Supplementary Table 1 | Statins: clinical studies mostly evaluating cancer as a secondary outcome of interest beyond cardiovascular events, and registry-based studies

Study	Tumour site	Design	Cases/Controls	Adjustments	Major findings
Clinical studies of the association between statin use and all cancer risk					
Shepherd *et al.* (1995)[1]	All	Double-blind RCT pravastatin or placebo	6,595 hyperlipidemic middle aged men	–	Mean follow-up 4.9 years. No significant difference in number of deaths from cancer.
Sacks *et al.* (1996)[2]	All	Double-blind RCT pravastatin or placebo (CARE)	4,159 coronary heart disease patients	–	Median follow-up 5 years. No significant difference in overall or cancer mortality.
LIPID study group (1998)[3]	All	Double-blind RCT pravastatin or placebo (LIPID)	9,014 coronary heart disease patients	–	Mean follow up 6.1 years. Non-statistically significant difference in cancer deaths.
Downs *et al.* (1998)[4]	All	Double-blind RCT lovastatin or placebo (AFCAPS and TexCAPS)	6,605 without CVD (primary prevention)	–	Mean follow up 5.2 years. No difference in cancer incidence except for a reduction in melanoma in lovastatin group ($P = 0.04$).
ALLHAT collaborative research group (2002)[5]	All	RCT pravastatin or usual care (ALLHAT-LLT)	10,355 participants drawn from ALLHAT with higher representation of older, women, ethnic minorities and diabetics	Not blinded	Mean follow up 4.8 years. Non-statistically significant differences in cancer deaths and in 6-year incidence cancer rate.
Shepherd *et al.* (2002)[6]	All	RCT pravastatin or placebo (PROSPER)	5,804 elderly	Single blindness	Mean follow up 3.2 years. More diagnoses of new cancers in pravastatin group RR = 1.25 (1.04-1.51).
Heart Protection Study Collaborative Group (2005)[7]	All	RCT simvastatin or placebo	20,536 vascular disease or diabetes patients	Single-blindness	Mean follow up 5 years. Cancer incidence rates similar
Pedersen *et al.* (2000)[8]	All	Post RCT observational for an additional 2 years following randomization to simvastatin or placebo for	4,444 coronary heart disease patients	Not accounted for: after the double blind period, most patients in both groups received simvastatin at the discretion of the treating physician.	Median follow up 7.4 years. Non-statistically significant fewer cancer deaths (2.3% vs 3.1%) in the simvastatin group compared

		5.4 years (4S)			to the placebo group.
Strandberg *et al.* (2004)[9]	All	Post RCT observational, for an additional 5 years following randomization to simvastatin or placebo for 5.4 years (4S)	4,444 coronary heart disease patients	Most participants on statins during the follow-up period	Median follow up 10.4 years. Non-statistically significant less cancer deaths and less incident cancers in the (original) simvastatin group.
Heart Protection study collaborative group (2011)[10]	All	Post RCT observational following randomization to simvastatin or placebo for a mean of 5 years (Heart Protection)	20,536 vascular disease or diabetes patients	single-blindness	Mean total follow up 11 years. No difference in cancer incidence or cancer deaths
Jacobs *et al* (2011)[11]	All	Prospective cohort	133,255 participants in the CPS-II nutrition cohort	Age, sex, race, education, smoking, NSAIDs, BMI, physical activity, cholesterol, diabetes, heart disease, hypertension, screening, HRT, alcohol, geographic region.	Lower risk of melanoma RR=0.70 (0.55-0.88), endometrial cancer RR=0.53 (0.32-0.87) and non-Hodgkin lymphoma RR=0.77 (0.62-0.94)
Kaye *et al.* (2004)[12]	All	Historical cohort	3,244 hyperlipidemic patients, 14,844 age-, sex-, general practice-, year of database entry-, index date-matched controls with no hyperlipidemia diagnosis	BMI, smoking, visit frequency	Median follow up 6.4 years. No increased cancer risk. Marginally increased risk for colorectal cancer in a subset of long term statin users (>60 months)
Friis *et al.* (2005)[13]	All	Historical cohort	12,251 statin users, 334,754 non-users, 1,257 other lipid-lowering drugs-users	Age, gender, calendar period, use of NSAIDs, hormone replacement therapy, CVD drugs	Mean follow up 3.3 years. adjusted RR for overall cancer in statin users 0.86 (0.78–0.95) compared to nonusers, and 0.73 (0.55–0.98) compared to other lipid-lowering users. No trend with longer duration of use

