SUPPLEMENTARY MATERIAL

Review and Meta-Analysis of Observational Studies

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Supplementary Material 1: Search Strategy

Five databases were searched: Medline (PubMed), Embase (Ovid), Scopus (SciVerse), Web of Science WoS (ISI Web of Knowledge, Thomson Reuters) and the Cochrane Library (Wiley). All searches were performed on 27 November 2012 without restrictions on language, publication date, or publication status. MESH and Emtree terms were used (PubMed, Embase, Cochrane Library) with search filter "Humans" (Medline, Embase). In addition, free text search limited to records published during the last year was used to identify records not yet indexed with MESH and Emtree terms. For Scopus and Web of Science, only free-text searches were used. Search terms for diabetes, insulin and cancer (or similar terms) were used in all searches, while terms for risk or incidence were added in free text searches. The specific search strategy for each database is presented below.

Medline (PubMed)

MESH search combined with free text search and filter:

1. "Diabetes Mellitus"[Mesh]
2. "Insulins"[Mesh]
3. "Neoplasms"[Mesh]
4. risk OR risk* OR incidence OR inciden*
5. #1 AND #2 AND #3 AND #4
6. Filters: Humans

295 records

Free text search in all fields with filter on publication date 2012 :

1. diabetes OR diabetes* OR diabetic* OR diabet*
2. insulin OR insulin*
3. tumor OR tumor* OR tumour OR tumour* OR cancer OR cancer* OR neoplasm OR neoplasm* OR carcinoma OR carcinom* OR sarcoma OR sarcom* OR lymphoma OR lymphom* OR leukemia OR leukem* OR myeloma OR myelom*
4. risk OR risk* OR incidence OR inciden*
5. #1 AND #2 AND #3 AND #4

6. Filters: Publication date from 2012 / 01 / 01 to 2012 / 12 / 31

284 records

Embase (Ovid)

Emtree search with limit:

1. exp diabetes mellitus
2. exp insulin derivative
3. exp cancer incidence OR exp cancer risk OR exp carcinogenicity OR exp drug induced cancer OR exp drug carcinogenicity OR exp carcinogenesis
4. 1 AND 2 AND 3
5. limit 4 to human

816 records

Free text search in title / abstract / keywords with limit on publication year 2012:

1. "diabet*".ti,ab,kw.
2. "insulin*".ti,ab,kw.
3. (risk* or inciden*).ti,ab,kw.
4. (cancer* or neoplasm* or tumor* or tumour* or carcinom* or sarcom* or lymphom* or leukem* or myelom*).ti,ab,kw.
5. 1 AND 2 AND 3 AND 4
6. limit 5 to yr="2012 -Current"

295 records

Scopus (SciVerse)

Free text search search in title / abstract / keywords:

1. TITLE-ABS-KEY(*diabet*)
2. TITLE(*insulin*)
3. TITLE-ABS-KEY(risk* OR inciden*)
4. TITLE(*cancer* OR *neoplasm* OR *tumor* OR *tumour* OR *carcinom* OR *sarcom* OR *lymphom* OR *leukem* OR *myelom*)
5. 1 and 2 and 3 and 4

313 records

Web of Science WoS (ISI Web of Knowledge, Thomson Reuters)

Free text search search in title / abstract / keywords (topic):

1. topic=(*diabet*)
2. title=(*insulin*)
3. topic=(risk* OR inciden*)
4. title=(*cancer* OR *neoplasm* OR *tumor* OR *tumour* OR *carcinom* OR *sarcom* OR *lymphom* OR *leukem* OR *myelom*)
5. 1 AND 2 AND 3 AND 4

239 records

The Cochrane Library (Wiley)

Databases selected: Cochrane Central Register of Controlled Trials (Clinical Trials), Cochrane Database of Systematic Reviews (Cochrane Reviews), Database of Abstracts of Reviews of Effects (Other Reviews), Cochrane Methodology Register (Methods

Studies), Health Technology Assessment Database (Technology Assessments), NHS Economic Evaluation Database (Economic Evaluations), About The Cochrane Collaboration (Cochrane Groups).

