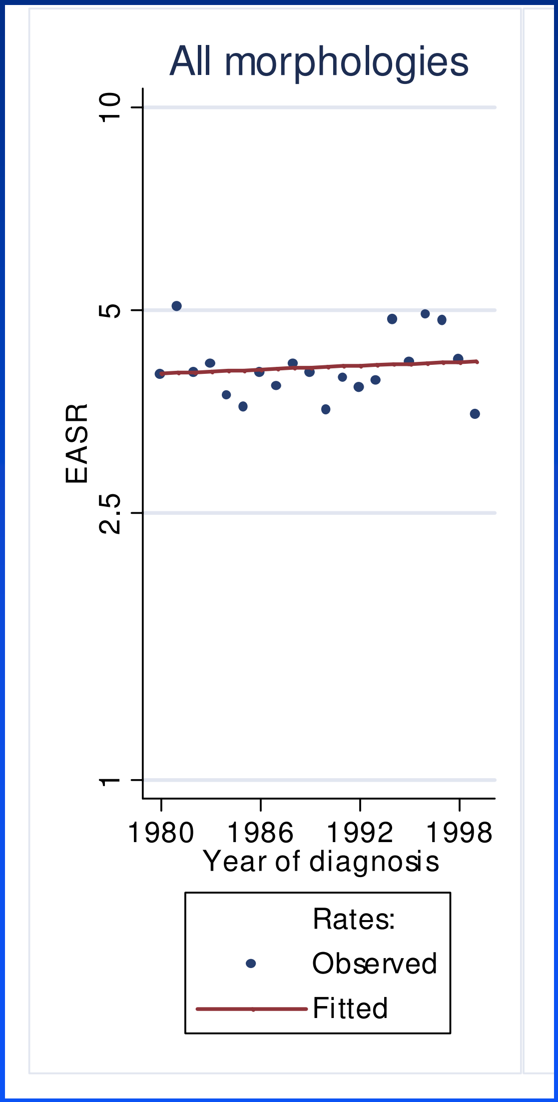


Thyroid Cancer
Papillary
BA
GA
GE
GG
NE
TI
VD
VS
ZH
ASR
1980
1986
1992
1998
Year of diagnosis
(min) asr1_es
fitted1
Graphs by Registry



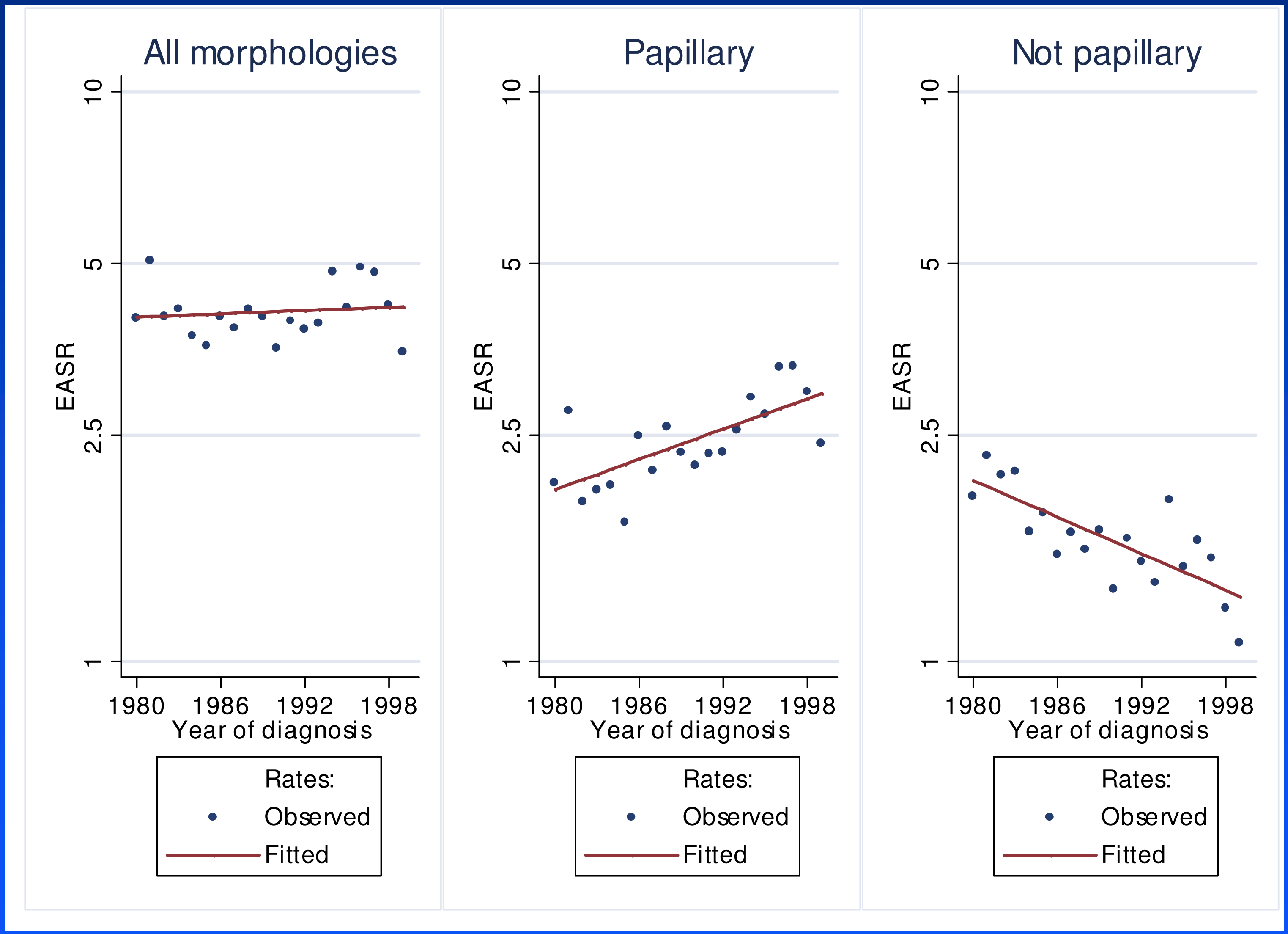
Thyroid Cancer
Not papillary
BA
GA
GE
GG
NE
TI
VD
VS
ZH
ASR
.1
510
1980
1986
1992
1998
Year of diagnosis
(min) asr0_es
fitted0
Graphs by Registry

Observed and fitted European age-standardized incidence rates (EASR, per 100,000, age 0-85+) of thyroid cancer in pooled Swiss cancer registries (1980-1999), linear regression modelling

