Alcohol rehabilitation and cancer risk: a nationwide hospital cohort study in France

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Summary

Background Even though alcohol consumption is an established risk factor for cancer, evidence regarding the effect of a reduction or cessation of alcohol consumption on cancer incidence is scarce. Our main study aim was to assess the effect of alcohol rehabilitation and abstinence on cancer incidence in people with alcohol dependence.

Methods We conducted a nationwide hospital retrospective cohort study which included all adults residing in mainland France and discharged in 2018–21. Multivariable Cox proportional hazards models were used to estimate the effect of rehabilitation treatment at hospital or a history of abstinence versus alcohol dependence without rehabilitation or abstinence on the risk for incident alcohol-associated cancers by sex, controlled for potential confounding risk factors.

Findings 10 260 056 men and 13 739 369 women were discharged from French hospitals in 2018–21. Alcohol dependence was identified in 645 720 (6·3%) men and 219 323 (1·6%) women. Alcohol dependence was strongly related to alcohol-associated cancer sites in both sexes (hepatocellular carcinoma and oral, pharyngeal, laryngeal, oesophageal, and colorectal cancers), except for breast cancer. Rehabilitation treatment or abstinence was associated with significantly lower risks compared with alcohol dependence without rehabilitation or abstinence (adjusted hazard ratios: 0·58, 99·89% CI 0·56–0·60 in men and 0·62, 0·57–0·66 in women). Relative risk reductions were significant for each alcohol-associated cancer site in both sexes and supported by all subgroup and sensitivity analyses.

Interpretation Our study results support the clear benefits of alcohol rehabilitation and abstinence in reducing the risk for alcohol-associated cancers. As only two in five patients with alcohol dependence were recorded with a history of rehabilitation treatment or abstinence, a large untapped potential exists for reducing cancer incidence.

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Introduction

Alcohol consumption is linked to multiple diseases and injuries,[1] including several cancer sites: oral, pharyngeal, laryngeal, oesophageal, liver (hepatocellular), colorectal, and female breast cancers.[2] The burden of alcohol-attributable cancer is substantial and accounted for 4·1% (95% CI 3·1–5·3) of all new cases of cancer globally in 2020.[3] Men accounted for approximately three-quarters of alcohol-attributable cancer cases due to their higher average alcohol consumption.[3]

A reduction or cessation of alcohol consumption should result in a reduction in the burden of alcohol-attributable cancer. In 2023, the International Agency for Research on Cancer (IARC) convened an International Expert Working Group to review published studies and evaluate the strength of epidemiological and mechanistic evidence on the potential for alcohol reduction or cessation to reduce alcohol-attributable cancer risk.[4] They found "sufficient evidence" for only two cancer sites (oral and oesophageal cancers), and "limited evidence" or "inadequate evidence" for other alcohol-attributable cancer sites. Overall, few studies exist on this topic, and even fewer high-quality studies with sufficient statistical power and adequate control for tobacco smoking as the main confounder.

The French National Hospital Discharge database offers a unique opportunity to fill some of these research gaps, especially given that the average annual level of adult alcohol consumption per capita in France (11·0 L of pure alcohol) was over twice the global average (5·3 L) in 2018–20.[5] Accordingly, a large number of patients with alcohol dependence—ie, the most severe form of alcohol use disorders[6]—are diagnosed and cared for in acute care or specialised hospitals in France.[7] In addition, all patients diagnosed with cancer are treated at hospital.[8] Our study aim was to test two main hypotheses for alcohol-associated cancers, overall and by cancer site: (1) alcohol dependence is associated with an increased risk compared with no alcohol dependence; (2) rehabilitation treatment or a history of abstinence is associated with a decreased risk compared with alcohol dependence without rehabilitation or abstinence.

Methods

Study design and participants

The data source for this retrospective cohort study was the French National Hospital Discharge (Programme de Médicalisation des Systèmes d'Information) database, which contains all billing claims for public and private

Research in context

Evidence before this study

In 2023, the International Agency for Research on Cancer (IARC) finalised its proceedings on the evidence of the effect of a reduction or cessation of alcohol consumption on alcohol-associated cancer risks, involving a comprehensive search of all published literature on this topic with no limits of language or time, and found "sufficient evidence" that a reduction or cessation of alcohol consumption reduces the risks for oral and oesophageal cancers, "limited evidence" for laryngeal, colorectal, and breast cancer risks, and "inadequate evidence" for pharyngeal and liver cancer risks. There is little evidence available on the role of alcohol reduction or cessation in reducing cancer risks. Moreover, there are almost no studies—and therefore no evidence—on the role of rehabilitation and abstinence in reducing cancer risks for people with alcohol dependence and heavy drinking. However, this evidence is crucial for policy makers to inform targeted interventions and policies aimed at cancer prevention.