MESH search:

1. "Diabetes Mellitus"[Mesh]
2. "Insulins"[Mesh]
3. "Neoplasms"[Mesh]
4. 1 AND 2 AND 3

11 records

Free text search search in title / abstract / keywords limited to dates 2011-2012:

1. (*diabet*):ti,ab,kw
2. (*insulin*):ti,ab,kw
3. (risk* OR inciden*):ti,ab,kw
4. (*cancer* or *neoplasm* or *tumor* or *tumour* or *carcinom* or *sarcom* or *lymphom* or *leukem* or *myelom*):ti,ab,kw
5. 1 AND 2 AND 3 AND 4
6. Limit Dates 2011-2012

32 records

Supplementary Material 2: Newcastle – Ottawa Quality Assessment Scale

http: / / www.ohri.ca / programs / clinical_epidemiology / oxford.asp

CASE CONTROL STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Selection

1) Is the case definition adequate?
   a) Yes, with independent validation *
   b) Yes, e.g. record linkage or based on self-reports *
   c) No description
2) Representativeness of the cases
   a) Consecutive or obviously representative series of cases *
   b) Potential for selection biases or not stated
3) Selection of Controls
   a) Community controls *
   b) Hospital controls
   c) No description
4) Definition of Controls
   a) No history of disease (endpoint) *
   b) No description of source

Comparability

1) Comparability of cases and controls on the basis of the design or analysis
   a) Study controls for age (user-defined) (Select the most important factor.) *
   b) Study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.) *

Exposure

1) Ascertainment of exposure
   a) Secure record (e.g. surgical records) *
   b) Structured interview where blind to case / control status *
   c) Interview not blinded to case / control status
   d) Written self-report or medical record only
   e) No description
2) Same method of ascertainment for cases and controls
   a) Yes *
   b) No
3) Non-Response rate
   a) Same rate for both groups *
   b) Non-respondents described
   c) Rate different and no designation

COHORT STUDIES

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

Selection

1) Representativeness of the exposed cohort
   a) Truly representative of the average diabetic population using insulin (user-defined) in the community *
   b) Somewhat representative of the average diabetic population using insulin (user-defined) in the community *
   c) Selected group of users e.g. nurses, volunteers
   d) No description of the derivation of the cohort
2) Selection of the non-exposed cohort

a) Drawn from the same community as the exposed cohort *
b) Drawn from a different source
c) No description of the derivation of the non-exposed cohort

3) Ascertainment of exposure
a) Secure record (e.g. surgical records) *
b) Structured interview *
c) Written self-report
d) No description

4) Demonstration that outcome of interest was not present at start of study
a) Yes *
b) No

Comparability

1) Comparability of cohorts on the basis of the design or analysis
a) Study controls for age (user-defined) (select the most important factor) *
b) Study controls for any additional factor (This criteria could be modified to indicate specific control for a second important factor.) *

Outcome

1) Assessment of outcome
a) Independent blind assessment *
b) Record linkage *
c) Self-report
d) No description

2) Was follow-up long enough for outcomes to occur
a) Yes, ≥ 5 years (user-defined) (select an adequate follow up period for outcome of interest) *
b) No

3) Adequacy of follow up of cohorts
a) Complete follow up - all subjects accounted for *
b) Subjects lost to follow up unlikely to introduce bias (small number lost): ≥90 % (user-defined) follow-up, or description provided of those lost *
c) Follow up rate <10 % (user-defined) and no description of those lost
d) No statement.

Supplementary Material 3

Presents all estimates extracted from each study for all cancer sites and exposure contrasts, sorted by author name and publication year. The same study can have several risk estimates for each combination of exposure contrast and cancer site if several study designs have been employed in the study (e.g. intention-to-treat and as-treated analysis, with and without latency periods, incident and prevalent users, diabetes types). If risk estimates for strata of dose / duration are presented, these are separated by " / " in tables.

1) Cohort studies (27 studies).

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval	
Blin 2012 [25]	any	glargine only	human only	both	0.59	0.28	1.25
Campbell 2010 [26]	colorectal	insulin	no insulin	men	1.11	0.82	1.51
Campbell 2010 [26]	colorectal	insulin	no insulin	women	0.94	0.60	1.48
Campbell 2010 [26]	colon	insulin	no insulin	men	1.13	0.79	1.61
Campbell 2010 [26]	colon	insulin	no insulin	women	1.04	0.62	1.73
Campbell 2010 [26]	rectal	insulin	no insulin	men	1.05	0.58	1.90