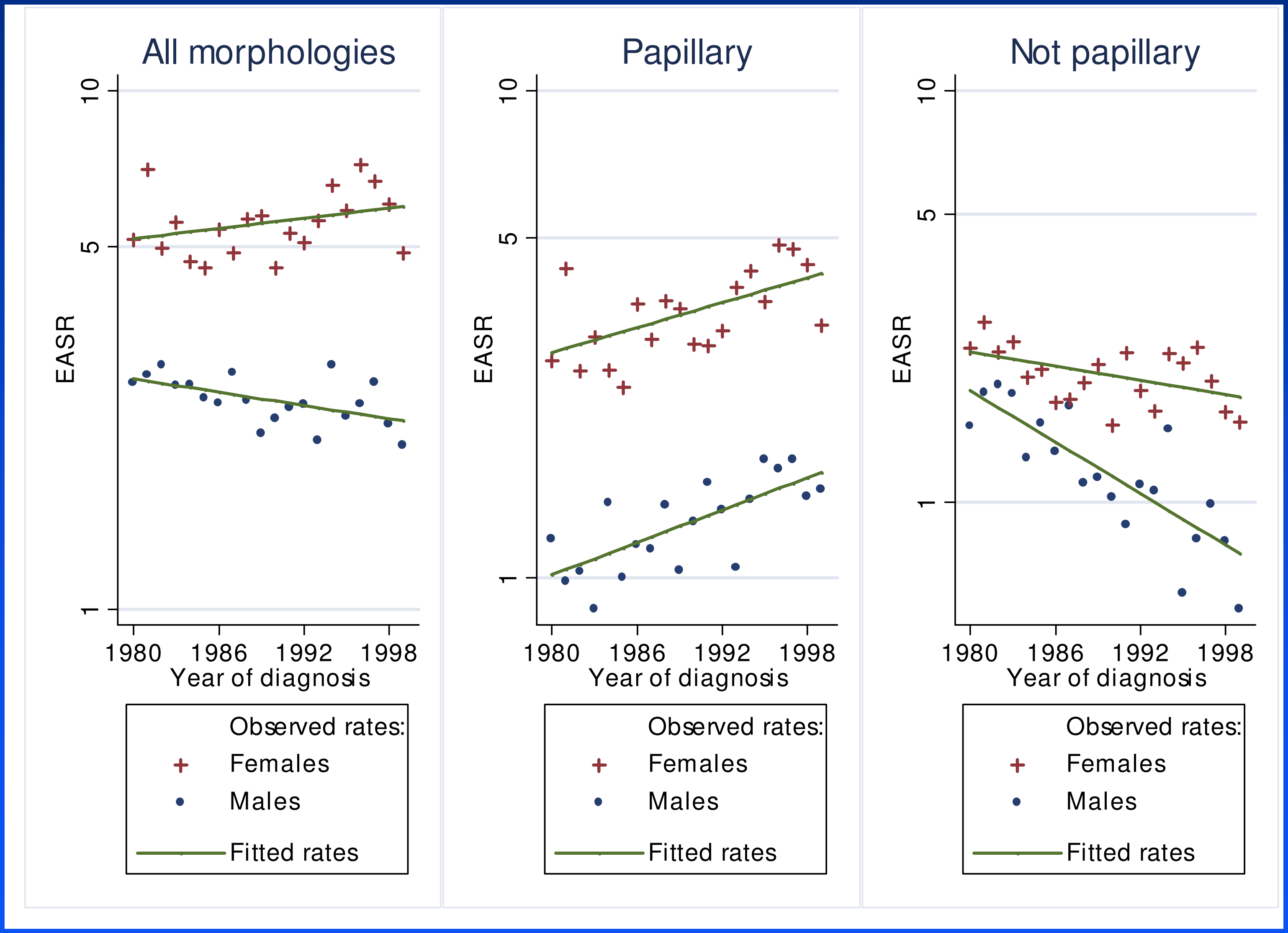


Average Annual Percent Change = 0.8%

Observed and fitted European age-standardized incidence rates (EASR, per 100,000, age 0-85+) of thyroid cancer in pooled Swiss cancer registries (1980-1999), linear regression modelling



Observed and fitted European age-standardized incidence rates (EASR, per 100,000, age 0-85+) of thyroid cancer in pooled Swiss cancer registries (1980-1999), linear regression modelling.



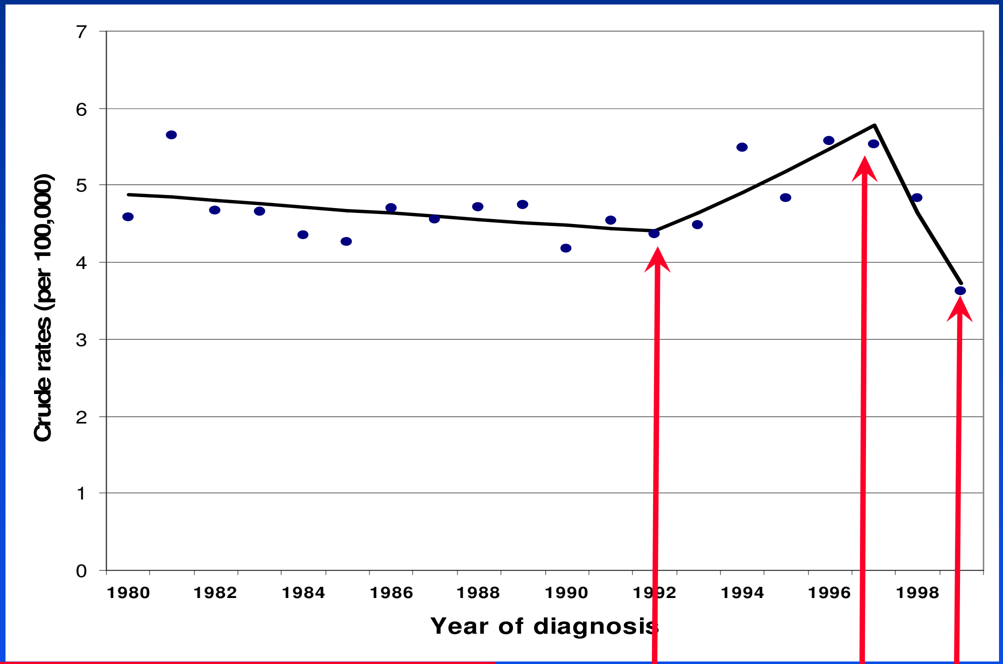
Average Annual Percent Changes (AAPC) (%)

		Papillary	Not papillary	All
Men	0-44	4.3	- 2.5	2.2
	45-69	2.0	- 3.6	- 0.4
	70+	**0.9**	- 6.9	**- 4.4**
	All ages	- 4.1	- 4.8	- 1.0
Women	0-44	2.4	2.2	2.3
	45-69	2.1	- 2.4	0.4
	70+	- 0.3	- 2.2	- 1.6
	All ages	2.0	- 1.3	0.8
Both sex	0-44	2.7	0.9	2.3
	45-69	2.0	- 2.9	0.1
	70+	- 0.2	- 3.7	- 2.5
	All ages	2.0	- 2.5	0.8

Joinpoint analysis

1. AAPC similar than those estimated for histological subtypes and for each sex with linear Poisson regression

2. No signifcant change in recent trends, except for both sex and all morphologies combined : two joinpoints are detected at 1992 and 1997