Setoguchi *et al.* (2007)[14]	All	Historical cohort	24,439 statin initiators, 7,284 controls	IBD, arthritis, mammary dysplasia, estrogen use, NSAIDs, obesity, BMI, smoking, functional status, aspirin, education, health care utilization, family history of cancer	Mean follow up 2.9 years. Similar incidence rates of colorectal, lung and breast cancers
Farwell *et al.* (2008)[15]	All	Historical cohort	37,248 statin users (mostly simvastatin and lovastatin) and 25,594 hypertensive controls	Comorbidities, aspirin use, sex, smoking, age, weight	Median follow up 5 years. Statin users had lower risk for overall cancer incidence HR = 0.74 (0.70–0.78) and specifically prostate, lung, and colorectal cancers. Decreased risk of lung, CRC and melanoma with increasing stain use
Smeeth *et al.* (2008)[16]	All	Historical cohort	129,288 statin prescribers, 600,241 sex-, age-, general practice-, propensity score-matched controls.	Smoking, BMI, comorbidities. Some in the control group were prescribed statin later.	Median follow up 4.4 years. No difference in incidence of all cancers, or GI, prostatic and breast cancers
Friedman *et al.* (2008)[17]	All	Historical cohort	361,859 statin prescribers, 3,881,208 controls	Smoking, HRT, NSAIDs	In more than 5 years of use: increased HR for all cancers HR 1.09 (1.02-1.17) only in men. Increased HR only in men for oesophagus, skin, bladder, thyroid cancers.
Haukka *et al.* (2009)[18]	All	Historical cohort	472,481 statin users and 472,481 sex-, age-, region-matched controls	BMI, comorbidities, other drugs	Mean follow up 8.8 years. No association with overall cancer incidence. Lower incidence of lung, colon and stomach cancers in lovastatin users with increased drug exposure
Marelli *et al.* (2011)[19]	All	Historical cohort	45,857 propensity-score-matched pairs of statin users and nonusers	Sex, age, race, smoking status, BMI, time in database, concomitant diagnoses, preventive screening, concomitant medications, calendar time	Mean follow up time 4.7 years. No difference in cancer incidence

Frohlich *et al.* (2012)[20]	All	Historical cohort	255 single-centre heart transplanted patients that survived the first year	Age, sex, type of cardiomyopathy, immunosuppressive therapy, cholesterol level	Median follow-up 12.6 years. Reduced occurrence of any malignancy HR = 0.33 (0.21–0.51). Patients receiving statins for >50% of the follow-up time had a lower risk of malignancy.
Nielsen *et al.* (2012)[21]	All	Historical cohort	295, 925 cancer patients. 18,721 statin users and sex-, age-, year of diagnosis-, cancer type-matched non statin user controls	Cancer stage, chemotherapy, CVD, diabetes, area-code, race, ethnic descent, education, size of residential area	Median follow-up 2.6 years. Cumulative incidence of death from cancer lower among statin users HR = 0.85 (0.82–0.87), with no dose–response relationship
Blais *et al.* (2000)[22]	All	Nested case-control	542 incident cases of malignant neoplasms, 5,420 randomly selected controls	Age, sex, calendar year, use of other medications, comorbidity, prior neoplasm	Median follow-up 2.7 years. Statin users were 28% less likely than controls to be diagnosed with cancer adjusted RR = 0.72 (0.57–0.92)
Graaf *et al.* (2004)[23]	All	Nested case-control	Within all patients prescribed cardiovascular medications, 3,129 incident cancer cases, 16,976 sex-, age-, geographic region-, duration of follow up, index date-ontrols	DM, prior hospitalization, comorbidity, use of diuretics, ace inhibitors, calcium channel blockers, NSAIDs, sex hormones, other lipid lowering drugs	Median follow-up 7.2 years. Statin use associated with 20% cancer risk reduction OR = 0.80 (0.66–0.96). OR = 0.64 (0.44–0.93) if 4 or more years of treatment. Site-specific reduction was significant only for renal cancer.
Vinogradova *et al.* (2011)[24]	All	Retrospective case-control	88,125 cancer patients, 362,254 age-, sex-, practice-, calendar time-matched non-cancer controls	DM, rheumatoid arthritis, hypertension, BMI, smoking, socioeconomic status, CVD, benign breast disease, family history of breast cancer, colitis, Crohn's disease, NSAIDs, COX-2 inhibitors, aspirin, HRT, oral contraceptives	At least 6 years follow-up. No association with overall risk of cancer. Atorvastatin: higher risk of colorectal cancer OR = 1.09 (1.01–1.18). Increased bladder risk OR = 1.29 (1.08–1.54) and increased lung cancer