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval	
Campbell 2010 [26]	rectal	insulin	no insulin	women	0.65	0.24	1.75
Carstensen 2012 [27]	any excl nmsc	insulin	no insulin	men	1.14	1.08	1.20
Carstensen 2013 [27]	any excl nmsc	insulin	no insulin	women	1.23	1.16	1.30
Carstensen 2013 [27]	oesophagus	insulin	no insulin	men	0.98	0.67	1.43
Carstensen 2013 [27]	oesophagus	insulin	no insulin	women	1.19	0.57	2.49
Carstensen 2013 [27]	stomach	insulin	no insulin	men	1.23	0.90	1.68
Carstensen 2013 [27]	stomach	insulin	no insulin	women	1.43	0.89	2.28
Carstensen 2013 [27]	colon	insulin	no insulin	men	1.00	0.84	1.19
Carstensen 2013 [27]	colon	insulin	no insulin	women	0.90	0.73	1.12
Carstensen 2013 [27]	rectal	insulin	no insulin	men	0.98	0.77	1.24
Carstensen 2013 [27]	rectal	insulin	no insulin	women	0.91	0.62	1.32
Carstensen 2013 [27]	colorectal	insulin	no insulin	men	0.99	0.86	1.14
Carstensen 2013 [27]	colorectal	insulin	no insulin	women	0.90	0.75	1.09
Carstensen 2013 [27]	liver	insulin	no insulin	men	2.41	1.93	3.00
Carstensen 2013 [27]	liver	insulin	no insulin	women	2.59	1.58	4.23
Carstensen 2013 [27]	pancreatic	insulin	no insulin	men	2.92	2.49	3.42
Carstensen 2013 [27]	pancreatic	insulin	no insulin	women	3.30	2.77	3.93
Carstensen 2013 [27]	respiratory	insulin	no insulin	men	1.28	1.13	1.45
Carstensen 2013 [27]	respiratory	insulin	no insulin	women	1.31	1.11	1.54
Carstensen 2013 [27]	melanoma	insulin	no insulin	men	0.80	0.57	1.12
Carstensen 2013 [27]	melanoma	insulin	no insulin	women	1.10	0.76	1.60
Carstensen 2013 [27]	kidney	insulin	no insulin	men	1.39	1.06	1.83
Carstensen 2013 [27]	kidney	insulin	no insulin	women	2.04	1.45	2.86
Carstensen 2013 [27]	bladder	insulin	no insulin	men	0.91	0.75	1.10
Carstensen 2013 [27]	bladder	insulin	no insulin	women	1.13	0.77	1.64
Carstensen 2013 [27]	brain	insulin	no insulin	men	1.00	0.69	1.44
Carstensen 2013 [27]	brain	insulin	no insulin	women	1.47	1.00	2.18
Carstensen 2013 [27]	thyroid	insulin	no insulin	men	1.38	0.57	3.35
Carstensen 2013 [27]	thyroid	insulin	no insulin	women	2.05	1.07	3.90
Carstensen 2013 [27]	HL	insulin	no insulin	men	1.07	0.50	2.29
Carstensen 2013 [27]	HL	insulin	no insulin	women	0.52	0.12	2.22
Carstensen 2013 [27]	NHL	insulin	no insulin	men	0.85	0.60	1.19
Carstensen 2013 [27]	NHL	insulin	no insulin	women	1.18	0.81	1.73
Carstensen 2013 [27]	multiple myeloma	insulin	no insulin	men	0.92	0.57	1.49

