

| 2015 | DIET, NUTRITION, PHYSICAL ACTIVITY AND LIVER CANCER | | |
|------------------|---|---|---|
| | | DECREASES RISK | INCREASES RISK |
| STRONG EVIDENCE | Convincing | | Aflatoxins ¹ Alcoholic drinks ² Body fatness ³ |
| | Probable | Coffee | |
| LIMITED EVIDENCE | Limited – suggestive | Fish Physical activity ⁴ | |
| | Limited – no conclusion | Cereals (grains) and their products, non-starchy vegetables, fruits, peanuts (groundnuts), meat and poultry, salted fish, tea, green tea, glycaemic index, calcium and vitamin D supplements, vitamin C, water source, low fat diet | |
| STRONG EVIDENCE | Substantial effect on risk unlikely | | |

- 1 Foods that may be contaminated with aflatoxins include cereals (grains), as well as pulses (legumes), seeds, nuts and some vegetables and fruits.
- 2 Based on evidence for alcohol intakes above around 45 grams per day (about 3 drinks a day). No conclusion was possible for intakes below 45 grams per day. There is insufficient evidence to conclude that there is any difference in effect between men and women. Alcohol consumption is graded by the International Agency for Research on Cancer (IARC) as carcinogenic to humans (Group 1) [2].
- 3 Body fatness is marked by body mass index (BMI).
- 4 Physical activity of all types.

Summary of nested case-control and cohort studies - aflatoxins (any biomarker of exposure)

| Study description | Publications | No. Cases / Controls | RR (95% CI) | Contrast |
|---|----------------|---|---------------------|---|
| Community-based Cancer Screening Cohort, Taiwan | Wu 2009 [18] | 241 HCC 1052 controls | 1.54 (1.01-2.36) | AFB ₁ -albumin adducts above vs. below mean (59.8 fmol/mg) |
| | | | 1.76 (1.18-2.58) | Urinary AFB ₁ above vs. below mean (55.2 fmol/mL) |
| | Sun 2001 [19] | HBsAg carriers 75HCC 140 controls | 2.0 (1.1-3.7) | AFB ₁ -albumin adducts detectable vs. non-detectable |
| | Wang 1996 [20] | 56 HCC 220 controls | 1.6 (0.4-5.5) | Serum level aflatoxin-albumin detectable vs. non-detectable |
| | | | 3.8 91.1-12.8) | Urinary levels of aflatoxin high vs. low |
| Shanghai Cohort Study, China | Yuan 2006 [21] | 213 HCC 1087 controls | 3.25 (1.63-6.48) | Urinary aflatoxin biomarker positive vs. negative |
| | Qian 1994 [22] | 55 HCC 267 controls | 5.0 (2.1–11.8) | Any urinary aflatoxin biomarker vs. none |
| | Ross 1992 [23] | 22 HCC 110 controls | 2.4 (1.0–5.9) | Any urinary aflatoxin biomarker vs. none |
| Qidong Cohort, China | Sun 1999 [24] | 22 HCC 149 controls | 3.3 (1.2–8.7) | Urinary AFM ₁ detectable (above 3.6 ng/L) vs. non-detectable |
| Cohort Gov. Clinics, Taiwan | Yu 1997 [25] | HBsAg carriers 21 HCC 63 controls | 12.0 (1.2–117.4) | Both markers (urinary AFM ₁ and AFB ₁ -N7-guanine adducts) vs. none |
| | Chen 1996 [26] | HSsAg carriers 32 HCC 73 controls | 3.8 (1.0–14.5) | AFB ₁ -albumin adducts high vs. undetectable |

Abbreviations: AFB₁, aflatoxin B₁; AFM₁, aflatoxin M₁; HBsAg, hepatitis B surface antigen; HCC, hepatocellular carcinoma

Summary of CUP 2014 stratified dose-response meta-analysis - coffee

| Analysis | Increment | RR (95% CI) | I ² | No. Studies | No. Cases |
|--------------|-----------------|---------------------|----------------|-------------|-----------|
| MEN | Per one cup/day | 0.84 (0.78-0.90) | 21% | 3 | 766 |
| WOMEN | Per one cup/day | 0.91 (0.83-1.01) | 0% | 3 | 377 |

