CRO AVIANO
Epidemiologia e Biostatistica
CENTRO DI RIFERIMENTO ONCOLOGICO

USE OF CANCER REGISTRIES DATA TO ESTIMATE THE CANCER RISK OF RECIPIENTS OF LIVER TRANSPLANT

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For the Italian Immunosuppression and Cancer Study Group

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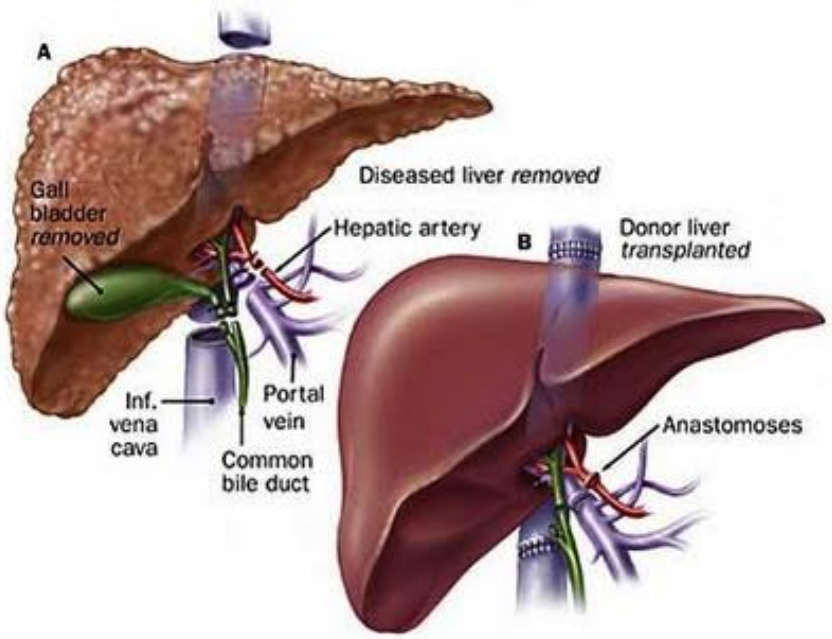
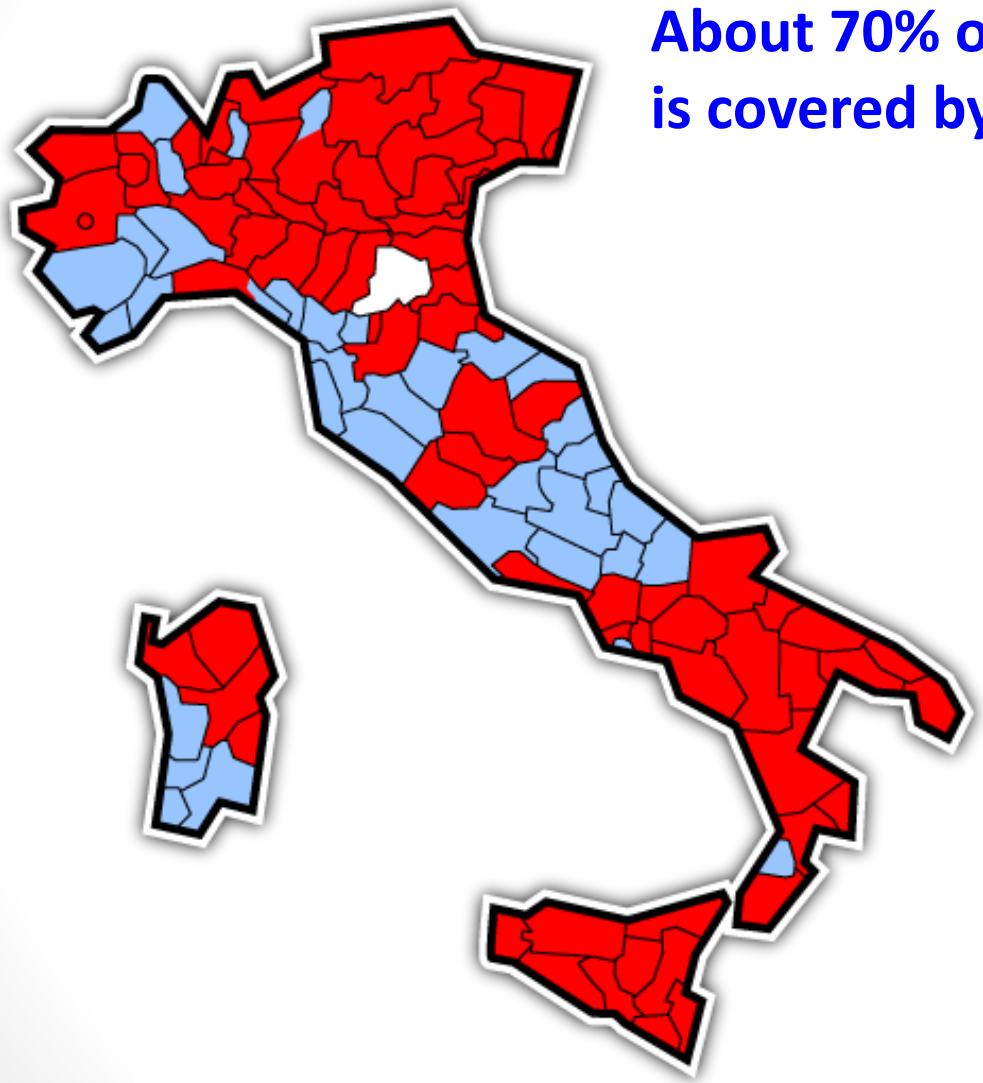
PRESENTATION