Added value of this study

Using a representative large cohort of all 25·3 million adults discharged from French hospitals between 2018 and 2021, we expectedly found a strong association between alcohol dependence and the risk for each alcohol-associated cancer site in both sexes, except for breast cancer. Rehabilitation treatment at hospital or a history of abstinence was associated with large benefits among patients with alcohol dependence, with about 40% relative reductions in the risk for alcohol-associated cancers in both sexes. Relative risk reductions were significant for each cancer site (hepatocellular carcinoma and oral, pharyngeal, laryngeal, oesophageal, colorectal, and breast cancer) and in all socioeconomic groups. Relative reductions in the risk for alcohol-associated cancers were even higher in patients having only a recorded history of abstinence compared with those receiving rehabilitation treatment at hospital, supporting that the benefits of alcohol reduction or cessation increase over time.

Implications of all the available evidence

Alcohol rehabilitation, which is linked to at least temporary reduction or cessation of alcohol consumption, was associated with a substantially lower risk in incidence in alcohol-associated cancer sites. Unfortunately, this intervention was only given to a minority of patients in French hospitals. To prevent future cancers, alcohol rehabilitation should be offered and used more widely.

acute, post-acute, and psychiatric day-case or inpatient hospital admissions in France on a 10-year rolling basis. The standardised discharge summary includes: patient demographics (sex, age at entry, postal code of residency linked to the 2015 update of a validated area deprivation index[9]); primary and associated discharge diagnosis codes according to the WHO International Classification of Diseases, 10th revision, French version (ICD-10-FR); medical procedures performed; entry and discharge dates; and in-hospital death. Using unique anonymous identifiers, medical information can be prospectively assessed over time for each individual patient from his or her multiple hospital admissions.[10]

We included all adult patients aged 20 years and older, residing in mainland France, who were discharged between Jan 1, 2018, and Dec 31, 2021. We excluded all patients discharged with any cancer diagnosis other than non-melanoma skin cancer in the preceding 5 years (between Jan 1, 2013, and Dec 31, 2017).[11] In addition, we excluded patients recorded with genital cancers and mismatch on sex in 2018–21. The full coding dictionary of the study is provided with supporting references in the appendix (p 7).

See Online for appendix

The study complies with French laws for secondary analyses of the French National Hospital Discharge database (reference methodology MR-005).[12] The approval of an Institutional Review Board was not required because the national discharge database is fully anonymous. For the same reason, informed consent was not possible and not required.

Procedures

Alcohol-associated cancer was identified at the first diagnosis record of hepatocellular carcinoma (C22.0) or cancers of the oral cavity (C01–C06), oropharynx (C09–C10), hypopharynx (C12–C13), larynx (C32), oesophagus (C15), colon (C18), rectum (C19–C20), or female breast (C50) in 2018–21.[2,11] To account for possible records of overlapping or second cancer sites over 4 years and double counting of patients in several cancer sites, we also assessed the overall risks for upper aerodigestive tract cancer (oral, oropharynx, hypopharynx, larynx, or oesophagus cancers),[13] colorectal cancer,[2] and any alcohol-associated cancer.

All cancer risk factors were assessed from 2013 to 2021, and, if applicable, before or at first diagnosis record of alcohol-associated cancer in 2018–21. Alcohol dependence was identified by respective ICD-10-FR codes (F10.2–F10.4, Z50.2) or selected via wholly alcohol-attributable diseases (E24.4, F10.5–F10.9, G31.2, G62.1, G72.1, I42.6, K29.2, K70, K85.2, K86.0).[10] This extended definition of alcohol dependence followed a preliminary analysis showing that patients recorded with wholly alcohol-attributable disease had usually been recorded with alcohol dependence in the past (appendix p 11). Among patients with alcohol dependence, rehabilitation treatment or a history of abstinence was identified at first use of rehabilitation services at hospital (Z50.2) and otherwise by any recorded history of abstinence (F10.20–F10.23). To avoid potential bias of reverse causation in patients newly diagnosed with cancer,

