

UPDATED MORTALITY ANALYSIS OF SELTINE, THE FRENCH COHORT OF NUCLEAR WORKERS, 1968–2014

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Background and aims

- Cohort studies of nuclear workers are key to assess the health effects of protracted exposures to low doses of ionizing radiation
- This is necessary to verify the adequacy of radiation protection standards
- In the 2000's, two cohorts were established by the IRSN of French nuclear workers, with a main focus on the effects of external exposure to IR: the EDF cohort and the CEA-AREVA cohort
- These French cohorts were integrated into the 15-Country study and, with extended follow-up, into the INWORKS study
- These two cohorts were merged into a single cohort, renamed SELTINE* and its follow-up has been extended through 31 December 2014

*Suivi Epidémiologique Longitudinal des Travailleurs de l'Industrie Nucléaire françaisE



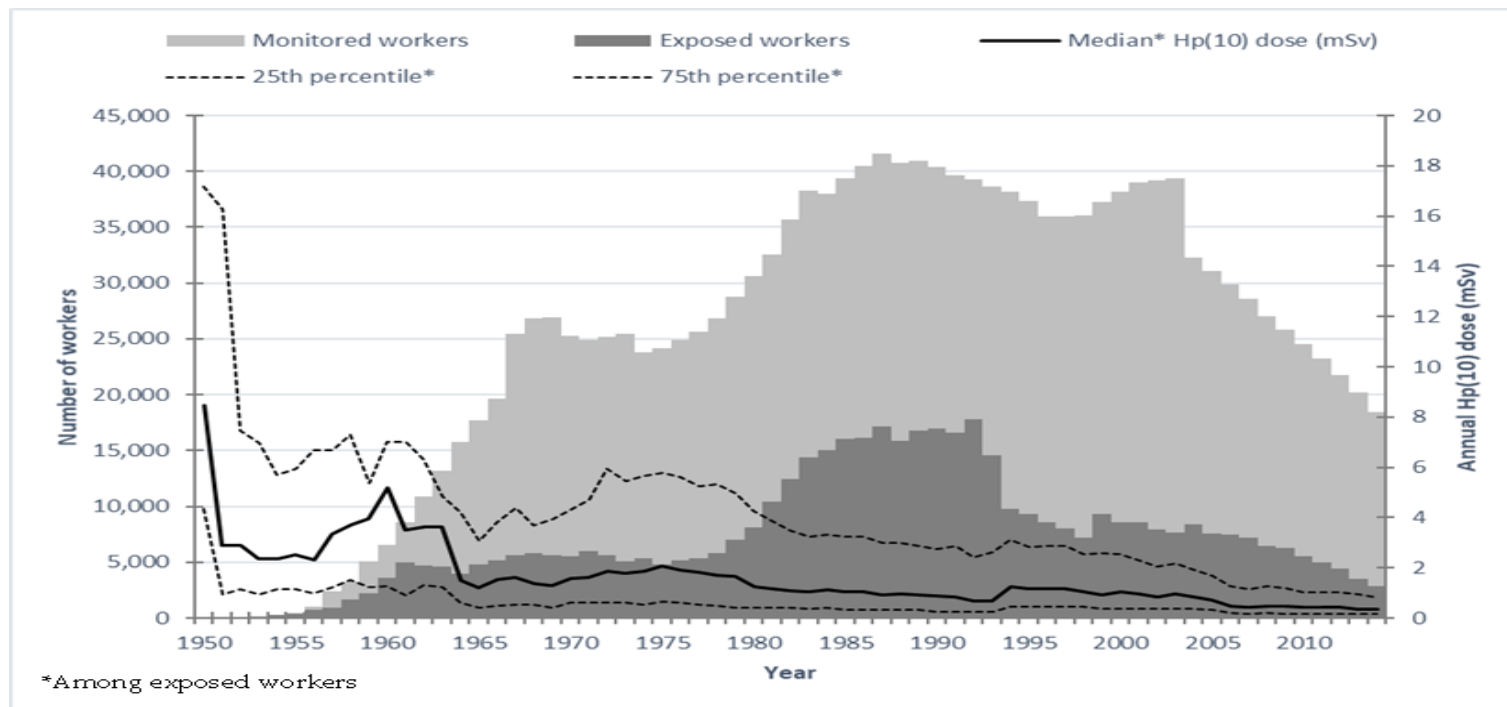
SELTINE: Study population

French nuclear worker cohort SELTINE, followed-up for mortality over period 1968–2014