Author (country)	Outcome[‡]	Exposure	Comparator	Gender	Risk estimate[†]	95% Confidence Interval		
Carstensen 2013 [27]	multiple myeloma	insulin	no insulin	women	0.74	0.36	1.52	
Carstensen 2013 [27]	leukaemia	insulin	no insulin	men	1.01	0.72	1.43	
Carstensen 2013 [27]	leukaemia	insulin	no insulin	women	1.08	0.70	1.66	
Carstensen 2013 [27]	breast	insulin	no insulin	men	2.59	0.84	7.94	
Carstensen 2013 [27]	breast	insulin	no insulin	women	0.96	0.84	1.09	
Carstensen 2013 [27]	cervical	insulin	no insulin	women	1.37	0.89	2.09	
Carstensen 2013 [27]	uterus	insulin	no insulin	women	1.05	0.82	1.36	
Carstensen 2013 [27]	ovarian	insulin	no insulin	women	1.07	0.76	1.50	
Carstensen 2013 [27]	prostate	insulin	no insulin	men	0.79	0.69	0.90	
Carstensen 2013 [27]	testis	insulin	no insulin	men	0.57	0.25	1.28	
Chang 2011 [28]	any	glargine	human int-/long-acting	both	0.86	0.73	1.02	
Chang 2011 [28]	liver	glargine	human int-/long-acting	both	0.76	0.54	1.08	
Chang 2011 [28]	colorectal	glargine	human int-/long-acting	both	0.78	0.49	1.26	
Chang 2011 [28]	pancreatic	glargine	human int-/long-acting	both	1.85	1.06	3.22	
Chang 2011 [28]	lung	glargine	human int-/long-acting	both	1.01	0.59	1.71	
Chang 2011 [28]	composite[‡]	glargine	human int-/long-acting	both	0.54	0.25	1.16	
Chang 2011 [28]	stomach	glargine	human int-/long-acting	both	0.62	0.27	1.42	
Chang 2011 [28]	skin	glargine	human int-/long-acting	both	1.08	0.48	2.46	
Chang 2011 [28]	breast	glargine	human int-/long-acting	women	0.53	0.21	1.31	
Chang 2011 [28]	prostate	glargine	human int-/long-acting	men	2.37	0.94	6.01	
Chang 2011 [28]	any	glargine	human int-/long-acting	both	0.81 / 0.75 / 0.79 / 1.18	0.6 / 0.5 / 0.54 / 0.83	1.07 / 1.11 / 1.16 / 1.67	cumulative dose (<50/50-135/135-300/>300 DDD)
Chang 2011 [28]	pancreatic	glargine	human int-/long-acting	both	1.23 / 1.19 / 1.15 /7.90	0.53 / 0.34 / 0.27 / 2.64	2.84 / 4.17 / 5.00 / 23.71	cumulative dose (<50/50-135/135-300/>300 DDD)
Chang 2011 [28]	prostate	glargine	human int-/long-acting	men	1.88 / 2.06 / 5.37 / 2.16	0.30 / 0.29 / 0.71 / 0.33	11.63 / 14.7 / 40.85 / 14.10	cumulative dose (<50/50-135/135-300/>300 DDD)
Chang 2011 [28]	any	glargine	human int-/long-acting	both	0.83 / 0.91	0.69 / 0.61	1.01 / 1.36	cumulative duration (<1/≥1 year)
Chang 2011 [28]	pancreatic	glargine	human int-/long-acting	both	1.75 / 2.58	0.98 / 0.50	3.12 / 13.23	cumulative duration (<1/≥1 year)
Chang 2011 [28]	prostate	glargine	human int-/long-acting	men	2.52 / 1.79	0.87 / 0.26	7.25 / 12.33	cumulative duration (<1/≥1 year)
Chang 2011 [28]	any	glargine	human int-/long-acting	both	0.68 / 1.05	0.52 / 0.84	0.89 / 1.32	mean daily dose (<0.5/≥0.5 DDD/day)
Chang 2011 [28]	pancreatic	glargine	human int-/long-acting	both	1.92 / 1.84	0.85 / 0.86	4.32 / 3.95	mean daily dose (<0.5/≥0.5 DDD/day)
Chang 2011 [28]	prostate	glargine	human int-/long-acting	men	2.95 / 1.98	0.83 / 0.47	10.43 / 8.40	mean daily dose (<0.5/≥0.5 DDD/day)
Colhoun 2010 [29]	any excl nmsc	glargine only	non-glargine insulins only	both	1.64	1.05	2.54	
Colhoun 2010 [29]	any excl nmsc	glargine + non-glargine	non-glargine insulins only	both	0.78	0.53	1.16	
Colhoun 2010 [29]	any excl nmsc	glargine	non-glargine insulins only	both	1.02	0.77	1.36	
Colhoun 2010 [29]	any excl nmsc	glargine	non-glargine insulins only	both	1.08	0.78	1.49	