	Men			Women		
	All (n=10 260 056)	Alcohol rehabilitation or a history of abstinence (n=245 550)	Alcohol dependence without rehabilitation or abstinence (n=400 170)	All (n=13 739 369)	Alcohol rehabilitation or a history of abstinence (n=87 723)	Alcohol dependence without rehabilitation or abstinence (n=131 600)
Age, years*	57 (42–69)	52 (43–62)	59 (48–69)	53 (35–70)	54 (44–64)	60 (48–70)
Area deprivation index quintile						
Q5 (most deprived)	2 056 645 (20·0%)	59 944 (24·4%)	101 366 (25·3%)	2 726 260 (19·8%)	19 777 (22·5%)	32 902 (25·0%)
Q4	2 134 927 (20·8%)	56 114 (22·9%)	92 696 (23·2%)	2 782 621 (20·3%)	19 011 (21·7%)	29 147 (22·1%)
Q3	2 104 801 (20·5%)	50 218 (20·5%)	80 058 (20·0%)	2 794 106 (20·3%)	18 173 (20·7%)	25 662 (19·5%)
Q2	2 029 401 (19·8%)	44 066 (17·9%)	69 630 (17·4%)	2 737 158 (19·9%)	16 157 (18·4%)	23 079 (17·5%)
Q1 (least deprived)	1 934 282 (18·9%)	35 208 (14·3%)	56 420 (14·1%)	2 699 224 (19·6%)	14 605 (16·6%)	20 810 (15·8%)
Residency covered by a cancer registry	2 281 552 (22·2%)	55 986 (22·8%)	90 999 (22·7%)	2 997 780 (21·8%)	19 870 (22·7%)	28 486 (21·6%)
Previous hospital admission(s) in 2013–17	5 818 274 (56·7%)	194 208 (79·1 %)	283 452 (70·8%)	8 035 268 (58·5%)	72 036 (82·1%)	96 557 (73·4%)
Any cancer risk factor	2 206 925 (21·5%)	181 601 (74·0%)	232 276 (58·0%)	2 556 165 (18·6%)	59 946 (68·3%)	69 100 (52·5%)
Tobacco smoking	1 124 487 (11·0%)	161 693 (65·8%)	178 193 (44·5%)	810 822 (5·9%)	50 295 (57·3%)	48 994 (37·2%)
Chronic bronchitis without smoking record	93 355 (0·9%)	2556 (1·0%)	6631 (1·7%)	67 276 (0·5%)	795 (0·9%)	1664 (1·3%)
BMI ≥40 kg/m²	172 380 (1·7%)	7821 (3·2%)	13 651 (3·4%)	432 596 (3·1%)	4645 (5·3%)	6911 (5·3%)
BMI 30 to <40 kg/m²	834 398 (8·1%)	32 271 (13·1%)	58 360 (14·6%)	1 141 992 (8·3%)	11 880 (13·5%)	16 969 (12·9%)
Any hereditary cancer syndrome	17 630 (0·2%)	556 (0·2%)	1003 (0·3%)	19 704 (0·1%)	208 (0·2%)	335 (0·3%)
Cancer survivor (>5 years)	170 112 (1·7%)	4847 (2·0%)	10 260 (2·6%)	246 093 (1·8%)	2685 (3·1%)	4523 (3·4%)
Transplant status†	53 017 (0·5%)	2527 (1·0%)	3700 (0·9%)	35 070 (0·3%)	662 (0·8%)	993 (0·8%)
HIV positive	50 273 (0·5%)	2279 (0·9%)	3963 (1·0%)	27 839 (0·2%)	508 (0·6%)	896 (0·7%)
Chronic hepatitis C	35 265 (0·3%)	7132 (2·9%)	6884 (1·7%)	23 807 (0·2%)	2213 (2·5%)	2062 (1·6%)
Chronic hepatitis B	18 670 (0·2%)	1409 (0·6%)	2069 (0·5%)	17 730 (0·1%)	350 (0·4%)	433 (0·3%)
Human papillomavirus positive	1393 (0·0%)	41 (0·0%)	67 (0·0%)	21 603 (0·2%)	242 (0·3%)	198 (0·2%)
Hospitalisation for COVID-19	252 296 (2·5%)	6982 (2·8%)	12 502 (3·1%)	239 683 (1·7%)	2150 (2·5%)	3594 (2·7%)
In-hospital death in 2018–21	584 967 (5·7%)	26 135 (10·6%)	64 195 (16·0%)	536 267 (3·9%)	7067 (8·1%)	16 903 (12·8%)

Data are median (IQR) or n (%). *In January, 2018. †Transplant recipients included 65 010 (73·8%) patients with solid organ transplants (47 335 [53·7%] kidney; 10 327 [11·7%] liver; 6810 [7·7%] heart; 3696 [4·2%] lung; 1531 [1·7%] pancreas) and 8154 (9·3%) patients with bone marrow transplants (counts are not mutually exclusive).