STUDY AIM

To assess, in Italy, the cancer risk of persons immunosuppressed after liver transplant by using data from population based cancer registries (PBCR)

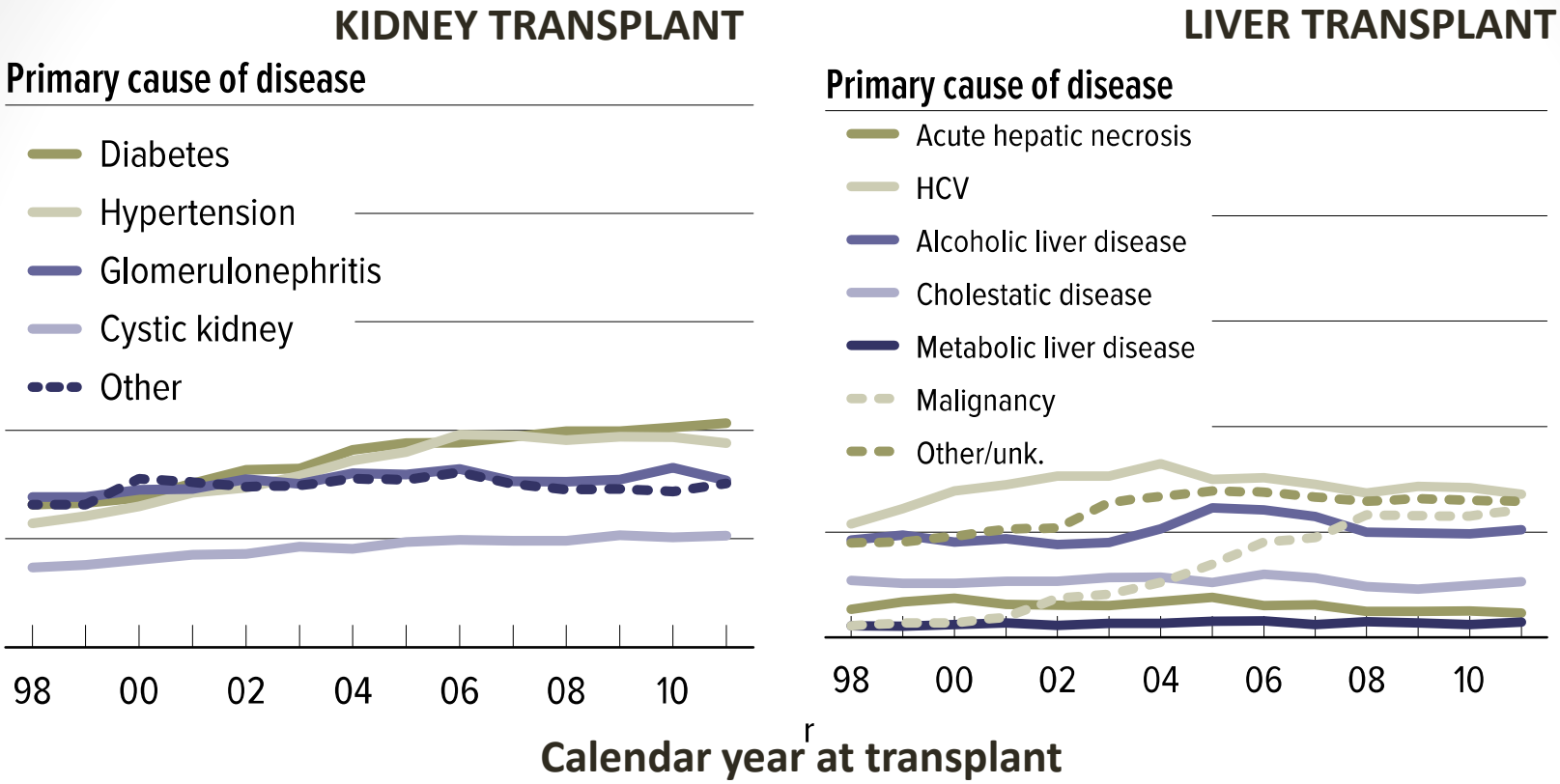
Italian Network of Population-Based Cancer Registries -AIRTUM