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval	
Colhoun 2010 [29]	any excl nmsc	glargine only	non-glargine insulins only	both	1.58	1.03	2.42
Colhoun 2010 [29]	any excl nmsc	glargine	non-glargine insulins only	both	1.02	0.50	2.09
Colhoun 2010 [29]	any excl nmsc	glargine only	non-glargine insulins only	both	1.73	0.98	3.05
Colhoun 2010 [29]	any excl nmsc	glargine + non-glargine	non-glargine insulins only	both	0.88	0.55	1.40
Colhoun 2010 [29]	breast	glargine	non-glargine insulins only	women	1.49	0.79	2.83
Colhoun 2010 [29]	breast	glargine only	non-glargine insulins only	women	3.65	1.05	12.68
Colhoun 2010 [29]	breast	glargine + non-glargine	non-glargine insulins only	women	1.10	0.38	3.16
Colhoun 2010 [29]	prostate	glargine only	non-glargine insulins only	men	1.16	0.16	8.50
Colhoun 2010 [29]	prostate	glargine + non-glargine	non-glargine insulins only	men	1.76	0.54	5.74
Colhoun 2010 [29]	colorectal	glargine only	non-glargine insulins only	both	1.43	0.45	4.57
Colhoun 2010 [29]	colorectal	glargine + non-glargine	non-glargine insulins only	both	0.36	0.09	1.45
Colhoun 2010 [29]	lung	glargine only	non-glargine insulins only	both	1.43	0.53	3.88
Colhoun 2010 [29]	lung	glargine + non-glargine	non-glargine insulins only	both	0.47	0.18	1.25
Colhoun 2010 [29]	pancreatic	glargine only	non-glargine insulins only	both	ne	-	-
Colhoun 2010 [29]	pancreatic	glargine + non-glargine	non-glargine insulins only	both	0.54	0.08	4.32
Colhoun 2010 [29]	any excl nmsc	glargine only	non-glargine insulins only	both	0.87	0.63	1.21
Colhoun 2010 [29]	any excl nmsc	glargine + non-glargine	non-glargine insulins only	both	1.20	0.69	2.09
Colhoun 2010 [29]	breast	glargine only	non-glargine insulins only	women	1.47	0.59	3.64
Colhoun 2010 [29]	breast	glargine + non-glargine	non-glargine insulins only	women	ne	-	-
Colhoun 2010 [29]	any excl nmsc	glargine only	non-glargine insulins only	both	1.49	1.09	2.03
Colhoun 2010 [29]	any excl nmsc	glargine + non-glargine	non-glargine insulins only	both	0.65	0.53	0.81
Colhoun 2010 [29]	breast	glargine only	non-glargine insulins only	women	1.99	0.88	4.49
Colhoun 2010 [29]	breast	glargine + non-glargine	non-glargine insulins only	women	1.19	0.72	1.94
Colhoun 2010 [29]	prostate	glargine only	non-glargine insulins only	men	1.14	0.45	2.84
Colhoun 2010 [29]	prostate	glargine + non-glargine	non-glargine insulins only	men	1.05	0.58	1.91
Colhoun 2010 [29]	colorectal	glargine only	non-glargine insulins only	both	1.13	0.62	2.04
Colhoun 2010 [29]	colorectal	glargine + non-glargine	non-glargine insulins only	both	0.58	0.36	0.93
Colhoun 2010 [29]	pancreatic	glargine only	non-glargine insulins only	both	1.34	0.64	2.78
Colhoun 2010 [29]	pancreatic	glargine + non-glargine	non-glargine insulins only	both	0.11	0.03	0.45
Colhoun 2010 [29]	any excl nmsc	glargine	non-glargine insulins only	both	0.69	0.60	0.79
Currie 2009 [30]	any	human long-acting only	glargine only	both	1.24	0.90	1.70
Currie 2009 [30]	any	human biphasic	glargine only	both	0.88	0.66	1.19
Currie 2009 [30]	any	analog biphasic	glargine only	both	1.02	0.76	1.37
Currie 2009 [30]	any	insulin	metformin only	both	1.42	1.27	1.60