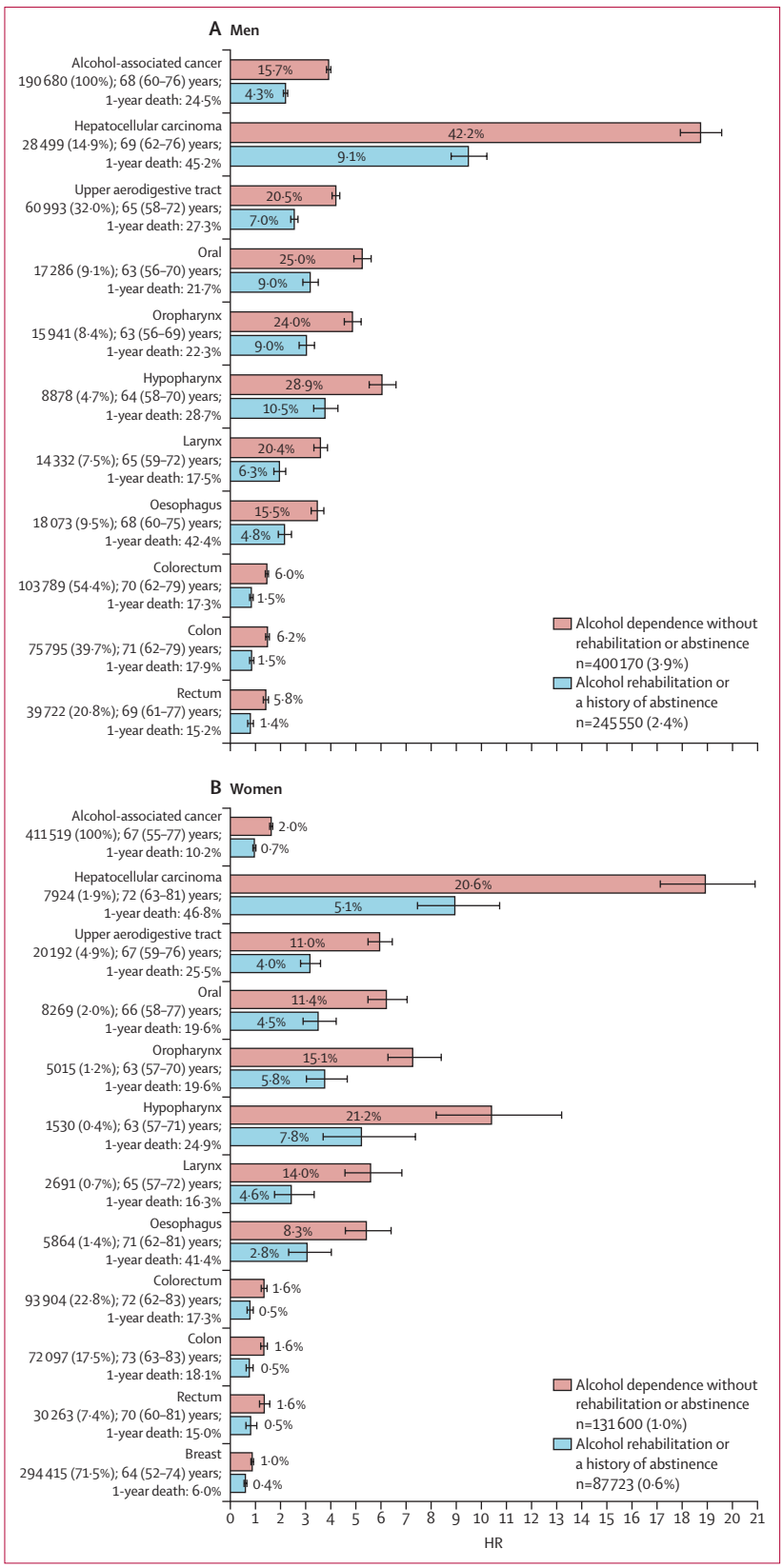
Table 1: **Hospital cohort characteristics, by sex and alcohol-dependence category**

rehabilitation treatment was ascertained strictly before the first diagnosis record of cancer in 2018–21. Examples of hospital records and alcohol exposure definitions are presented in the appendix (p 12).

Other cancer risk factors included tobacco smoking, obesity (BMI ≥30 kg/m²), any hereditary cancer syndrome,[14] cancer survivorship (>5 years), transplant status,[15] HIV infection, and chronic viral infections causally related to several cancer sites (chronic hepatitis C or B for hepatocellular carcinoma; human papillomavirus for oral and oropharynx cancers).[16] To limit residual confounding from unrecorded smoking status and past smoking in particular, we also assessed chronic bronchitis status in patients without smoking records.[17] To account for possible delays in genetic diagnosis, hereditary cancer syndromes were conservatively assessed over the whole study period. To account for competing mortality effects of the COVID-19 pandemic in vulnerable populations at risk for cancer, we recorded inpatient admissions for symptomatic COVID-19 in 2020–21.[18]

Statistical analysis

The effects of alcohol dependence categories (rehabilitation treatment or a history of abstinence *vs* alcohol dependence without rehabilitation or abstinence) on cancer risks were contrasted in multivariable Cox proportional hazards models. Age was used as the time-scale to estimate adjusted hazard ratios (HRs) and 99·89% CIs, with follow-up starting from Jan 1, 2018 (with left truncation) until first diagnosis record of cancer site (or category), in-hospital death, or last hospital discharge in 2018–21.[19] In patients lost to follow-up in 2018–21 and readmitted in 2022, the follow-up date was recorded as Dec 31, 2021. All models were stratified by area deprivation index quintile and residency in a territory covered by a cancer registry.[8] All covariates were controlled for using age-varying variables: the use of alcohol rehabilitation services at hospital, transplantation, and admission for symptomatic COVID-19 were identified at first record, and other cancer risk factors were considered in the risk set starting from Jan 1, 2018.



We did several sensitivity analyses to ascertain the potential benefits of alcohol rehabilitation or a history of abstinence on alcohol-associated cancer risk. First, we studied different population subgroups as defined by area deprivation index quintile, residency in a territory covered by a cancer registry, or previous hospital admission(s) in 2013–17. Second, we assessed the effects of rehabilitation treatment or a history of abstinence in patients recorded with wholly alcohol-attributable disease versus other patients only recorded with alcohol dependence. Third, we contrasted the effects of rehabilitation treatment versus a history of abstinence. Finally, we assessed the effects of alcohol dependence categories over the lifespan with use of third-order polynomials of age attained on Jan 1, 2018.

All significance tests were two-sided. To correct for multiple comparisons, we used a Bonferroni corrected α-threshold of 0·0011 (two alcohol dependence categories, 11 cancer sites by sex and breast cancer in women). The same correction was conservatively used in sensitivity analyses. All analyses were performed with SAS software, version 9.4.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Of the 49 175 541 adults residing in mainland France on Jan 1, 2018, 25 291 344 (51·4%) were discharged from acute, post-acute, or psychiatric hospitals in 2018–21. Of these, we excluded 1 291 767 (5·1%) patients discharged with a cancer diagnosis in 2013–17 and 152 patients recorded with genital cancers and a mismatch on sex in 2018–21.