(1980-1992) = - 0.86 (- 2.42 to 0.73)

(1992-1997) = 5.56 (- 1.98 to 13.68)

(1997-1999) = - 19.62 (- 40.27 to 8.18)

Descriptive analysis and geographical comparison

Pooled time trend analysis

Age period cohort modelling

Age-period-cohort analysis of thyroid cancer incidence (Swiss people aged 20-79 years old during 1980-99)

Models	Deviance	DF	Change in deviance (Δdf)[1]	p-value for change in deviance[1]	Deviance /DF ratio (GOF)[2]
	Females				
All morphologies					
Age (A)					
Age + drift (AD)					
Age + period (AP)					
Age + cohort (AC)					
Age + cohort + period (APC)					

1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When $p<0.05$, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
2. *Goodness of fit indicator: when ratio > 1.5, the model does not fit well the data.*

Age-period-cohort analysis of thyroid cancer incidence (Swiss people aged 20-79 years old during 1980-99)

Models	Deviance	DF	Change in deviance (Δdf)[1]	p-value for change in deviance[1]	Deviance /DF ratio (GOF)[2]
	Females				
All morphologies					
Age (A)	53.32	36			1.481
Age + drift (AD)	48.33	35	4.99 (1)	**0.0255**	1.381
Age + period (AP)					
Age + cohort (AC)					
Age + cohort + period (APC)					

1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When $p<0.05$, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
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All morphologies					
Age (A)	53.32	36			1.481
Age + drift (AD)	48.33	35	4.99 (1)	**0.0255**	1.381
Age + period (AP)	45.39	33	2.94 (2)	0.2295	1.375
Age + cohort (AC)					
Age + cohort + period (APC)					

1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When p<0.05, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
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Age-period-cohort analysis of thyroid cancer incidence (Swiss people aged 20-79 years old during 1980-99)

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	Females				
All morphologies					
Age (A)	53.32	36			1.481
Age + drift (AD)	48.33	35	4.99 (1)	**0.0255**	1.381
Age + period (AP)	45.39	33	2.94 (2)	0.2295	1.375
Age + cohort (AC)	22.12	22	26.21 (13)	**0.0159**	1.005
Age + cohort + period (APC)					

1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When $p<0.05$, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
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Age-period-cohort analysis of thyroid cancer incidence (Swiss people aged 20-79 years old during 1980-99)

Models	Deviance	DF	Change in deviance (Δdf)[1]	p-value for change in deviance[1]	Deviance /DF ratio (GOF)[2]
	Females				
All morphologies					
Age (A)	53.32	36			1.481
Age + drift (AD)	48.33	35	4.99 (1)	**0.0255**	1.381
Age + period (AP)	45.39	33	2.94 (2)	0.2295	1.375
Age + cohort (AC)	22.12	22	26.21 (13)	**0.0159**	1.005
Age + cohort + period (APC)	20.99	20	1.126 (2)	0.5694	1.050

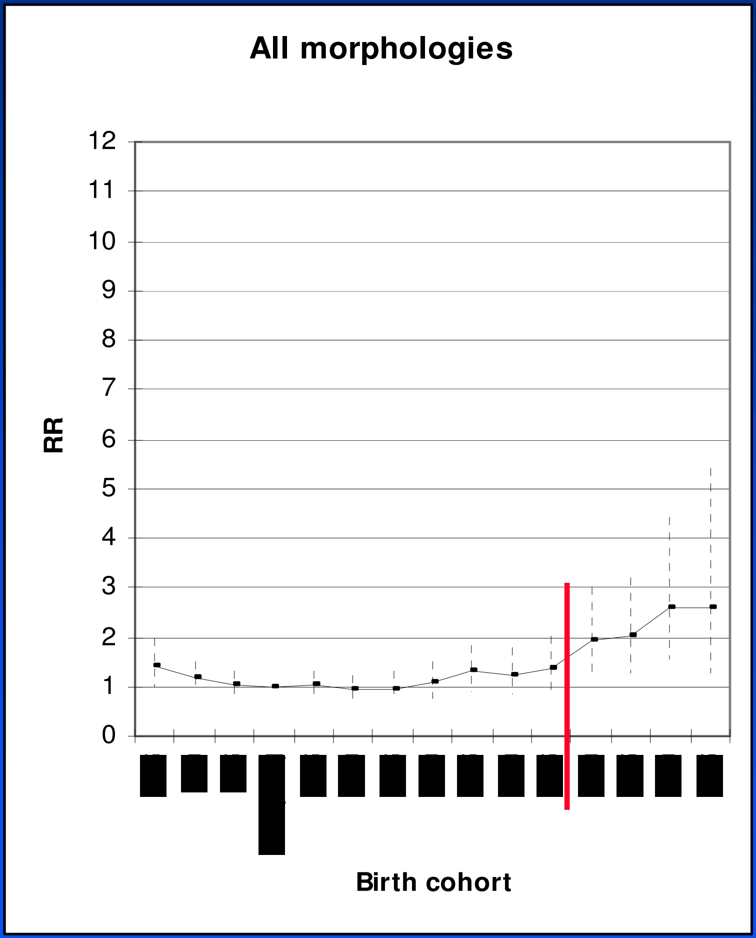
1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When $p<0.05$, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
2. *Goodness of fit indicator: when ratio > 1.5, the model does not fit well the data.*

Age-period-cohort analysis of thyroid cancer incidence (Swiss people aged 20-79 years old during 1980-99)

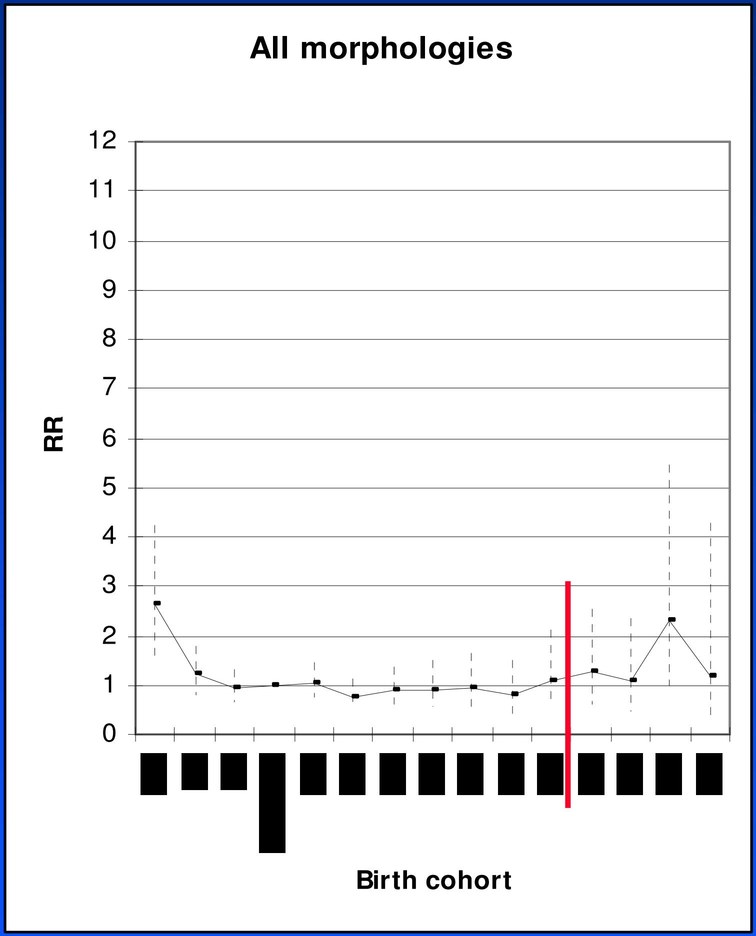
Models	Deviance	DF	Change in deviance (Δdf)[1]	p-value for change in deviance[1]	Deviance /DF ratio (GOF)[2]
	Males				
All morphologies					
Age (A)	46.41	36			1.289
Age + drift (AD)	45.79	35	0.61 (1)	0.4341	1.308
Age + period (AP)	44.08	33	1.71 (2)	0.4245	1.336
Age + cohort (AC)	14.86	22	30.93 (13)	**0.0035**	0.676
Age + cohort + period (APC)	14.86	20	0.25 (2)	0.8842	0.731