Author (country)	Outcome[‡]	Exposure	Comparator	Gender	Risk estimate[†]	95% Confidence Interval		
Currie 2009 [30]	any	insulin	metformin only	both	1.35	1.19	1.54	
Currie 2009 [30]	colorectal	insulin	metformin only	both	1.69	1.23	2.33	
Currie 2009 [30]	pancreatic	insulin	metformin only	both	4.63	2.64	8.10	
Currie 2009 [30]	prostate	insulin	metformin only	men	1.10	0.79	1.52	
Currie 2009 [30]	breast	insulin	metformin only	women	1.07	0.79	1.44	
Currie 2009 [30]	breast	glargine only	non-glargine insulin	women	0.86	0.42	1.75	
Currie 2009 [30]	composite[‡]	human long-acting only	glargine only	both	1.17	0.70	1.94	
Currie 2009 [30]	composite[‡]	human biphasic	glargine only	both	0.76	0.47	1.24	
Currie 2009 [30]	composite[‡]	analog biphasic	glargine only	both	1.01	0.63	1.63	
Fagot 2012 [31]	any	glargine	other int-/long-acting insulins	both	1.04	0.93	1.16	
Fagot 2012 [31]	any	glargine	other int-/long-acting insulins	both	1.04 / 1.01 / 1.06	0.91 / 0.88 / 0.91	1.18 / 1.16 / 1.24	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	any	detemir	other int-/long-acting insulins	both	1.01	0.89	1.13	
Fagot 2012 [31]	any	detemir	other int-/long-acting insulins	both	1.05 / 0.91 / 1.06	0.88 / 0.73 / 0.85	1.23 / 1.12 / 1.32	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	any	human int-/long-acting	other int-/long-acting insulins	both	0.91	0.76	1.08	
Fagot 2012 [31]	any	human int-/long-acting	other int-/long-acting insulins	both	0.93 / 0.89 / 0.89	0.73 / 0.65 / 0.63	1.18 / 1.21 / 1.24	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	breast	glargine	other int-/long-acting insulins	women	1.08	0.72	1.62	
Fagot 2012 [31]	breast	glargine	other int-/long-acting insulins	women	0.88 / 1.02 / 1.49	0.54 / 0.62 / 0.91	1.45 / 1.67 / 2.45	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	breast	detemir	other int-/long-acting insulins	women	1.08	0.72	1.62	
Fagot 2012 [31]	breast	detemir	other int-/long-acting insulins	women	1.13 / 1.02 / 1.04	0.66 / 0.51 / 0.48	1.96 / 2.03 / 2.26	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	breast	human int-/long-acting	other int-/long-acting insulins	women	1.03	0.56	1.88	
Fagot 2012 [31]	breast	human int-/long-acting	other int-/long-acting insulins	women	1.21 / 1.51 / -	0.56 / 0.61 / -	2.60 / 3.72 / -	cumulative dose (<14000/14000-27000/27000+ IU)
Fagot 2012 [31]	colorectal	glargine	other int-/long-acting insulins	both	0.98	0.72	1.32	
Fagot 2012 [31]	liver	glargine	other int-/long-acting insulins	both	1.07	0.72	1.59	
Fagot 2012 [31]	kidney	glargine	other int-/long-acting insulins	both	1.11	0.54	2.26	
Fagot 2012 [31]	bladder	glargine	other int-/long-acting insulins	both	1.06	0.67	1.66	
Fagot 2012 [31]	lung	glargine	other int-/long-acting insulins	both	1.10	0.78	1.57	
Fagot 2012 [31]	head+neck	glargine	other int-/long-acting insulins	both	0.91	0.48	1.72	
Fagot 2012 [31]	prostate	glargine	other int-/long-acting insulins	men	1.01	0.68	1.48	
Ferrara 2011 [32]	prostate	insulin	no insulin	men	0.80	0.70	0.90	
Ferrara 2011 [32]	breast	insulin	no insulin	women	1.00	0.90	1.20	
Ferrara 2011 [32]	lung+bronchus	insulin	no insulin	both	1.10	0.90	1.30	

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval		
Ferrara 2011 [32]	colon	insulin	no insulin	both	1.10	0.90	1.30	
Ferrara 2011 [32]	NHL	insulin	no insulin	both	1.00	0.80	1.30	
Ferrara 2011 [32]	uterus	insulin	no insulin	women	1.00	0.80	1.30	
Ferrara 2011 [32]	pancreatic	insulin	no insulin	both	3.10	2.40	4.00	
Ferrara 2011 [32]	kidney+renal pelvis	insulin	no insulin	both	1.30	0.90	1.70	
Ferrara 2011 [32]	rectal	insulin	no insulin	both	1.00	0.70	1.40	
Ferrara 2011 [32]	melanoma	insulin	no insulin	both	1.10	0.80	1.50	
hemkens 2009 [33]	any	aspartat only	human only	both	1.00 / 1.02 / 1.04	0.82 / 0.85 / 0.87	1.21 / 1.22 / 1.24	mean daily dose (10/30/50 IU mean daily dose)
hemkens 2009 [33]	any	lispro only	human only	both	0.99 / 0.98 / 0.98	0.82 / 0.83 / 0.83	1.19 / 1.16 / 1.16	mean daily dose (10/30/50 IU mean daily dose)
hemkens 2009 [33]	any	glargine only	human only	both	1.09 / 1.19 / 1.31	1.00 / 1.10 / 1.20	1.19 / 1.30 / 1.42	mean daily dose (10/30/50 IU mean daily dose)
Hense 2011 [34]	any	human only	no use human insulin	both	1.25	1.17	1.33	
Hense 2011 [34]	any	insulin analogs	no use insulin analogs	both	0.89	0.79	1.01	
Hsieh 2012 [35]	any	insulin only	metformin only	both	1.78	1.41	2.26	
Hsieh 2012 [35]	colorectal	insulin only	metformin only	both	2.14	1.23	3.72	
Hsieh 2012 [35]	lung	insulin only	metformin only	both	1.06	0.51	2.18	
Hsieh 2012 [35]	liver	insulin only	metformin only	both	1.82	1.08	3.08	
Hsieh 2012 [35]	stomach	insulin only	metformin only	both	1.86	0.78	4.42	
Hsieh 2012 [35]	pancreatic	insulin only	metformin only	both	0.69	0.09	5.55	
Hsieh 2012 [35]	breast	insulin only	metformin only	women	1.63	0.60	4.40	
Hsieh 2012 [35]	prostate	insulin only	metformin only	men	0.89	0.34	2.36	
Kostev 2012 [36]	breast	glargine	nph insulin	women	0.93	0.68	1.27	
Kostev 2012 [36]	breast	detemir	nph insulin	women	1.17	0.66	2.06	
Lai 2012 [37]	pancreatic	insulin	no insulin	both	2.20	1.40	3.45	
Lai 2012 [38]	lung	insulin	no insulin	both	1.00	0.68	1.45	
Lai 2012 [39]	hcc	insulin	no insulin	both	0.98	0.74	1.28	
Lind 2012 [40]	breast	glargine	no glargine	women	1.54	0.90	2.67	
Lind 2012 [40]	prostate	glargine	no glargine	men	1.37	0.78	2.39	
Ljung 2011 [41]	any	glargine only	non-glargine insulins only	both	1.10	0.96	1.26	
Ljung 2011 [41]	gastrointestinal	glargine only	non-glargine insulins only	both	0.86	0.61	1.23	
Ljung 2011 [41]	colorectal	glargine only	non-glargine insulins only	both	0.88	0.61	1.28	