					OR = 1.18 (1.05–1.34) with long-tern usage. Reduced risk of haematological malignancies OR = 0.78 (0.71–0.86).
Clinical studies of the association between statin use and breast cancer risk					
Cauley *et al.* (2003)[25]	Breast	Prospective cohort SOF study	7,528 community dwelling women	BMI, ages at menarche, first birth and menopause, parity, family history of breast cancer, alcohol, physical activity, smoking, HRT, education, health status, mammography use, bone density	Mean follow-up 6.8 years. RR = 0.28 (0.09–0.86) for statin users (mostly lovastatin), 0.36 (0.13–0.97) for users of other non-statin lipid-lowering drugs vs no users.
Cauley *et al.* (2006)[26]	Breast	Prospective cohort and clinical trials (Women's Health Initiative)	156,351 postmenopausal women	Ethnicity, DM, hypercholesterolemia, IHD, benign breast disease, educational level, family history of breast cancer, hysterectomy, oophorectomy, ages at menarche and first birth, parity, NSAIDs, aspirin, smoking, physical activity, alcohol, fat in diet, BMI	Mean follow up 6.7 years. HR = 0.91 (0.80–1.05) of breast cancers among statin users, compared with no users. No trend with increased duration of use. Hydrophobic statins associated HR = 0.82 (0.70–0.97).
Kwan *et al.* (2008)[27]	Breast	Prospective cohort (Life After Cancer Epidemiology [LACE] study)	1,811 early stage breast cancer survivors	Age, race, education, height, weight, smoking, family history of breast cancer, breast cancer treatment, tumour stage, nodal status, tumour hormone receptor status	Mean follow-up 5 years. Risk of recurrence decreased with increasing duration of statin use after diagnosis (*P* for linear trend 0.02). Lipophilic statins mainly used.
Boudreau *et al.* (2007)[28]	Breast	Historical cohort	92,788 women, 7.4% of which were statin-users for >1 year	Weight, height, race, education, parity, menopause, family history of breast cancer, DM, HRT	Median follow-up 6.4 years. Lovastatin and simvastatin mostly used. No difference in breast cancer risk HR = 1.07 (0.88–1.29)