Alcohol dependence was identified in 645 720 (6·3%) of 10 260 056 men and 219 323 (1·6%) of 13 739 369 women (table 1). Among patients with alcohol dependence, the proportions of patients with a record of rehabilitation treatment or a history of abstinence were similar across sexes (men: 245 550 [38·0%]; women: 87 723 [40·0%]). Of them, 141 682 (57·7%) men and 48 167 (54·9%) women

Figure 1: **Alcohol dependence and cancer risks, by sex, cancer site or category, and alcohol dependence category**

(A) Men (n=10 260 056). (B) Women (n=13 739 369). Figure shows the effects of alcohol dependence, with and without rehabilitation or abstinence, for each cancer risk (newly diagnosed at hospital in 2018–21 without any cancer recorded in 2013–17). Each cancer risk is described by the number of incident cases recorded in 2018–21 (percentage of the total number of alcohol-associated cancer cases); median (IQR) age at first diagnosis; and 1-year in-hospital mortality rate following diagnosis. The proportions of patients recorded with and without rehabilitation or abstinence are reported overall (key) and for each cancer risk (bars). Adjusted HRs and 99·89% CIs were estimated in multivariable Cox models. The reference group (HR=1) is constituted by adults without any alcohol dependence record at hospital in 2013–21. Error bars show 99·89% CIs. HR=hazard ratio.

had used rehabilitation services at hospital with a median follow-up of 3·8 years (IQR 1·4–6·2) since the first treatment in 2013–21, and other patients were only recorded with a history of abstinence in 2013–21. The median length of inpatient stay was 13 days (IQR 8–25) for rehabilitation treatment. Alcohol dependence categories were associated with higher area deprivation, previous hospital admission(s) in 2013–17, any cancer risk factor, and in-hospital death in 2018–21 in both sexes (table 1). Patients identified with rehabilitation treatment or a history of abstinence had the highest rates of cancer risk factors, including tobacco smoking and chronic hepatitis C infection, in both sexes.

Overall, 602 199 (2·5%) patients were newly diagnosed in 2018–21 with cancer sites identified as being causally related to alcohol consumption. Alcohol-associated cancers included heterogeneous cancer sites, with sites differing in frequency, sex ratio, median age at diagnosis, and prognosis (description provided in the label of each cancer risk in figure 1). Hepatocellular carcinoma and upper aerodigestive tract cancers were mostly diagnosed in men (28 499 [78·2%] of 36 423 and 60 993 [75·1%] of 81 185, respectively) and were associated with poor prognosis (overall 1-year in-hospital mortality rate of 45·5% [16 583 of 36 423] and 26·9% [21 807 of 81 185], respectively). Colorectal and female breast cancers targeted by national screening programmes accounted for the majority of alcohol-associated cancers (colorectal cancer in men: 103 789 [54·4%] of 190 680; colorectal and breast cancers in women: 385 182 [93·6%] of 411 619) and were associated with better prognosis (overall 1-year in-hospital mortality rate of 17·3% [34 195 of 197 693] for colorectal cancer and 6·0% [17 700 of 294 415] for breast cancer).

Alcohol dependence was more frequently recorded in men than in women for all alcohol-associated cancer sites and categories: hepatocellular carcinoma (men: 14 621 [51·3%]; women: 2036 [25·7%]), upper aerodigestive tract cancers (men: 16 743 [27·5%]; women: 3031 [15·0%]), and colorectal cancer (men: 7795 [7·5%]; women: 1958 [2·1%]; total proportions shown in the two bars per cancer risk in figure 1). In multivariable Cox models, alcohol dependence without any hospital record of rehabilitation treatment or abstinence in 2013–21 was a major risk factor for all alcohol-associated cancers in both sexes, except for breast cancer (first bar per cancer risk in figure 1; the full results of each Cox model are presented by cancer site or category in appendix pp 14–25).

Rehabilitation treatment or a history of abstinence was associated with lower risks compared with alcohol dependence without rehabilitation or abstinence (second bar per cancer risk in figure 1 and appendix pp 14–25), with about 40% relative reductions in the risk for alcohol-associated cancer (adjusted HR 0·58, 99·89% CI 0·56–0·60 in men and 0·62, 0·57–0·66 in women; table 2). Relative risk reductions were significant for each cancer site or category in both sexes (table 2).