1. *Models are compared according to change in deviance, differences in degrees of freedom (Δdf) and related p-value for change in deviance. When $p<0.05$, the effects of the added term are significant. AD vs. A, AP vs. AD, AC vs. AD, APC vs. AC*
2. *Goodness of fit indicator: when ratio > 1.5, the model does not fit well the data.*

Relative Risks (RRs) for different Swiss birth cohorts related to people born around 1920 (Ref.)
Cohort effects estimated using the age-cohort model

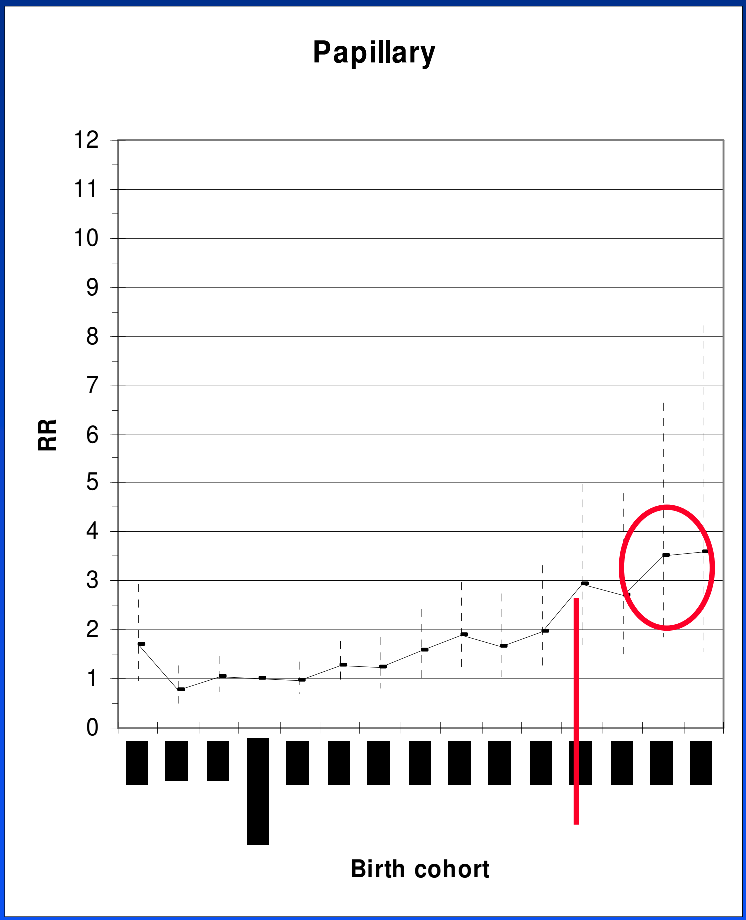


Women

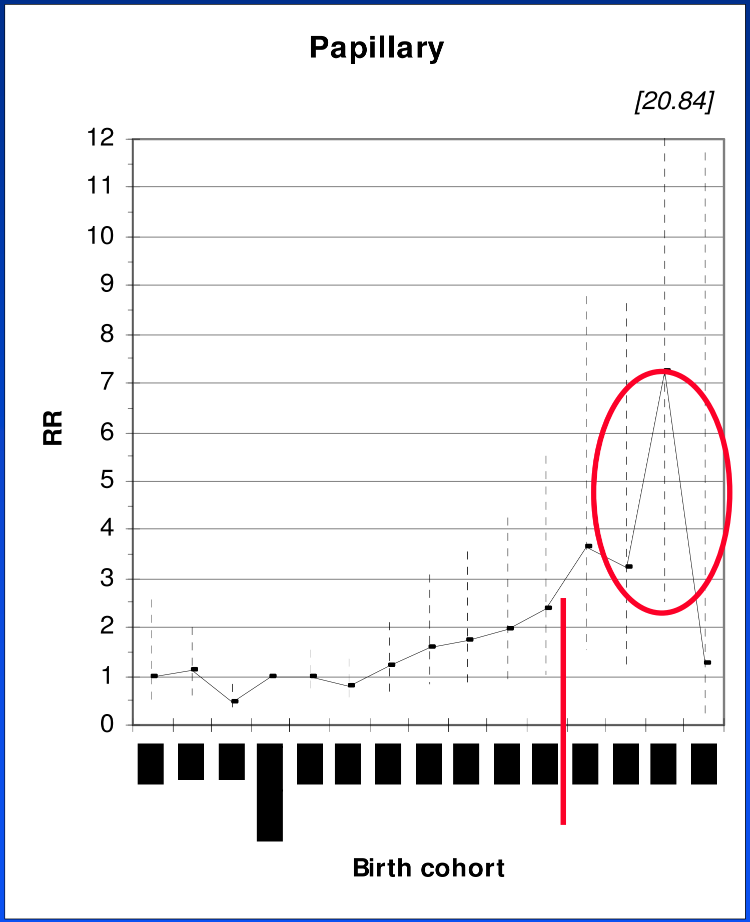


Men

Relative Risks (RRs) for different Swiss birth cohorts related to people born around 1920 (Ref.)
Cohort effects estimated using the age-cohort model