Characteristics			
Number of workers		80,348	
Number of person-years		2,554,554	
Percentage of females		13%	
Median year of birth (range)		1951 (1893–1984)	
Follow-up (1968–2014), in years	Mean		SD
Duration	31.8		11.6
Age at beginning of follow-up	31.1		8.2
Age at end of follow-up	62.9		3.9
Vital status on 12/31/2014,	N		%
Alive	64,298		80.0
Deceased	15,695		19.5
Lost to follow-up	355		0.5
Employment	Mean		SD
Duration	26.2		9.2
Number of person-years by main employing company			%
CEA	1,418,821		55.5
Orano	249,662		9.8
EDF	808,188		31.6
Other**	77,883		3.1

SELTINE: Exposure history

Distribution by calendar year of monitored and exposed workers with median Hp(10) dose in milliSievert (mSv)



Mean
cumulative
dose :
15.7 mSv
(SD: 37.5)

SELTINE: Dose-risk relationship for solid cancers

Excess relative rates of death per Gray (ERR/Gy) of cumulative organ dose (males only)

Cause of Death	Target Tissue	Observed Deaths	ERR/Gy	95% CI	p-Value
All cancers	Colon	5,618	0.53	-0.40; 1.55	0.28
All cancers excluding leukaemia	Colon	5,414	0.46	-0.48; 1.50	0.35
Solid cancers	Colon	5,130	0.71	-0.28; 1.80	0.16
Solid cancers excluding lung cancer	Colon	3,778	0.45	-0.65; 1.69	0.44
Oral cavity cancer	Skin	201	4.54	-0.92; 12.8	0.12
Oesophagus cancer	Stomach	206	1.26	ne; 7.97	0.63
Stomach cancer	Stomach	198	2.82	ne; 10.7	0.32
Colon cancer	Colon	383	1.48	-1.71; 6.03	0.42
Rectum cancer	Colon	142	4.31	-1.24; 13.1	0.15
Liver cancer	Liver	286	1.20	ne; 7.17	0.63
Gallbladder cancer	Gallbladder	35	NC	NC	NC
Pancreas cancer	Pancreas	338	-2.41	ne; 1.19	0.15
Peritoneum cancer	Colon	74	6.58	ne; 23.9	0.18
Nasal cancer	Skin	45	8.87	ne; 33.5	0.15
Larynx cancer	Stomach	102	5.23	ne; 18.6	0.22
Lung cancer	Lung	1,352	1.09	-0.83; 3.39	0.29
Pleural cancer	Lung	95	-1.79	-2.14; 7.03	0.61
Bones, connective, and other soft tissues cancers	Colon	48	3.67	ne; 22.8	0.52
Melanoma	Skin	86	3.68	ne; 17.0	0.37
Prostate cancer	Bladder	473	-1.66	ne; 1.42	0.25
Bladder cancer	Bladder	212	-1.14 **	ne; 4.63	0.65
Kidney cancer	Bladder	160	3.59	ne; 13.8	0.32
Brain and central nervous system cancer	Brain	169	-1.68	ne; 5.31	0.56
Brain and central nervous system tumours including benign tumours	Brain	250	0.87	ne; 7.71	0.75

(Linear models,
10-year lag)

SELTINE: Dose-risk relationship for hematopoietic and lymphatic cancers

Excess relative rates* of death per Gray (ERR/Gy) of cumulative red bone marrow dose (males only)

Cause of Death	Observed Deaths	Lag	ERR/Gy	95% CI	p-Value
Leukaemia excluding CLL	157	2	3.31	0.94; 13.38	<0.01
Acute myeloid leukaemia	59	2	5.26	ne; 24.17	0.05
Acute myeloid leukaemia and MDS	96	2	3.86	0.43; 21.36	0.02
Leukaemia (excluding CLL) and MDS	194	2	2.87	0.95; 11.55	0.01
Chronic lymphocytic leukaemia	44	10	NC	NC	NC
Non-Hodgkin lymphoma	184	10	NC	NC	NC
Multiple myeloma	80	10	-0.57	ne; 11.94	0.90

* estimated from a linear model of cumulative penetrating photon dose lagged by 2 or 10 years, adjusted on calendar year, age, company, and duration of employment, and allowing for modification effect of attained age for leukaemia analyses; CI: likelihood-based confidence interval; CLL: chronic lymphocytic leukaemia; MDS: myelodysplastic syndromes; NC: convergence not achieved; ne: not estimated.