	Men		Women	
	HR (99·89% CI)	p value	HR (99·89% CI)	p value
Alcohol-related cancer	0·58 (0·56–0·60)	<0·0001	0·62 (0·57–0·66)	<0·0001
Hepatocellular carcinoma	0·52 (0·48–0·56)	<0·0001	0·49 (0·41–0·59)	<0·0001
Upper aerodigestive tract	0·63 (0·60–0·67)	<0·0001	0·56 (0·49–0·64)	<0·0001
Oral cavity	0·63 (0·57–0·70)	<0·0001	0·59 (0·48–0·72)	<0·0001
Oropharynx	0·65 (0·59–0·72)	<0·0001	0·55 (0·44–0·69)	<0·0001
Hypopharynx	0·65 (0·57–0·74)	<0·0001	0·53 (0·37–0·75)	<0·0001
Larynx	0·57 (0·50–0·64)	<0·0001	0·46 (0·33–0·64)	<0·0001
Oesophagus	0·64 (0·57–0·73)	<0·0001	0·59 (0·44–0·79)	<0·0001
Colorectum	0·59 (0·54–0·65)	<0·0001	0·60 (0·51–0·72)	<0·0001
Colon	0·59 (0·53–0·66)	<0·0001	0·58 (0·48–0·72)	<0·0001
Rectum	0·58 (0·50–0·68)	<0·0001	0·62 (0·46–0·84)	<0·0001
Female breast	..	..	0·72 (0·65–0·81)	<0·0001

Table shows adjusted HR and 99·89% CI of rehabilitation treatment or a history of abstinence versus alcohol dependence without rehabilitation or abstinence estimated in a multivariate Cox model for each cancer risk (the full results of multivariate Cox models are presented in appendix pp 12–23). HR=hazard ratio.

Table 2: **Cancer risk reduction with alcohol rehabilitation or abstinence, by sex and cancer site or category**

The benefits of alcohol rehabilitation and abstinence on alcohol-associated cancer risk were supported by all subgroup and sensitivity analyses. Relative reductions in the risk for alcohol-associated cancer were similar in population subgroups defined by area deprivation index quintile or residency in a territory covered by a cancer registry (appendix p 26).

Compared with 13 853 542 patients with previous hospital admission(s) in 2013–17, 10 145 883 patients newly discharged in 2018–21 were, as expected, younger (median age of 51 years [IQR 35–65] *vs* 58 years [40–71] on Jan 1, 2018) and less comorbid (alcohol dependence: 218 790 [2·2%] *vs* 646 253 [4·7%]; any cancer risk factor: 1 219 629 [12·0%] *vs* 3 543 461 [25·6%]). Alcohol dependence without rehabilitation or abstinence was similarly associated with increased risks for alcohol-associated cancer in both population subgroups (appendix pp 27–28). In contrast, relative risk reductions with rehabilitation or abstinence were even higher in patients newly discharged in 2018–21 (adjusted HR 0·35, 99·89% CI 0·31–0·38 in men and 0·38, 0·32–0·46 in women) compared with those with previous hospital admission(s) in 2013–17 (0·70, 0·67–0·73 in men and 0·73, 0·67–0·79 in women).

Patients recorded with wholly alcohol-attributable disease (237 842 [36·8%] men; 77 121 [35·2%] women) were at increased risk for alcohol-associated cancer compared with other patients recorded with alcohol dependence (407 878 [63·2%] men; 142 202 [64·8%] women), although the benefits of rehabilitation and abstinence on alcohol-associated cancer risk were similar in both patient groups (men: adjusted HR 0·57, 99·89% CI 0·54–0·60 and 0·53, 0·50–0·57, respectively; women: 0·66, 0·60–0·73 and 0·61, 0·55–0·68, respectively; appendix p 29).

We also found that relative reductions in the risk for alcohol-associated cancer were even higher in patients