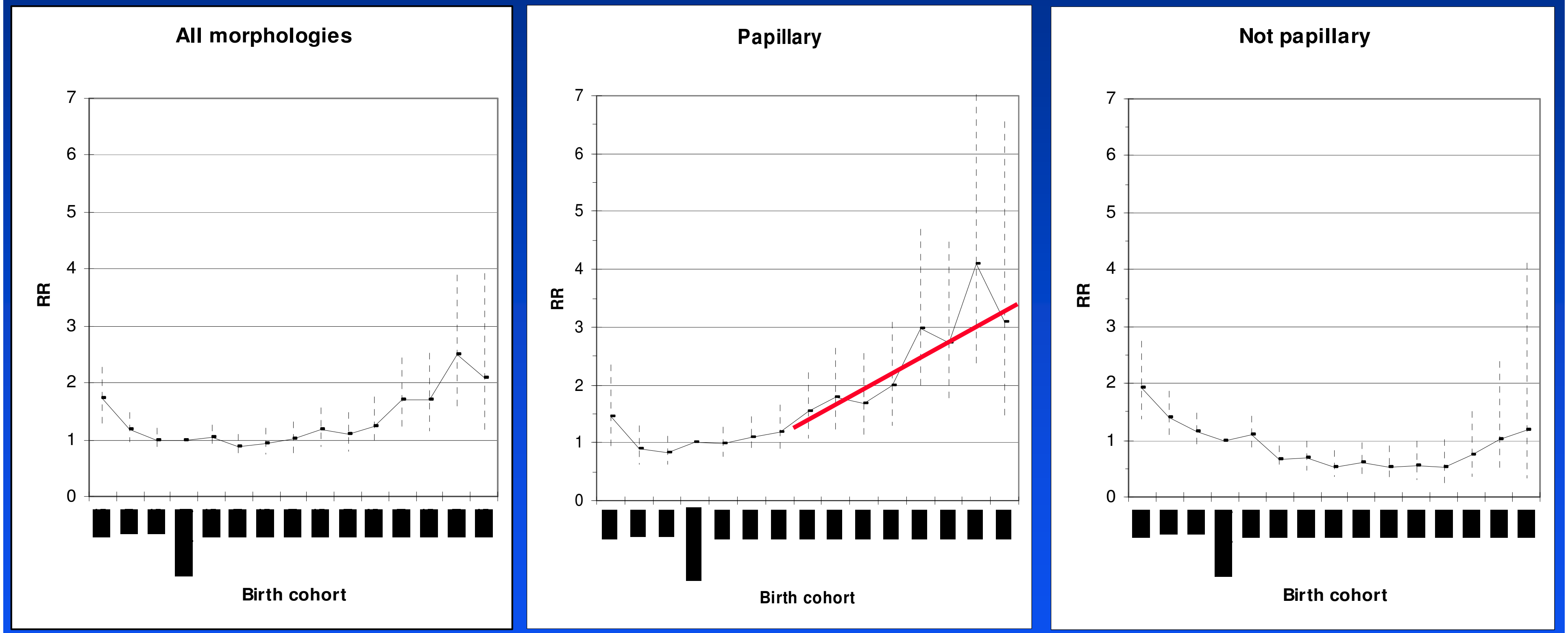


Women



Men

Relative Risks (RRs) for different Swiss birth cohorts related to people born around 1920 (Ref.) Cohort effects estimated using the age-cohort model



Both sex

Montanaro et al, European Journal of Cancer Prevention, 2006, in press

First comments

1. No "period" effect
2. Apparent global regular increase ≈ 1% per year, but
   - Opposite trends for histological subtypes
   - Heterogeneous trends for young vs elderly
   - Different trends by gender

Explanations ?

Impact of changing the rules for coding (1988) : observed and corrected incidence rates in Geneva

	1970-80		1990-98	
	Observed	Corrected[a]	Observed	Corrected[b]
Papillary	1.48	2.46	3.06	3.21
Follicular	1.29	0.35	0.62	0.43
Other cancers	1.15	1.39	0.82	0.86
Total	4.32	4.20[c]	4.50	4.50

[a] : 45% of follicular cancer reclassified as papillary cancers, 18% reclassified as other cancer, 27% remained follicular cancers

[b] : 25% of follicular cancer reclassified as papillary cancers, 6% reclassified as other cancer, 69% remained follicular cancers

[c] : 9% of thyroid cancers diagnosed as follicular carcinoma between 1970 and 1980 were reclassified as benign

Verkooijen et al, Cancer Causes and Controls, 2003

Proportion of papillaries among all thyroid cancers

Code	*Label*	*1980-84*	*1985-89*	*1990-94*	*1995-99*
8050	Papillary carcinoma NOS	13%	13%	13%	18%
8260	Papillary adenocarcinoma, NOS	10%	15%	17%	24%
8290	Papillary carcinoma with oxyphilic cells	5%	6%	7%	4%
8340	Papillary carcinoma, follicular variant	21%	20%	23%	21%

Impact of radiation exposure on histological subtypes : Belarus Vs Italy/France (1986)

TABLE 1. Histotype and tumor extension of thyroid cancer in children and adolescents (Belarus *vs.* Italy and France)

	Belarus (n = 472)		Italy/France (n = 369)		
	n	(%)	n	(%)	
Histology					
Papillary	443	(93.9)	303	(82.1)	$P = 0.0001^a$
Follicular	25	(5.3)	56	(15.2)	
Medullary	2	(0.4)	(2)[b]		
Hürthle	1	(0.2)	0		
Anaplastic	1	(0.2)	0		
Unknown	0		10	(2.7)	
Extension					
Extrathyroid	232	(49.1)	92	(24.9)	$P = 0.0001$
Lymph nodes	305	(64.6)	199	(53.9)	$P = 0.002$
Distant met.[c]	37	(7.8)	64	(17.3)	

[a] By χ^2 limited to papillary and follicular.
[b] Excluded from analysis because detected by genetic screening of medullary thyroid carcinoma.
[c] In Belarus patients the presence of distant metastases was assessed by x-rays; in Italy/France, by x-rays and ^{131}I-WBS.

Pacini et al, Journal of clinical endocrinology and metabolism, 1997

Trends in Canada, 1970-1996

Table 1 Age-specific incidence rate of thyroid cancer (per 100 000 population) and average annual percent change (AAPC) in Canada excluding Quebec, 1970–72 to 1994–96[a]

Age (year)	Female			Male		
	1970–72	1994–96	AAPC[b]	1970–72	1994–96	AAPC[b]
10–24	1.55	2.92	2.54**	0.37	0.74	1.67*
25–44	4.43	11.04	3.65**	1.27	2.84	2.74**
45–64	5.84	12.78	3.36**	1.97	4.56	2.93**
65–84	8.16	10.69	0.66*	4.08	5.88	1.68**
All ages[a]	3.26	6.82	3.50**	1.12	2.23	3.15**

*$P < 0.05$; **$P < 0.01$ [a]Rates were adjusted to the World Standard Population. [b]Trends were estimated by Poisson regression. See the Methods.