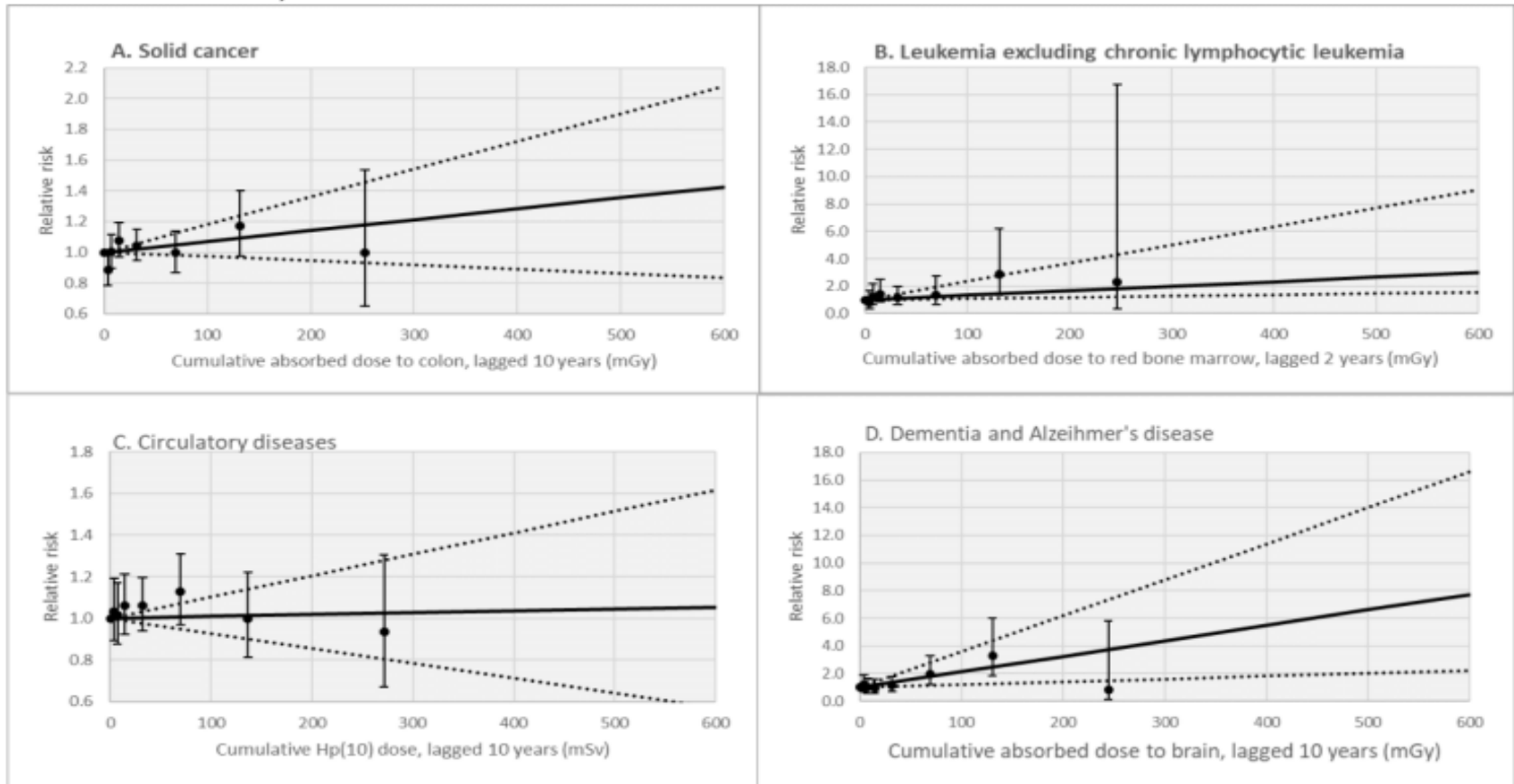
SELTINE: Dose-risk relationship for non-cancer outcomes

Excess relative rates* of death per unit of cumulative dose to target tissues (in Gy or Sv) (males only)