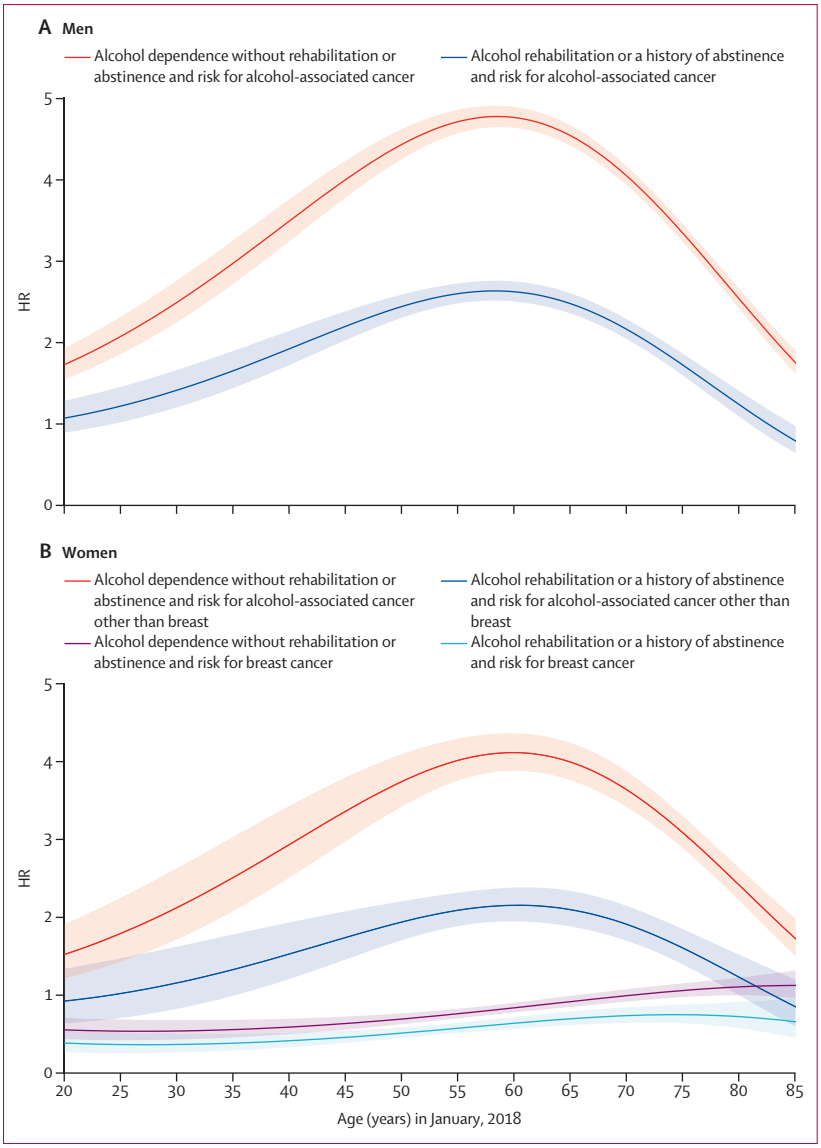


Figure 2: **Cancer risk in people with alcohol dependence over the lifespan, by sex and alcohol dependence category**

(A) Men (n=10 260 056). (B) Women (n=13 739 369). Figure shows the effects of alcohol dependence, with and without rehabilitation or abstinence, on the risk for alcohol-related cancer by sex over the lifespan. Adjusted HRs and 99·89% CIs were estimated with use of a third-order polynomial of age attained in January, 2018 in multivariable Cox models. The reference group (HR=1) is constituted by adults without any alcohol dependence record at hospital in 2013–21. Shaded areas show 99·89% CIs. HR=hazard ratio.

having only a recorded history of abstinence (adjusted HR 0·51, 99·89% CI 0·48–0·54 in men and 0·57, 0·52–0·62 in women) compared with those receiving rehabilitation treatment at hospital in 2013–21 (0·68, 0·64–0·71 in men and 0·67, 0·61–0·74 in women; appendix p 31).

With the exception of breast cancer, we found that rehabilitation treatment or a history of abstinence was associated with decreasing risks for alcohol-associated cancer over the lifespan, with maximum benefits seen in middle-aged patients (figure 2).

Discussion

In this nationwide hospital cohort study, we found a marked association of alcohol dependence with alcohol-associated cancers after controlling for potential confounding risk factors. Our study results also support the benefits of alcohol rehabilitation and abstinence in reducing the risk for alcohol-associated cancers, overall and for each cancer site.

The study results corroborate and expand on previous studies, which were limited to cancer risks associated with different levels of drinking recorded at cohort inception.[1–3,20] Alcohol dependence is strongly associated with heavy drinking (>60 g of pure ethanol per day, the equivalent of more than six alcoholic drinks per day)[21,22] and thus—with the exception of female breast cancer—has predictably been associated in this study with risks at the high end of the exponential dose–response curve for alcohol-associated cancers.[1,3,20] Alcohol rehabilitation or abstinence should be associated with a decreased risk for any alcohol-associated cancer but the evidence is scarce and limited,[4] while a recent study on patterns of drinking over the life course suggested that heavy drinking remains associated with higher risks for alcohol-associated cancer despite alcohol reduction or cessation.[23]

Several potential limitations of our study based on hospital billing claims data should be acknowledged. One potential limitation relates to possible misclassifications of cancer sites. Cancers treated before 2013 could not be identified in 2013–21 hospital discharge databases and long-term relapses might have been misclassified as new cancer cases in 2018–21. To limit misclassification bias, all study results were controlled for any record of cancer survivorship (>5 years) and we found strong associations of cancer survivorship with the risks for upper aerodigestive tract and colorectal cancers, and even more so with the risk for female breast cancer (appendix pp 16, 22, 25).

Furthermore, colorectal and female breast cancers are targeted by national screening programmes in France. Screening programmes might be associated with over-recording of cancer diagnoses (C codes) for neoplasms screened at in situ or unknown behaviour stages (D codes) and overdiagnosis of indolent cancers that would not have progressed to a symptomatic stage before death.[24] Assuming that patients with alcohol dependence are less likely to participate in voluntary cancer screening programmes compared with others, the strength of the association with alcohol dependence should decrease with increasing participation rates in population screening programmes (colorectal cancer: around 35%;[25] female breast cancer: around 50%[26]). Indeed, we found that alcohol dependence was associated with the risk for colorectal cancer but was no longer associated with the risk for female breast cancer, except after age 70 years (figure 2B). When we restricted our cancer definition to only include patients recorded with metastasis, we found that the strengths of association of alcohol dependence

significantly increased with the risk for metastatic colorectal or female breast cancers, while the benefits of rehabilitation treatment and abstinence were even larger (appendix pp 32–33).