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval		
Ljung 2011 [41]	pancreatic	glargine only	non-glargine insulins only	both	1..52	0.82	2.83	
Ljung 2011 [41]	prostate	glargine only	non-glargine insulins only	men	1.11	0.81	1.52	
Ljung 2011 [41]	breast	glargine only	non-glargine insulins only	women	1.60	1.10	2.32	
Ljung 2011 [41]	breast	glargine only	non-glargine insulins only	women	1.58	1.09	2.29	
Ljung 2011 [41]	breast	glargine only	non-glargine insulins only	women	1.60	1.07	2.39	
Ljung 2011 [41]	any	glargine only	non-glargine insulins only	both	1.10	0.90	1.35	
Ljung 2011 [41]	gastrointestinal	glargine only	non-glargine insulins only	both	0.80	0.46	1.38	
Ljung 2011 [41]	colorectal	glargine only	non-glargine insulins only	both	0.76	0.41	1.38	
Ljung 2011 [41]	pancreatic	glargine only	non-glargine insulins only	both	1.04	0.32	3.31	
Ljung 2011 [41]	prostate	glargine only	non-glargine insulins only	men	1.19	0.76	1.87	
Ljung 2011 [41]	breast	glargine only	non-glargine insulins only	women	0.87	0.41	1.85	
Morden 2011 [42]	any	glargine only	non-glargine insulins only	both	0.94	0.88	1.01	
Morden 2011 [42]	any	glargine + non-glargine	non-glargine insulins only	both	0.94	0.87	1.01	
Morden 2011 [42]	colon	glargine only	non-glargine insulins only	both	0.79	0.60	1.05	
Morden 2011 [42]	colon	glargine + non-glargine	non-glargine insulins only	both	0.95	0.74	1.23	
Morden 2011 [42]	pancreatic	glargine only	non-glargine insulins only	both	0.95	0.67	1.35	
Morden 2011 [42]	pancreatic	glargine + non-glargine	non-glargine insulins only	both	0.71	0.47	1.07	
Morden 2011 [42]	prostate	glargine only	non-glargine insulins only	men	1.12	0.88	1.42	
Morden 2011 [42]	prostate	glargine + non-glargine	non-glargine insulins only	men	0.89	0.68	1.18	
Morden 2011 [42]	breast	glargine only	non-glargine insulins only	women	1.03	0.83	1.29	
Morden 2011 [42]	breast	glargine + non-glargine	non-glargine insulins only	women	1.08	0.86	1.36	
Neumann 2012 [43]	bladder	insulin	no insulin	both	1.08	0.97	1.21	
Neumann 2012 [43]	colorectal	insulin	no insulin	both	1.05	1.01	1.11	
Neumann 2012 [43]	kidney	insulin	no insulin	both	1.09	1.00	1.20	
Neumann 2012 [43]	lung	insulin	no insulin	both	1.23	1.17	1.29	
Neumann 2012 [43]	head+neck	insulin	no insulin	both	1.24	1.14	1.36	
Neumann 2012 [43]	breast	insulin	no insulin	women	0.86	0.81	0.91	
Newton 2012 [44]	bladder	insulin	no insulin	both	1.70	1.13	2.54	
Oliveria 2008 [45]	bladder	insulin only	no insulin	both	1.09	0.72	1.64	
Oliveria 2008 [45]	liver	insulin only	no insulin	both	1.19	0.54	2.65	
Oliveria 2008 [45]	pancreatic	insulin only	no insulin	both	0.64	0.34	1.21	
Oliveria 2008 [45]	colorectal	insulin only	no insulin	both	0.99	0.74	1.33	
Oliveria 2008 [45]	colorectal	insulin only	other ad drug	both	1.48 / 1.24	0.58 / 0.57	3.78 / 2.68	time of use (past/current)