Cause of Death	Target Tissue	Observed Deaths	ERR/Gy or ERR/Sv	95% CI	p-Value
Non-cancer diseases (all)	H _p (10)	8577	0.02	-0.49; 0.57	0.95
Diabetes mellitus	H _p (10)	169	-0.91	ne; 2.62	0.54
Mental and behavioural disorders	Brain	235	2.74	-1.95; 10.33	0.32
Diseases of the nervous system	Brain	531	3.47	-0.48; 8.56	0.09
Dementia, Alzheimer's disease, Parkinson's disease, motoneuron disease	Brain	469	4.99	0.74; 10.52	0.02
Dementia, Alzheimer's disease	Brain	269	9.62	3.05; 18.68	<0.01
Parkinson's disease	Brain	124	-1.30	ne; 7.44	0.71
Circulatory diseases	H _p (10)	3261	0.09	-0.72; 1.03	0.83
Ischemic diseases	H _p (10)	1258	-0.23	ne; 1.38	0.76
Cerebrovascular diseases	H _p (10)	684	1.41	ne; 4.05	0.19
Hypertensive diseases	H _p (10)	120	2.31	ne; 9.98	0.37
Respiratory diseases	Lung	558	0.22	ne; 3.71	0.88
Chronic obstructive pulmonary diseases	Lung	164	0.15	ne; 7.52	0.96
Digestive diseases	Colon	583	0.96	-1.72; 4.58	0.53
Cirrhosis	Liver	166	3.72	ne; 13.64	0.29

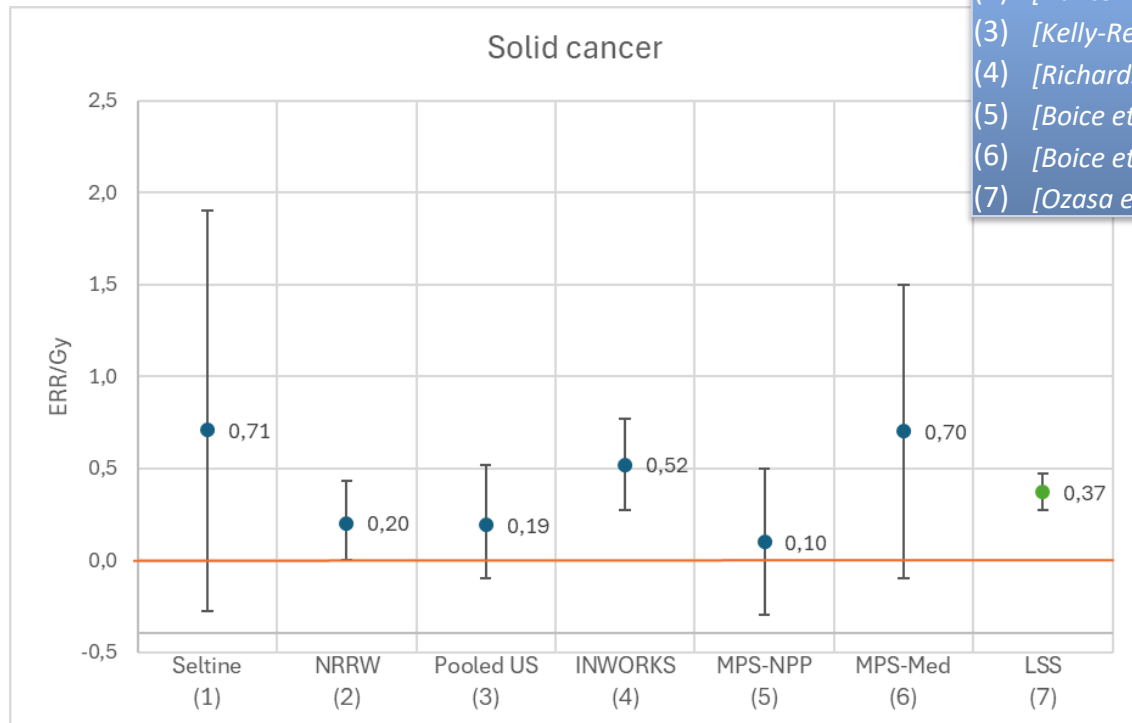
* estimated from a linear model of cumulative penetrating photon dose lagged by 10 years, adjusted on calendar year, age, sex, company, duration of employment, and socioeconomic status; CI: likelihood-based confidence interval; ne: not estimated.