Another potential limitation relates to possible under-recording of cancer risk factors in hospital billing claims data, resulting in a systematic underestimation of associated cancer risks. To limit coding bias and residual confounding, we assessed a large set of cancer risk factors that could be readily identified from all hospital records over a 9-year period. We found well known associations between tobacco smoking and the risk for each of the upper aerodigestive tract cancer sites (appendix pp 16–21) as well as between obesity and chronic hepatitis C or B infections and the risk for hepatocellular carcinoma (appendix p 15).[2] Given the associations of alcohol dependence with all cancer risk factors and tobacco smoking in particular, and the strengths of independent associations found between alcohol dependence and cancer risks in both sexes, overall and by population subgroups, we do not believe that the bias due to under-recorded cancer risk factors would be large. In addition, we set a uniform cohort entry date of Jan 1, 2018, to reduce possible bias from exposure durations based on the first hospitalisation record in 2013–21.

Finally, we need to discuss the potential limitations of our assessment of alcohol exposure via alcohol dependence, alcohol rehabilitation, and abstinence status from hospital discharge records. As indicated above, these assessments are indicators of heavy drinking, but the exact association cannot be quantified as the level of alcohol consumption cannot be assessed from ICD-10 diagnosis codes alone and the duration of exposure cannot be derived from a single discharge record. In particular, 116 173 (81·0%) of 143 424 patients identified with a history of abstinence had a single discharge record of abstinence status (F10.20–F10.23) in 2013–21. Accordingly, abstinence duration could not be assessed from repeated records over multiple hospital stays, although abstinence was likely achieved before 2013 in most patients as none were recorded with rehabilitation treatment at hospital over 2013–21. In addition, we might have missed outpatient interventions that have the same effectiveness as those provided by the hospital.[27] However, not having records of outpatient interventions would actually lead to an underestimation of the benefits of rehabilitation at hospital. Altogether, the study results support that the benefits of alcohol reduction or cessation increase over time as we found that relative reductions in the risk for alcohol-associated cancer were even higher in patients having only a recorded history of abstinence compared with those receiving rehabilitation treatment at hospital in 2013–21.

Overall, the study results point to a potent effect of alcohol rehabilitation and abstinence to reduce alcohol-associated cancer risks. While the hospital cohort study involved a large sample of the French adult population,[10] the study results were robust across sexes and in all other subgroup or sensitivity analyses, supporting high generalisability to the whole population. Accordingly, we might expect future editions of the *IARC Handbooks of Cancer Prevention*[28] to include more alcohol-associated cancer risks where there is sufficient evidence for a positive effect derived from reduction or cessation of alcohol consumption.[4]

Only 333 273 (38·5%) of 865 043 patients with alcohol dependence and discharged from French hospitals in 2018–21 had received rehabilitation treatment at hospital or were recorded with a history of abstinence in 2013–21. In 2007, the French Government aimed to improve hospital-based addiction care by implementing financial incentives that are all captured in this study.[29] However, for a variety of reasons including persisting stigma and a shrinking medical workforce,[18] the provision of rehabilitation services at hospital often remains limited to the most severe or comorbid patients with alcohol dependence. We found indeed that rehabilitation treatment at hospital or a history of abstinence were disproportionately recorded in older and more comorbid patients with previous hospital admission(s) in 2013–17 (appendix pp 27–28), although relative reductions in the risk for alcohol-associated cancer were much higher in patients newly discharged in 2018–21. Accordingly, the benefits of rehabilitation treatment should be expected to be larger if extended to an earlier stage of alcohol dependence. The results also suggest that observed reductions in alcohol-attributable cancer risk were similar across population subgroups defined by area deprivation index quintile, emphasising the importance of alcohol rehabilitation services for reducing health inequalities.

In conclusion, effective alcohol interventions are underused in French hospitals, as is the case elsewhere.[30] Screening for alcohol consumption at hospital, followed by brief interventions for hazardous drinking or with rehabilitation treatment for alcohol use disorders is a major step towards preventing many cancer cases.[31] In addition, delivering routine screening and outpatient interventions upstream in primary health care should also be considered.[27] However, considering the relatively high costs of all individual-level interventions, cancer prevention should start with the implementation of population-level strategies, which aim to reduce alcohol consumption and alcohol-attributable burden of disease, including cancer, across the entire population. These are WHO's so-called best buys—ie, raising taxes to make alcohol less affordable, reducing availability, and banning marketing.[32]

Contributors

MS conceptualised the study, had full access to all the hospital discharge data and verified the data, did the database management and statistical analyses on the secured platform of the Agence Technique de

l'Information Hospitalière, contributed to the interpretation of the data, and co-wrote the first draft of the paper. CF-B, MN, and FA contributed to the interpretation of the data and co-edited the drafts. In addition, FA accessed and verified the underlying data of the study. JR contributed to the interpretation of the data and co-wrote the first draft of the paper. All authors had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

The French National Hospital Discharge (Programme de Médicalisation des Systèmes d'Information) database cannot be shared publicly because of legal restrictions on sharing potentially re-identifying patient information. According to French laws for secondary analyses of the National Hospital Discharge database (reference methodology MR-005), data are available from the Agence Technique de l'Information Hospitalière (https://www.atih.sante.fr/acces-aux-donnees-pour-les-etablissements-de-sante-les-chercheurs-et-les-institutionnels) for researchers who meet all criteria for access to the database.

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