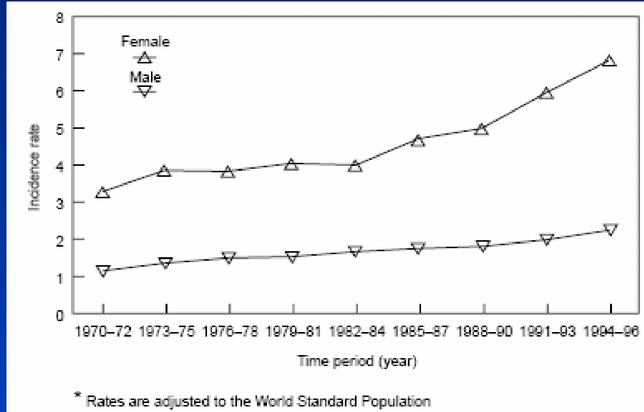


Figure 1 Age-adjusted incidence rates of thyroid cancer by sex in Canada, 1970–72 to 1994–96, per 100 000

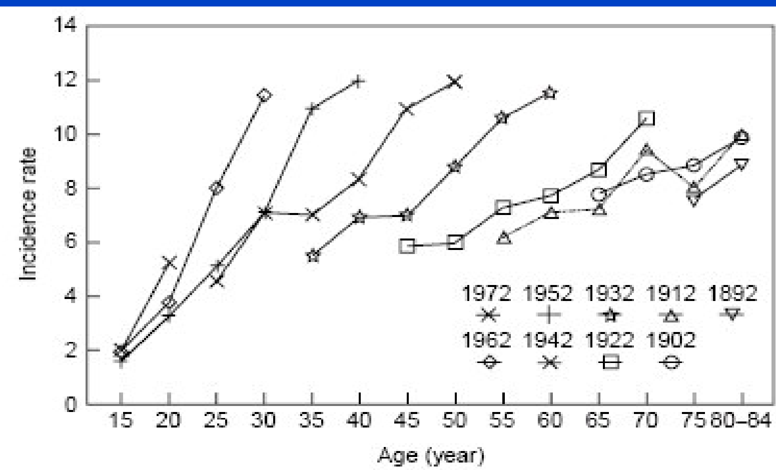


Figure 2 Age-specific incidence rates of thyroid cancer by birth cohort among women in Canada, per 100 000

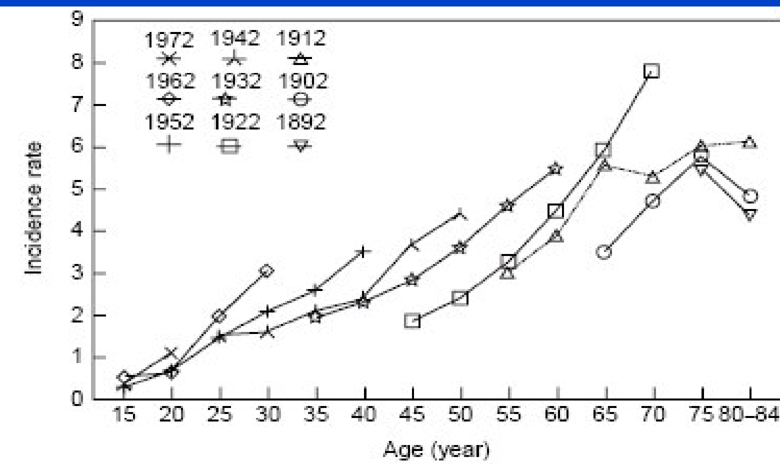
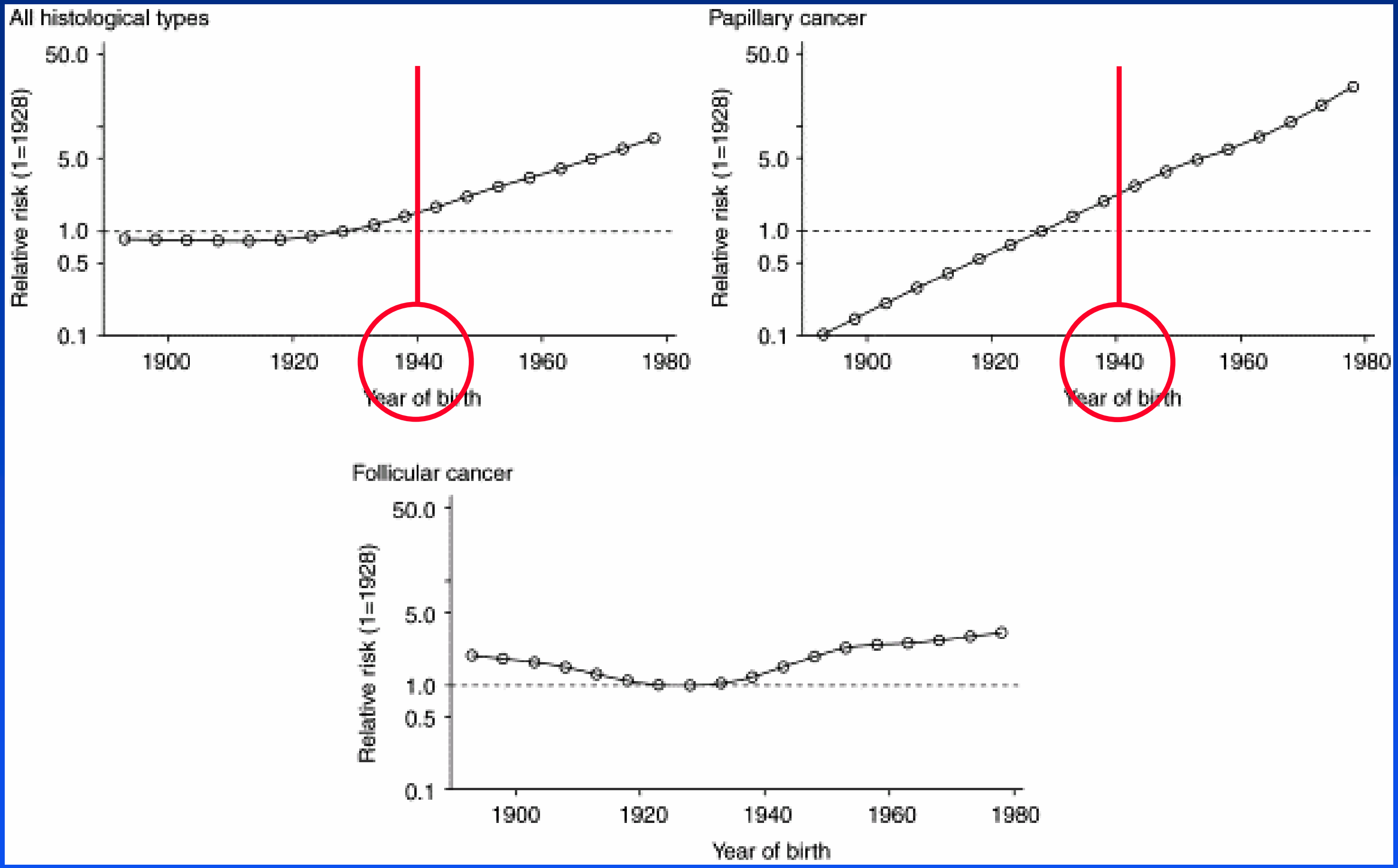