Ahern *et al.* (2011)[29]	Breast	Historical cohort	18,769 invasive breast cancer women	Age, menopause, histological grade, tumour receptor status, adjuvant therapy, type of surgery, HRT, aspirin, ACE inhibitors, NSAIDs, anticoagulants, comorbidity	Median follow up 6.8 years. 10-year adjusted HR = 0.73, (0.60–0.89) for recurrences in exclusive lipophilic statins users.
Kaye *et al.* (2002)[30]	Breast	Retrospective case-control	224 incident breast cancer cases (including *in situ)*, 1,009 age-, sex-, general practice-, duration of history-, index date-matched controls	BMI, HRT, history of benign breast disease	Risk of breast cancer increased in untreated hyperlipidemic RR = 1.6 (1.1–2.5). RR = 1.0 (0.6–1.6) for breast cancer among statin users.
Boudreau *et al.* (2004)[31]	Breast	Retrospective case-control	975 women ages 65-79 years with invasive breast carcinoma, 1,007 controls	Age, reference date, county, HRT, weight, BMI, hypertension, hypertensive medications, smoking, income, education, alcohol, menopause, age at menopause, mammograms, family history of breast cancer, parity, age at first birth, use of other cholesterol-lowering medications	Lower breast cancer risk in long-term statin users (>5 years) OR = 0.7 (0.4–1.0)
Woditschka *et al.* (2010)[32]	Breast	Retrospective case-control	22,488 invasive breast cancer cases, 224,860 age-, duration of data base coverage-controls	Oral contraceptives, HRT, obesity, alcohol, race	No association between lipophilic statin use of ≥2 years and breast cancer risk
Clinical studies of the association between statin use and colorectal cancer risk					
Jacobs *et al.* (2006)[33]	CRC	Prospective cohort (Cancer Prevention Study II Nutrition Cohort)	132,136 participants	Sex, NSAIDs, colorectal endoscopy, stage of colorectal cancer, cancer anatomic subsite	Follow-up 4 years. No association demonstrated.
Ng *et al.* (2011)[34]	CRC	Prospective cohort (post CALGB RCT study)	842 stage III CRC patients	Age, sex, family history of colorectal cancer, ECOG performance status, cancer stage, CEA level, type of treatment arm, BMI, physical activity, diet, aspirin, COX-2 inhibitors.	Median follow-up 6.5 years. Disease-free survival, recurrence-free survival and overall survival were similar in statin users and non-users, regardless of *KRAS* mutation. (The study had

					80% power to detect HR of 0.55).
Lee *et al.* (2011)[35]	CRC	Prospective cohort (Nurses' Health Study, and Health Professionals Follow up Study)	1,818 CRC cases within 131,922 participants	Study, age, calendar year, BMI, aspirin, multivitamins, endoscopy, smoking, alcohol	Current statin use was not associated with colon cancer, but was inversely associated with rectal cancer RR = 0.59 (0.41–0.84), with no association with *KRAS* mutation, *PTGS2* (COX-2) expression, microsatellite instability status, CIMP (DNA methylation) status.
Simon *et al.* (2012)[36]	CRC	Prospective cohort and clinical trials (WHI)	159,219 postmenopausal women	Age, race/ethnicity, DM, hypercholesterolemia, CAD, educational level, family history of CRC, NSAIDs, aspirin, smoking, physical activity, alcohol, diet, BMI, calcium and selenium supplements, current health-care provider, last medical visit, history of colon polyp removal, hypertension, history of stroke, colon screening, HRT, nonstatin lipid lowering medications	Reduction in CRC risk associated with lovastatin HR = 0.62 (0.39-0.99)
Bertagnolli *et al.* (2010)[37]	Colorectal adenomas	Prospective cohort (secondary analysis of RCT to celecoxib or placebo [APC trial])	2,028 patients at high risk for recurrent colorectal adenomas	Age, sex, aspirin, CVD events, hypertension, diabetes	Follow up of 5 years. Statin use >3 years increased (recurrent) adenoma risk RR = 1.39 (1.04–1.86). Celecoxib treatment eliminated the risk.