About 70% of the Italian population is covered by a PBCR

COVERAGE = 70 %

Primary causes of diseases for kidney or liver transplant : USA, 1998-2010



Anti-rejection immunosuppressive drugs

METHODS 1- the role of PBCR

Design: ongoing, retrospective, cohort study of 2832 recipients of liver transplant from 9 Italian centres -1985 to 2014.

Follow-up and outcomes:

- cancer diagnosis: clinical charts, **record linkage with population-based cancer registries (based on the residence of recipients)**
- Vital status: clinical charts, administrative docs, death certificates

Exclusion criteria:

- *At enrolment*:
  - Age less than 18 years
  - Individuals with a history of cancer preceding transplant (except non-melanoma skin cancer and hepatocellular carcinoma in liver transplants).
- *At analysis*:
  - Cancer diagnosed within 30 days after transplant
  - Follow-up less than 30 days.

Examined variables:

- Demographic (e.g., sex, age, birthplace and residence)
- Life styles (e.g., alcohol, smoking)
- Related to transplantation (e.g., baseline disease, immunosuppressive therapy)
- Related to the neoplasm (e.g., histology, date of diagnosis, treatment, outcome)

METHODS-2 the role of PBCR

Standardized Incidence Ratio (SIR and 95% CI)

The number of observed incident cancer cases was compared with the expected one computed from sex- and age-specific incidence rates from all Italian cancer registries as published by the International Agency for Cancer (IARC) ***Cancer Incidence in Five Continents volumes***

Person-years (PYs)

- from 30 days after the date of transplantation to the date of the last follow-up visit, the date of death, the date of tumour diagnosis or the end date of the study (December 31, 2016), whichever came first.