Figure 3 Age-specific incidence rates of thyroid cancer by birth cohort among men in Canada, per 100 000

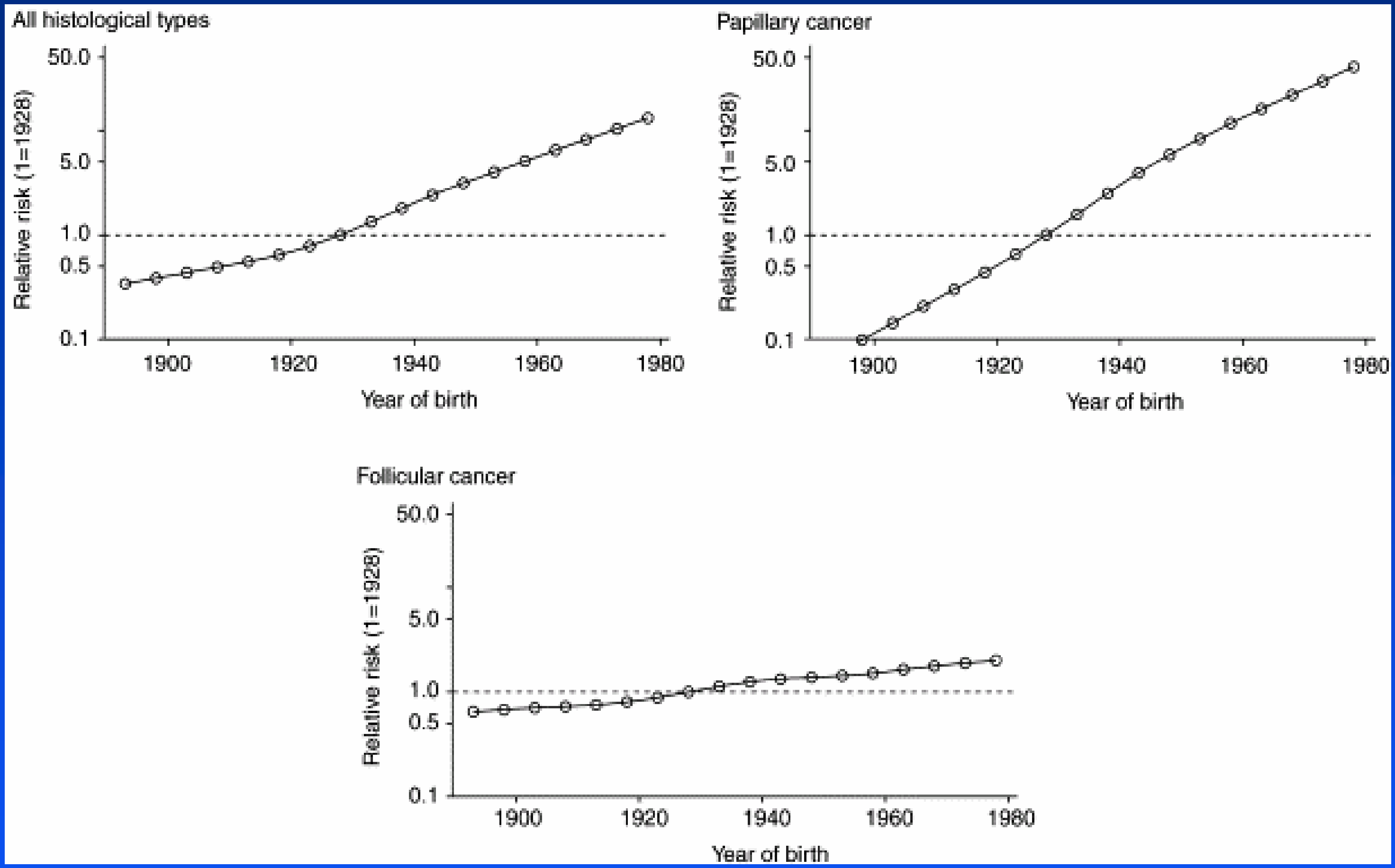
S. Liu et al. British Journal of Cancer, 2000

Trends in France 1978-1997 (Men)



Colonna et al, European Journal of Cancer, 2002

Trends in France 1978-1997 (Women)



Colonna et al, European Journal of Cancer, 2002

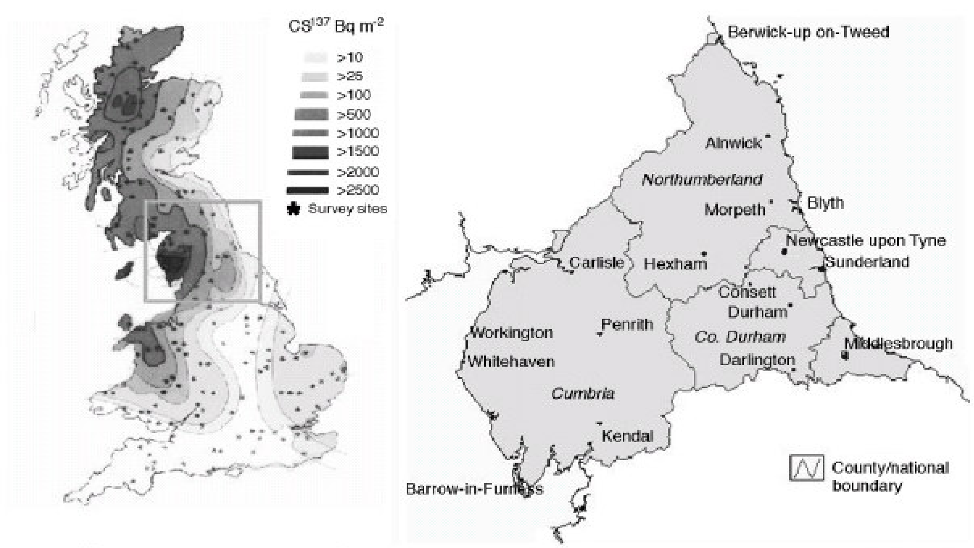
Colonna et al. 's comment (2002)

" As in many countries, the increasing number of diagnostic investigations over time can be proposed as an explanation for the upward trends in the incidence of thyroid cancer. The exposure to radiation therapy for benign conditions in early childhood might explain a small part of this increase.