SELTINE: Relative risk by dose categories for selected outcomes



SELTINE: Comparison of results with other recent studies

Excess relative rates of death per Gy of cumulative dose and 95% confidence intervals, estimated from a linear model

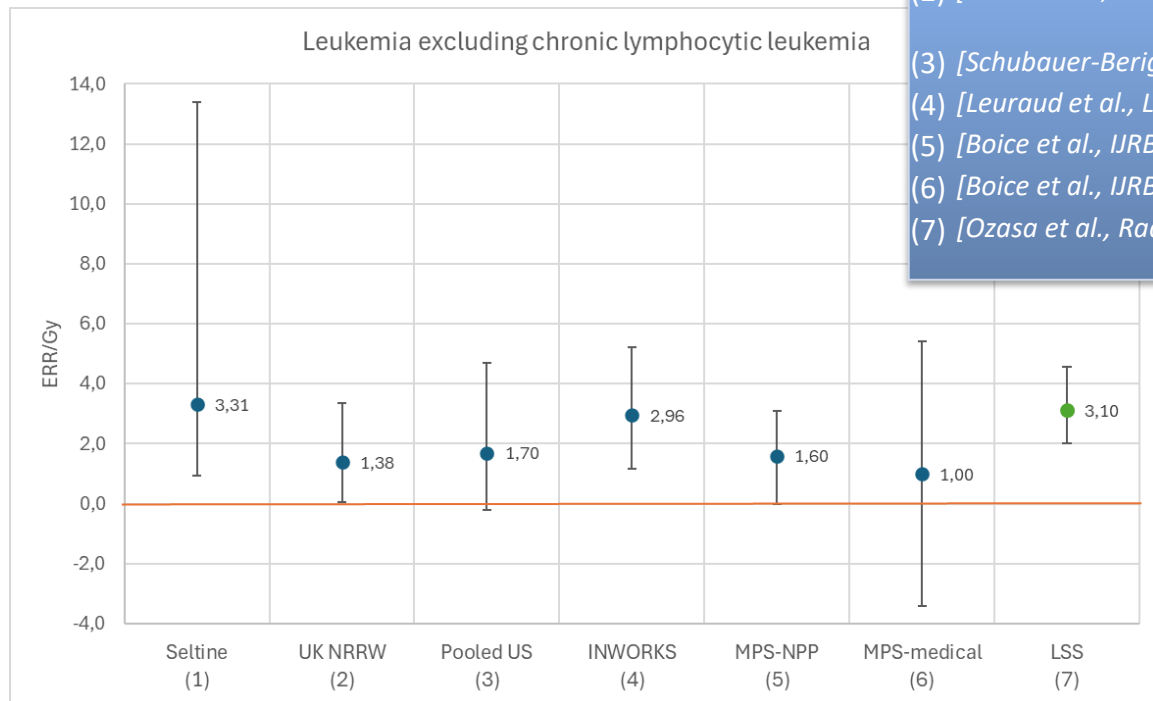


- (1) [Laurent et al., *Cancers* 2023] males only
- (2) [Hunter et al., *Radiat Res* 2023] incidence, dose in Sv
- (3) [Kelly-Reif et al., *Int J Epidemiol* 2023] 90%CI, dose in Sv
- (4) [Richardson et al., *BMJ* 2023] 90%CI
- (5) [Boice et al., *IJR* 2022] -
- (6) [Boice et al., *IJR* 2023] -
- (7) [Ozasa et al., *Radiat Res* 2012] age at exposure ≥ 20 y

SELTINE: Comparaison of results with recent studies

Excess relative rates of death per Gy of cumulative dose and 95% confidence intervals, estimated from a linear model

- (1) [Laurent et al., *Cancers* 2023] males only
- (2) [Gillies et al., *Radiat Res* 2019] incidence, males only, 90%CI, dose in Sv
- (3) [Schubauer-Berigan et al., *Radiat Res* 2015] dose in Sv
- (4) [Leuraud et al., *Lancet Haematol* 2015] 90%CI
- (5) [Boice et al., *IJR* 2022] -
- (6) [Boice et al., *IJR* 2023] -
- (7) [Ozasa et al., *Radiat Res* 2012] age at exposure ≥ 20 y, all leukemia



Conclusion

Overall healthy worker effect (36% mortality deficit)

Consolidates the evidence of an excess risk of solid cancer and leukaemia (excluding CLL) after low-dose protracted exposure to low-LET external radiation

Results coherent with those obtained in other major nuclear workers studies, and with those from the A-Bomb survivors