Poynter *et al.* (2005)[38]	CRC	Prospective case-control. Pharmacy records confirmed.	1,953 CRC patients and 2,015 age-, sex-, clinic-, ethnicity-matched controls	Aspirin, NSAIDs, physical activity, hypercholesterolemia, family history of CRC, ethnicity, vegetable consumption, level of education, red meat consumption	Use of statins (mostly simvastatin and pravastatin) for at least 5 years was associated with reduced relative risk of CRC adjusted OR = 0.53 (0.38–0.74). Strength of association similar for pravastatin and simvastatin.
Samadder *et al.* (2011)[39]	CRC	Prospective case-control. Pharmacy records confirmed.	1,921 matched pairs of CRC cases and controls	Aspirin, NSAIDs, family history of cancer, ethnicity, physical activity, smoking, vegetable consumption	Long term statin use (mostly simvastatin) was associated with reduced IBD-associated CRC OR = 0.07 (0.01-0.78) and non-IBD CRC OR = 0.49 (0.39–0.62).
Coogan *et al.* (2007)[40]	CRC	Retrospective case-control	1,809 CRC patients, 1,809 age-, sex-, precinct-matched controls	Education, exercise, occupational physical activity, family history of CRC, alcohol, smoking, race, BMI, use of vitamin E, multivitamin, calcium supplements, HRT, NSAIDs cholecystectomy, screening colonoscopy, diet.	No association between use of statins (mostly atorvastatin) and overall CRC risk. Risk of stage IV CRC lower among statin users OR = 0.49 (0.26–0.91).
Vinogradova *et al.* (2007)[41]	CRC	Retrospective case-control	5,686 incident CRC cases, 24,982 age-, calendar time-, sex-, practice-matched controls	Morbidity, smoking, BMI, socioeconomic status, ulcerative colitis, DM, IHD, hypertension, stroke, rheumatoid arthritis, osteoarthritis	Median follow up 7.3 years. Association between simvastatin use but not atorvastatin and CRC, OR = 0.83 (0.72–0.96). No significant trend with number of prescriptions. Prolonged use of NSAIDs and COX-2 inhibitors was associated with reduced CRC risk.
Hoffmeister *et al.* (2007)[42]	CRC	Retrospective case-control	537 CRC cases, 612 sex-, age-, county of residence-matched controls	Other medications, former colorectal endoscopy, family history of CRC, rheumatic disease, DM, hyperlipidemia, HRT, diet, NSAIDs, alcohol, smoking,	Non statistically significant reduction of CRC risk for regular use of low dose aspirin, OR = 0.77 (0.55–1.07).

				educational level, BMI, general health screening examination, physical activity	Stronger association with regular statin use OR = 0.65 (0.43–0.99), strongest with simvastatin. Combined use of aspirin and statin for 5 years or more associated with risk reduction by 62% OR = 0.38 (0.15–0.97)
Yang *et al.* (2008)[43]	CRC	Retrospective case-control	4,432 incident CRC cases, 44,292 practice-, duration of follow up-, calendar time-matched controls	Smoking, alcohol, BMI, NSAIDs, aspirin, HRT, endoscopy	Mean follow up 7.4 years. No association between statin use and CRC risk
Hachem *et al.* (2009)[44]	CRC	Retrospective case-control	6,080 CRC cases with DM, 24,320 sex-, age-matched controls	IBD, DM severity, cholecystectomy, liver disease, DM medications, aspirin, NSAIDs, colorectal evaluation, previous colorectal polyps, cancer site, race.	Less statin prescription (mostly simvastatin) in colon cancer cases than in controls adjusted OR = 0.91 (0.86–0.96). Regular use (filled prescription greater than 80% of the time) was associated with further risk reduction OR = 0.83 (0.76–0.91). No duration-response relationship was observed.
Robertson *et al.* (2010)[45]	CRC	Retrospective case-control	9,979 CRC cases, 99,790 age-, gender-, county of residence-, matched controls	Aspirin, NSAIDs, cholecystectomy, DM, alcoholism	Statin use slightly reduced CRC risk IRR = 0.87 (0.80–0.96), specifically simvastatin IRR = 0.88 (0.79–0.98). The association was not seen in long term users.
Cheng *et al.* (2011)[46] (73)	CRC	Retrospective case-control	1,156 CRC cases and, 4,624 age-, sex-, index date-matched	DM, cholecystectomy, liver disease, colorectal polyps, IBD, other lipid lowering medications,	No association between statin use and CRC.