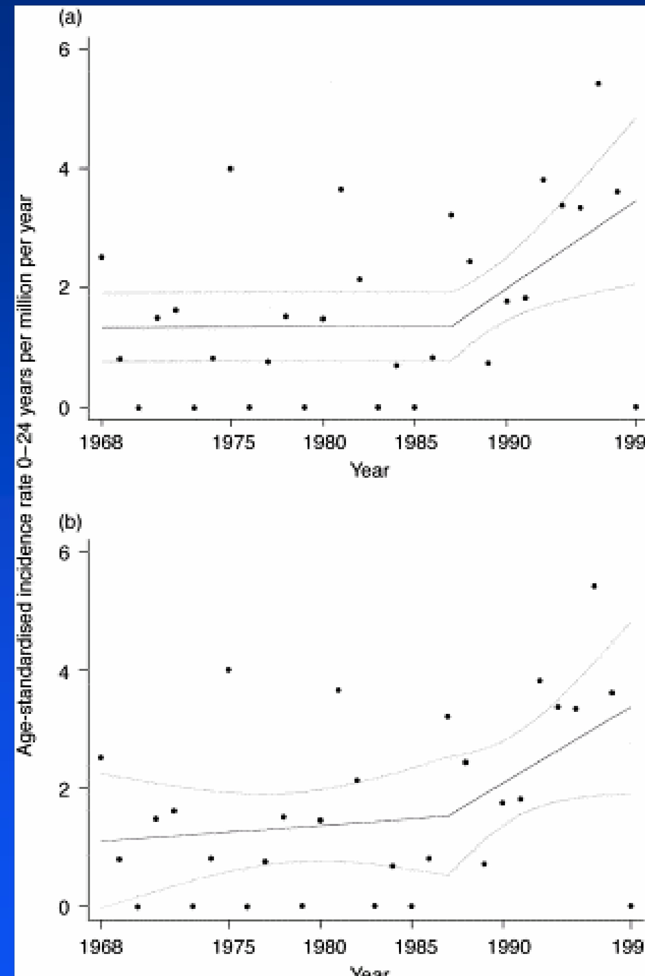
Our analysis showed that there was no change in the recent trends in thyroid cancer following the Chernobyl accident. It does not exclude that such changes will occur later when the children who were possibly exposed in 1986 might develop the disease after a long latent period "

Trends in the North of England 1968-1997

« Regression models showed a significant increase in the incidence of thyroid cancer […] (*p*=0.002) »

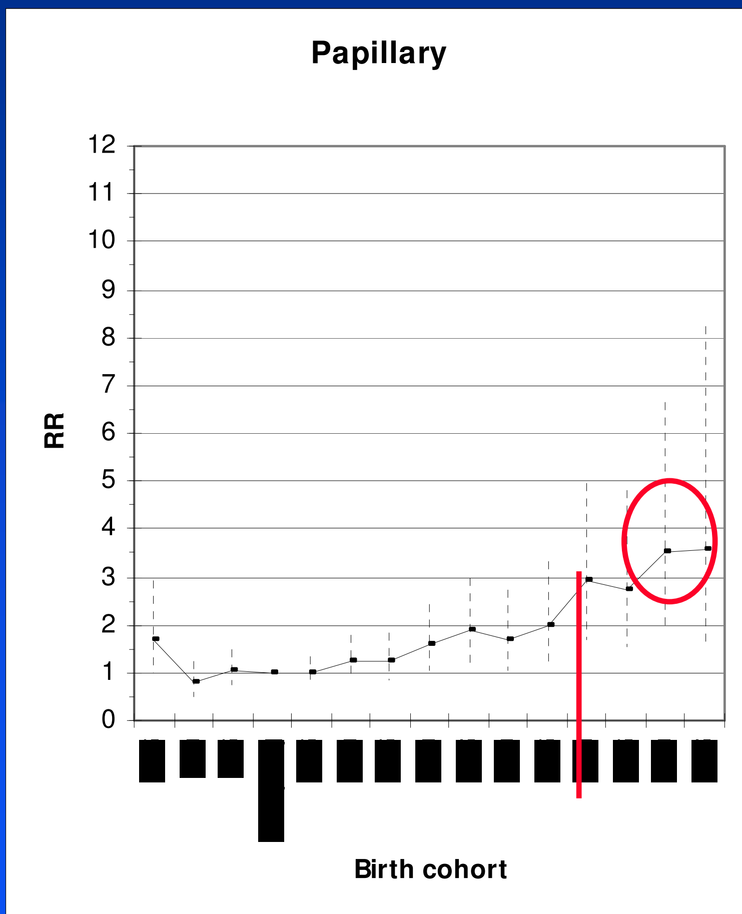


Casesium^{137} deposition on vegetation (Bq m^{-2}).
Figure by kind permission of the Institute of Terrestrial Ecology

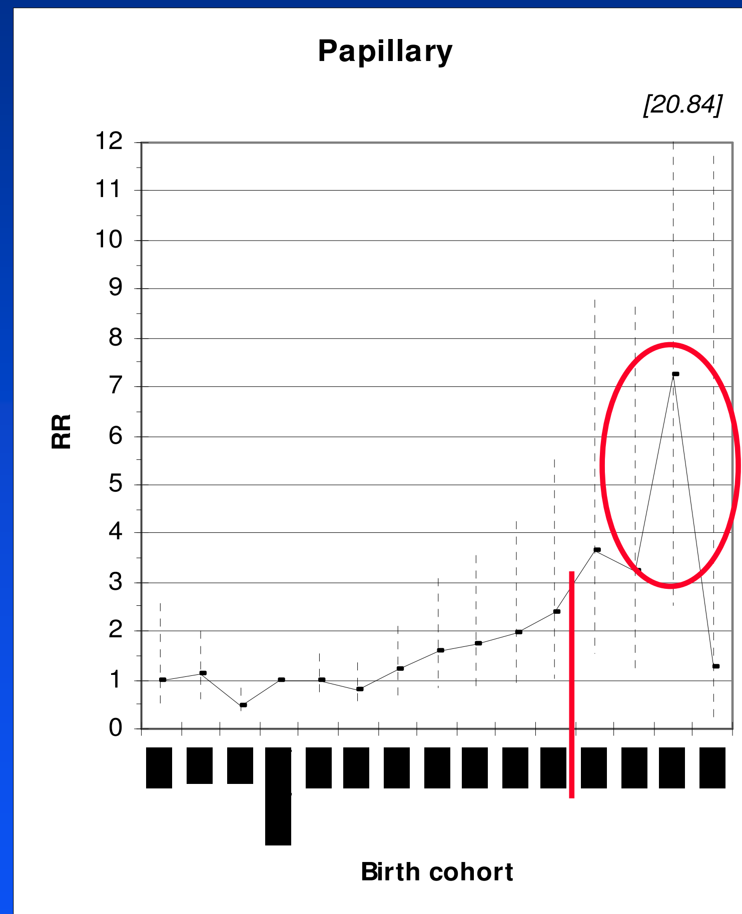


S. J. Cotterill et al. European Journal of Cancer, 2001

Relative Risks (RRs) for different Swiss birth cohorts related to people born around 1920 (Ref.)
Cohort effects estimated using the age-cohort model



Women



Men

Conclusions

- No "period" effect
- Apparent global regular increase ≈ 1% per year
- We do observe an unexpected (non significant) increase among recent birth cohorts, more marked for males, which cannot be only explained by a "screening effect" or any other bias.

Conclusions

Radiation exposure in childhood and adolescence might be responsible for increasing risk of developing papillary carcinoma.

Other unrecognized etiologic factors remain to be identified. The differential age and cohort effect provide clues for etiologic heterogeneity in the pathogenesis of thyroid cancer between females and males.