The Liver Transplant Cohort, n=2832

- **Females:** 716 (25.3%)
- **Median age at transplant:** 53.5 yrs (IQR: 46.0-59.3)
- **Total follow-up:** 18642 Person Years (PYs)
- **Median follow-up:** 4.7 years (IQR: 2.3-8.9)

- **Prevalence of infections**: HCV-pos: (49.9%), HBV-pos (42.1%)
- **Heavy alcohol consumption:** 26.7%
- **Liver cancer as a cause of transplant**: 952 (34.4%)

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Risk of virus and non-virus related malignancies following immunosuppression in a cohort of liver transplant recipients. Italy, 1985–2014

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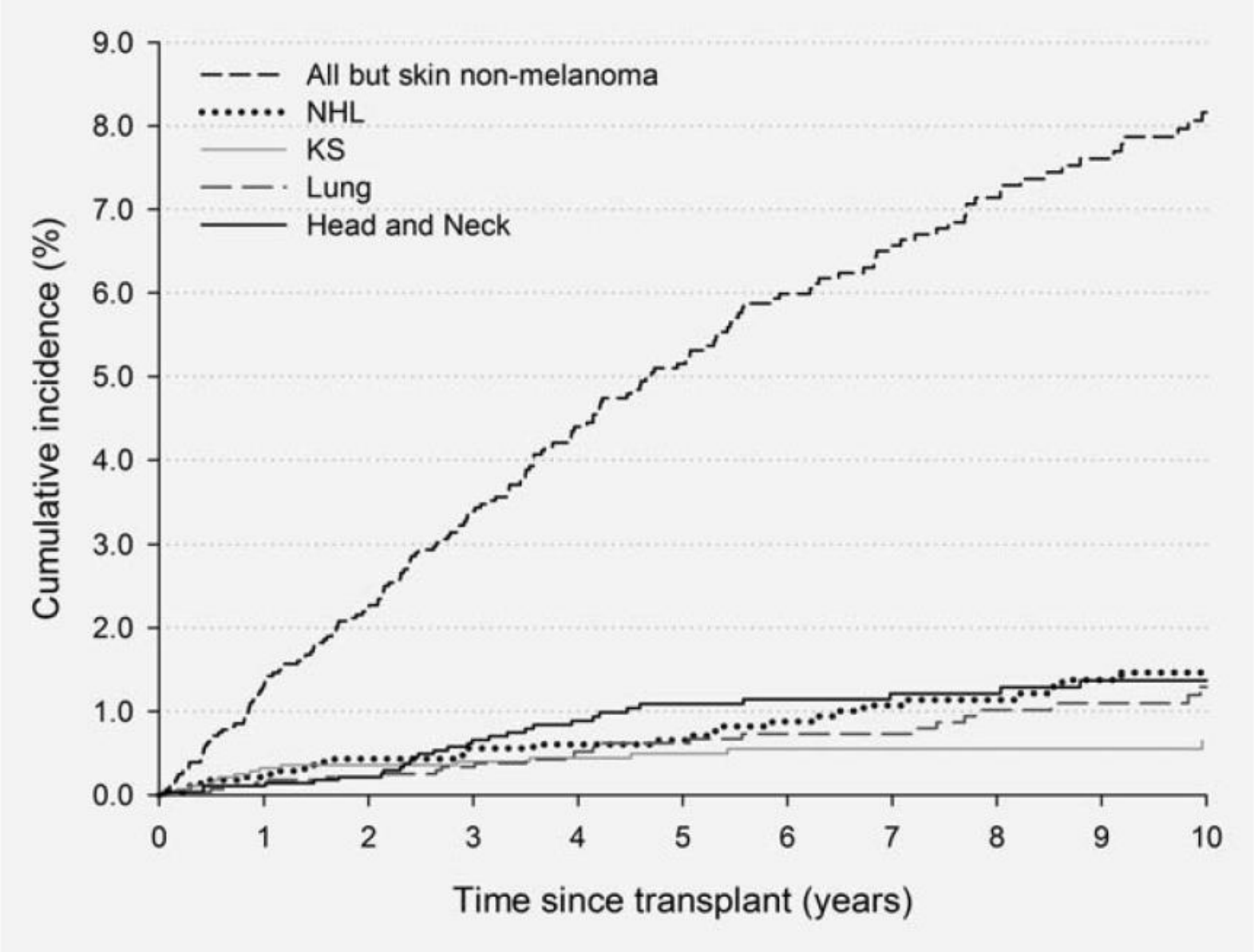
Figure 1. Cumulative cancer incidence by time since liver transplantation and cancer type. Abbreviations: KS: Kaposi's sarcoma; NHL: non-Hodgkin lymphoma