			controls who were admitted to hospital for reasons unrelated to statins.	NSAIDs, colonoscopy, FOBT, number of hospitalizations.	
Broughton *et al.* (2012)[47]	CRC	Retrospective case-control	101 CRC patients and 132 controls, of symptomatic patients attending for diagnostic colonoscopy	Age, gender, alcohol, DM, aspirin, metformin, NSAIDs, calcium channel blockers, diabetes medications, indications for colonoscopy.	Inverse association between previous statin use (mostly simvastatin) and a diagnosis of CRC OR = 0.43 (0.25–0.80). Association stronger with higher statin doses OR = 0.19 (0.07–0.47), and greater duration of statin use: use over 5 years OR = 0.18 (0.06–0.55)
Lakha *et al.* (2012)[48]	CRC	Retrospective case-control	309 CRC cases, 294 age-, sex-, region of residence-matched controls.	Family history of CRC, previous cancer, bowel disease, BMI, smoking, physical activity, energy intake, deprivation category, NSAIDs, HRT, hormonal contraception.	Statins use associated with reduced CRC risk OR 0.33–0.42.
Broughton *et al.* (2012)[49]	Colorectal adenomas	Retrospective case-control	132 adenomatous polyp patients, 132 age-, sex-matched controls without polyps, attending diagnostic colonoscopy.	Aspirin, NSAIDs, metformin, other diabetic medications, calcium channel blockers, DM, IBD, family history of CRC, smoking, alcohol, BMI, HRT, parity.	Negative association between prior statin use (mostly simvastatin) and a diagnosis of adenomatous polyps OR = 0.40 (0.24–0.76). Significantly stronger with higher doses OR = 0.33 (0.10–0.53), and longer duration of use OR = 0.36 (0.10–0.67)
Clinical studies of the association between statin use and risk of cancer in other sites:					

Kawata *et al.* (2001)[50]	Liver	RCT pravastatin/ no pravastatin along with standard chemotherapy	83 consecutive unresectable HCC patients	–	Median survival longer in HCC cases assigned to pravastatin use
Kastelein *et al.* (2011)[51]	Oesophagus	Prospective cohort. Pharmacy records confirmed.	570 Barrett's oesophagus patients	Age, gender, Barrett's oesophagus length, BMI, smoking, alcohol, family history, symptoms, histology, PPIs, NSAIDs, COX-2 inhibitors, aspirin.	Median follow up 4.5 years. NSAIDs and statin use were each associated with a reduced risk of neoplastic progression HR = 0.47, HR = 0.46 respectively. Use of both NSAIDs and statins was associated with even lower risk HR = 0.22 (0.06–0.85).
Kantor *et al.* (2012)[52]	Oesophagus	Prospective cohort	395 Barrett's oesophagus patients	Age, sex, smoking, NSAIDs, waist-hip ratio, education	Inverse association between statin use and risk of progression to oesophageal carcinoma significant for high-grade dysplasia patients HR = 0.31 (0.11–0.86)
Liu *et al.* (2012)[53]	Renal	Prospective cohorts (Nurses' Health Study, Health Professional Follow up Study).	80,782 women, 37,869 men.	Age, BMI, smoking, hypertension, DM, NSAIDs, physical activity, diet, alcohol, calendar year.	After 14-16 years of follow up, statin use was associated with reduced incidence of renal cell carcinoma in women with no dose-response relation.
Tsan *et al.* (2012)[54]	Liver	Historical cohort	33,413 HBV infected patients	Age, sex, income, level of urbanization, other lipid lowering agents, aspirin, ACE inhibitors, alcohol related disease, cirrhosis, DM, anti-HBV treatment	Follow up 328,946 person-years. Dose-response relationship between statin use and reduced HCC risk HR = 0.66 (0.44–0.99), 0.41 (0.27–0.61), 0.34 (0.18–0.67) for