Additional analyses warranted to fully understand factors of variations of the dose-risk relationship in low dose studies


The association observed between radiation exposure and dementia needs further investigation

To know more



Article

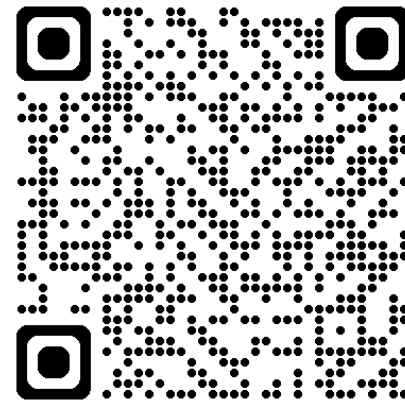
Updated Mortality Analysis of SELTINE, the French Cohort of Nuclear Workers, 1968–2014

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**THANK YOU
FOR YOUR
ATTENTION**

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- IRSN's BASEP unit who helped to extract dose recordings from the SISERI system
- Isabelle Thierry-Chef and François Trompier for their help in the estimation of dose conversion coefficients
- This work was carried out by IRSN with partial funding from EDF and Orano



SELTINE: Global mortality

External analysis : Standardized Mortality Ratio

○ Overall healthy worker effect (36% mortality deficit)

- All cause (n=15695) SMR = 0.64 CI95% [0.63 – 0.65]

○ Specific excesses

- Pleural mesothelioma (n=98) SMR = 1.68 CI95% [1.36 – 2.05]
- Skin melanoma (n=94) SMR = 1.22 CI95% [0.99– 1.50]

Results : external analysis for all causes and solid cancers

Cause of death	Observed deaths	Expected deaths	SMR	95%CI
All causes	15,695	24,379.4	0.64	0.63-0.65
Solid cancers	5,691	8,054.7	0.71	0.69-0.73
Mouth and pharynx	206	485.7	0.42	0.37-0.49
Oesophagus	211	403.7	0.52	0.45-0.60
Stomach	210	314.8	0.67	0.58-0.76
Colon	428	562.8	0.76	0.69-0.84
Rectum	155	223.6	0.69	0.59-0.81
Liver	307	497.6	0.62	0.55-0.69
Gallbladder	41	53.3	0.77	0.55-1.04
Pancreas	367	400.7	0.92	0.82-1.01
Peritoneum	84	112.6	0.75	0.59-0.92
Nasal cavity	48	109.9	0.44	0.32-0.58
Larynx	103	236.2	0.44	0.36-0.53
Trachea, bronchus and lung	1,421	2,115.7	0.67	0.64-0.71
Pleura	98	58.3	1.68	1.36-2.05
Bones and articular cartilage	32	39.4	0.81	0.56-1.15
Soft tissue	19	34.7	0.55	0.33-0.86
Skin melanoma	94	76.9	1.22	0.99-1.50
Skin other	15	23.2	0.65	0.36-1.07

SMR: mortality ratio standardized on calendar period, age, and sex; CI: confidence interval;

Results : external analysis for non-cancer causes of death

Cause of death	Observed deaths	Expected deaths	SMR	95%CI
Non-cancer causes of death				
Diabetes mellitus	188	380.0	0.49	0.43-0.57
Mental and behavioural disorders	269	603.9	0.45	0.39-0.50
Diseases of the nervous system	618	778.7	0.79	0.73-0.86
Dementia, Alzheimer's disease, Parkinson's disease, moto-neuron disease	553	650.8	0.85	0.78-0.92
Dementia and Alzheimer's disease	334	414.6	0.81	0.72-0.90
Parkinson's disease	139	140.4	0.99	0.83-1.17
Circulatory diseases	3,582	5,805.9	0.62	0.60-0.64
Ischemic heart diseases	1,333	2,032.0	0.66	0.62-0.69
Cerebrovascular diseases	781	1,270.8	0.61	0.57-0.66
Respiratory diseases	628	1,314.9	0.48	0.44-0.52
COPD	186	436.9	0.43	0.37-0.49
Asthma	28	56.5	0.50	0.33-0.72
Digestive diseases	633	1,489.6	0.42	0.39-0.46
Cirrhosis	177	547.8	0.32	0.28-0.37
External causes	1,559	2,491.7	0.63	0.60-0.66

SMR: mortality ratio standardized on calendar period, age, and sex; CI: confidence interval;