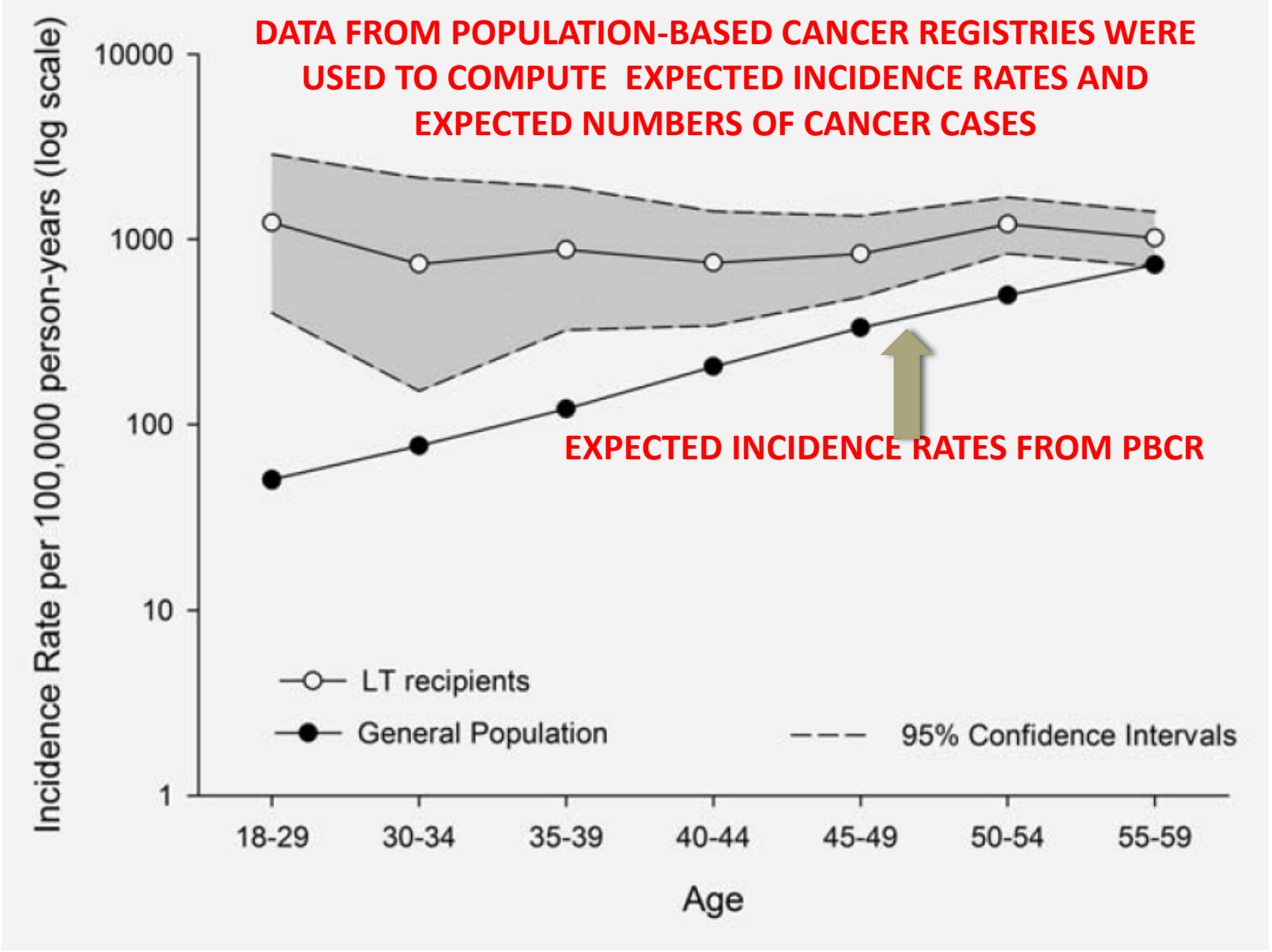


Figure 2. Age-specific incidence rates for *de novo* malignancies observed in liver transplant (LT) recipients and in the Italian general population.

PBCR=Exp. N° of cases

Table 2. SIRs and 95% CIs for *de novo* malignancies in liver transplant recipients

Type/site	ICD-10 codes	Total		
		Obs.	Exp.	SIR (95% CI)
Virus-related malignancies				
Non-Hodgkin lymphoma	C82–85, C96	31	4.4	7.1 (4.8–10.1)***
Kaposi's sarcoma	C46	15	0.3	53.6 (30.0–88.5)***
Liver	C22	6	5.5	1.1 (0.4–2.4)
Cervix uteri	C53	3	0.6	5.4 (1.1–15.8)*
Hodgkin lymphoma	C81	2	0.6	3.5 (0.4–12.6)
Virus-unrelated malignancies				
Head and neck	C00–14, C30–32	34	7.7	4.4 (3.1–6.2)***
Bronchus and lung	C34	28	19.4	1.4 (1.0–2.1)
Colon–rectum	C18–20	21	15.9	1.3 (0.8–2.0)
Bladder	C67, D09.0, D30.3, D41.4	9	11.4	0.8 (0.4–1.5)
Esophagus	C15	8	1.2	6.7 (2.9–13.3)***
Stomach	C16	7	5.7	1.2 (0.5–2.5)
Skin melanoma	C43	7	2.7	2.6 (1.0–5.3)*
Thyroid gland	C73	5	2.3	2.2 (0.7–5.0)
Breast female	C50	4	8.6	0.5 (0.1–1.2)
Kidney	C64	4	4.2	1.0 (0.3–2.5)
Pancreas	C25	3	3.3	0.9 (0.2–2.6)
Leukemia	C91–95	3	2.9	1.0 (0.2–3.0)
Prostate	C61	2	14.0	0.1 (0.0–0.5)***
Testis	C62	2	0.4	5.2 (0.6–18.7)
Adrenal gland	C74	2	0.1	22.9 (2.8–82.7)**
Unspecified sites	C76–C80	5	1.9	2.6 (0.8–6.0)
Skin non-melanoma	C44	50	18.3	2.7 (2.0–3.6)***
All lymphohematopoietic malignancies[1]	C81–96	37	9.6	3.8 (2.7–5.3)***
All solid tumors but skin non-melanoma[1,2]		149	112.6	1.3 (1.1–1.6)***
All but skin non-melanoma[1,2]		199	117.5	1.7 (1.5–1.9)***
All[1,2]		246	136.5	1.8 (1.6–2.0)***

CONCLUSION

What's new?

Liver transplantation often requires long-term immunosuppressive therapy, which increases the risk of certain infections and malignancies. The extent to which chronic immunosuppressant use impacts cancer risk following liver transplantation, however, remains unclear. In this multicenter cohort study in Italy, liver transplant recipients had an overall 1.8-fold higher cancer risk compared with the general population. Risk was elevated for virus-related malignancies, as well as for several cancers not associated with viral infections, including cancers of the head and neck, esophagus, and adrenal gland. The findings support further investigation into the prevention and early detection of cancer in liver transplant recipients.

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- THE AVAILABILITY OF DATA FROM PBCR ALLOWED US TO IMPROVE COMPLETENESS, ACCURACY AND RISKS OF CANCERS ASSOCIATED WITH IATROGENIC IMMUNE DEPRESSION FOLLOWING LIVER TRANSPLANT

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