					increasing cumulative defined daily doses. No effect with pravastatin.
Khurana *et al.* (2007)[55]	Lung	Retrospective case-control	7,280 lung cancer patients, 476,453 controls with no lung cancer	Age, sex, BMI, smoking, diabetes, race (note: there is possible time-window bias that was not adjusted for). In a time dependent analysis of a similar cohort there was no effect to statins[56]	Statins use >6 months was associated with a 55% risk reduction OR = 0.45 (0.42–0.48)
Nguyen *et al.* (2010)[57]	Oesophagus	Retrospective case-control	116 oesophageal adenocarcinoma patients, 696 no adenocarcinoma controls, all with Barrett's oesophagus	Age, race, outpatient encounters, comorbidity, socio-economic status, PPI, NSAID/aspirin (for statin analysis)	Reduction in adenocarcinoma risk in statin users IRR = 0.55 (0.36–0.86). Greater risk reduction with longer duration of statin use.
Beals *et al.* (2012)[58]	Oesophagus	Retrospective case-control	112 oesophageal adenocarcioma patients, 448 age-, sex-matched controls attending upper GI endoscopy gastroscopy.	BMI, gender, smoking, alcohol, DM, aspirin, metformin, NSAID.	Statin use was associated with lower adenocarcinoma risk OR = 0.52 (0.27–0.92). Aspirin use was also associated with reduced risk, and further reduction with aspirin and statin combination OR = 0.27 (0.05–0.67). Greater risk reduction with longer duration and higher doses of statins. Both hydrophilic and lipophilic statins associated with reduced risk.
Chiu *et al.* (2011)[59]	Stomach	Retrospective case-control.	337 gastric cancer cases, 1,348 age-, sex-, index date-matched controls, who were admitted to the hospital for diagnoses unrelated to statins.	Helicobacter Pylori eradication, peptic ulcer, aspirin, NSAIDs, PPI, other lipid lowering drugs	Ever-use of statin associated with decreased gastric cancer risk OR = 0.68 (0.49–0.95). Trend toward decreasing risk with increasing cumulative dose.
Khurana *et al.* (2007)[60]	Pancreas	Retrospective case-control	475 pancreatic cancer patients, 483,258	Age, sex, BMI, smoking, DM, race (note: time-window	Statins use >6 months associated with

			controls with no pancreatic cancer.	bias not accounted for).	a risk reduction of pancreatic cancer, OR = 0.33 (0.26–0.41). OR = 0.2 (0.13–0.29) with statins use >4 years.
Bradley *et al.* (2010)[61]	Pancreas	Retrospective case-control.	1,141 pancreatic cancer cases, 7,954 general practice site-, sex-, age-matched controls.	Smoking, BMI, alcohol, pancreatitis, DM, history of cancer, systemic steroids, HRT.	Mean follow up 10.6 years. Use of statins (mostly simvastatin and atorvastatin) not associated with pancreatic cancer risk reduction
El-Serag *et al.* (2009)[62]	Liver	Retrospective case-control	1,303 HCC patients, 5,212 age-, gender-, date –matched controls, all DM patients.	Race, alcoholism, cirrhosis, hepatitis C, hepatitis B, obesity, alcoholic liver disease, aspirin, NSAIDs, ACE inhibitors, cirrhosis, diabetes medications, propensity score.	Statin use (mostly simvastatin) associated with a HCC risk reduction OR = 0.74 (0.64–0.87).
Chiu *et al.* (2011)[63]	Liver	Retrospective case-control	1,166 liver cancer cases, 1,166 age-, sex-, index date-matched controls hospitalized for non-statin related reasons.	Hepatitis B, hepatitis C, cirrhosis, alcoholic liver disease, DM, NSAIDs, ACE inhibitors, other lipid-lowering drugs.	Use of statins associated with reduced liver cancer risk OR = 0.62 (0.45–0.83). The association among high dose users was not significant.
Yu *et al.* (2009)[64]	Female reproductive organ	Cross-sectional	586 endometrial cancer cases within 73,336 women, 326 ovarian cancer cases within 93,619 women	Age, BMI, smoking, parity, DM, hormonal therapy, other lipid lowering drugs, hyperlipidaemia, endometriosis	Median follow up 5.6-5.8 years. Non-significant decrease of gynaecological cancers in statin users (mostly simvastatin and lovastatin)
Abbreviations: ACE, angiotensin converting enzyme; CAD, coronary artery disease; CIMP, CpG island methylator phenotype; COX-2, cyclooxygenase-2; CRC, colorectal cancer; CVD, cardiovascular disease; DM, diabetes mellitus; FOBT, faecal occult blood test; GI, gastrointestinal; HBV, hepatitis B virus; HCC, hepatocellular cancer; HR, hazard ratio; HRT, hormonal replacement therapy; IBD, inflammatory bowel disease; IHD, ischemic heart disease; IRR, incidence rate ratio; PPI, proton pump inhibitor; NSAIDs, non-steriodal anti-inflammatory drugs; OR, odds ratio; RCT, randomized controlled trial; RR, relative risk, rate ratio.					

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