Summary of CUP 2014 stratified dose-response meta-analyses – alcohol

| Analysis | Increment | RR (95% CI) | I ² | No. Studies | No. Cases |
|---------------------------------------|--------------|---------------------|----------------|-------------|-----------|
| Incidence | Per 10 g/day | 1.12 (1.05-1.18) | 69% | 9 | 1,738 |
| Mortality | Per 10 g/day | 1.02 (1.01-1.03) | 0% | 5 | 3,912 |
| Men | Per 10 g/day | 1.03 (1.01-1.05) | 51% | 8 | 4,132 |
| Women | Per 10 g/day | 1.19 (1.04-1.35) | 12% | 4 | 637 |
| North America & Europe | Per 10 g/day | 1.08 (1.00-1.16) | 74% | 3 | 930 |
| Asia | Per 10 g/day | 1.04 (1.02-1.07) | 63% | 11 | 4,720 |

Summary of CUP 2014 meta-analyses and published pooled analysis – alcohol

| Analysis | Increment | RR (95% CI) | I ² | No. Studies | No. Cases | Factors adjusted for |
|--|----------------------|----------------------|----------------|----------------|--------------|--|
| CUP Liver Cancer SLR 2014 | Per 10 g/day | 1.04 (1.02-1.06) | 64% | 14 | 5,650 | |
| Pooled analysis of Japanese cohort studies [72] | Per 10 g/day (men) | 1.02 (1.004-1.04) | - | 4 | 605 | Geographical location, age, history of diabetes, smoking and coffee intake |
| | Per 10 g/day (women) | 1.11 (0.96-1.29) | - | 4 | 199 | |
| Liver Cancer SLR 2014 additional analysis: pooled analysis of Japanese cohort studies [72] comined with studies for the CUP* | Per 10 g/day | 1.04 (1.02-1.06) | 0% | 17 | 6,372 | |

**The Miyagi Cohort [74] was the only study in the pooled analysis of Japanese cohort studies that was also included in the Liver Cancer SLR 2014.*

Summary of CUP 2014 stratified dose-response meta-analyses – BMI

| Analysis | Increment | RR (95% CI) | I ² | No. Studies | No. Cases |
|------------------|-------------------------|---------------------|----------------|-------------|-----------|
| Incidence | Per 5 kg/m ² | 1.43 (1.19-1.70) | 84% | 8 | 11,530 |
| Mortality | Per 5 kg/m ² | 1.13 (1.00-1.28) | 43% | 4 | 2,543 |
| Men | Per 5 kg/m ² | 1.21 (1.02-1.44) | 84% | 8 | 11,180 |
| Women | Per 5 kg/m ² | 1.21 (1.10-1.33) | 11% | 4 | 2,337 |
| Europe | Per 5 kg/m ² | 1.59 (1.35-1.87) | 42% | 4 | 588 |
| Asia | Per 5 kg/m ² | 1.18 (1.04-1.34) | 60% | 7 | 12,520 |

Summary of CUP 2014 meta-analysis and published pooled analyses – BMI

| Analysis | Increment | RR (95% CI) | I ² | No. Studies | No. Cases | Factors adjusted for |
|--|---|------------------|----------------|-------------|------------|--|
| CUP Liver Cancer SLR 2014 | Per 5 kg/m ² | 1.30 (1.16-1.46) | 78% | 12 | 14,311 | |
| Asia-Pacific Cohort Studies Collaboration [99] | ≥25 vs. 18.5–22.9 kg/m ² | 1.27 (0.93-1.74) | - | 44 | 420 deaths | Age, sex, study, alcohol, blood pressure, smoking, serum cholesterol and diabetes |
| Prospective Studies Collaboration [100] | Per 5 kg/m ² | 1.47 (1.26-1.71) | - | 57 | 422 deaths | Study, baseline age and smoking |
| Asia-Pacific Cohort Studies Collaboration [101] | 30–60 vs. 18.5–24.9 kg/m ² | 1.10 (0.63-1.91) | - | 39 | 774 | Age, smoking |
| | Per 5 kg/m ² | 1.11 (0.63-1.91) | - | | | |
| European cohorts [102] | HvL quintile (median) BMI 31.3 vs. 20.7 kg/m ²) | 1.92 (1.23-2.96) | - | 7 | | Age, smoking status and BMI, stratified by birth years, sex and sub-cohorts, and corrected for regression dilution ratio |