Author (country)	Outcome[‡]	Exposure	Comparator	Gender	Risk estimate[†]	95% Confidence Interval		
Redaniel 2012 [46]	breast	insulin only	no ad drugs	women	0.72	0.60	0.87	
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	women	1.14	0.54	2.39	
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	women	1.33	0.63	2.83	
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	women	1.01 / 0.54 / 2.25	0.11 / 0.18 / 0.72	8.97 / 1.68 / 6.99	duration since start exp (<1/1-5/>5 years)
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	women	1.33	0.63	2.78	
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	women	1.67	0.70	3.99	
Ruiter 2012 [47]	any	glargine only	human only	both	0.75	0.71	0.80	
Ruiter 2012 [47]	any	non-glargine analogs only	human only	both	0.85	0.82	0.89	
Ruiter 2012 [47]	colon	glargine only	human only	both	0.55	0.39	0.76	
Ruiter 2012 [47]	colon	non-glargine analogs only	human only	both	1.07	0.93	1.25	
Ruiter 2012 [47]	bladder	glargine only	human only	both	1.89	0.69	3.21	
Ruiter 2012 [47]	bladder	non-glargine analogs only	human only	both	0.48	0.34	0.69	
Ruiter 2012 [47]	respiratory	glargine only	human only	both	1.03	0.84	1.24	
Ruiter 2012 [47]	respiratory	non-glargine analogs only	human only	both	0.64	0.54	0.77	
Ruiter 2012 [47]	prostate	glargine only	human only	men	2.76	1.32	5.80	
Ruiter 2012 [47]	prostate	non-glargine analogs only	human only	men	0.83	0.70	1.03	
Ruiter 2012 [47]	breast	glargine only	human only	women	1.58	1.22	2.05	
Ruiter 2012 [47]	breast	non-glargine analogs only	human only	women	0.95	0.83	1.08	
Ruiter 2012 [47]	any	glargine	human	both	0.77	0.73	0.82	
Ruiter 2012 [47]	any	non-glargine analogs only	human	both	0.85	0.82	0.88	
Ruiter 2012 [47]	colon	glargine	human	both	0.61	0.43	0.88	
Ruiter 2012 [47]	colon	non-glargine analogs only	human	both	0.87	0.78	0.97	
Ruiter 2012 [47]	bladder	glargine	human	both	1.77	1.04	3.00	
Ruiter 2012 [47]	bladder	non-glargine analogs only	human	both	0.69	0.57	0.84	
Ruiter 2012 [47]	respiratory	glargine	human	both	0.92	0.74	1.16	
Ruiter 2012 [47]	respiratory	non-glargine analogs only	human	both	0.70	0.62	0.78	
Ruiter 2012 [47]	prostate	glargine	human	men	1.17	0.84	1.62	
Ruiter 2012 [47]	prostate	non-glargine analogs only	human	men	0.82	0.69	0.97	
Ruiter 2012 [47]	breast	glargine	human	women	1.39	1.08	1.79	
Ruiter 2012 [47]	breast	non-glargine analogs only	human	women	1.00	0.93	1.09	
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	women	0.80	0.30	2.10	
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	women	1.0 / 0.9 / 0.8 / ne	0.3 / 0.3 / 0.2 / ne	3.1 / 2.7 / 3.1 / ne	duration since start exp (<1 / 1-3 / 3-5 / >5 yrs)
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	women	1.00	0.70	1.40	
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	women	0.9 / 1.0 / 0.8 / 1.8	0.5 / 0.6 / 0.5 / 0.8	1.5 / 1.7 / 1.6 / 4.0	duration since start exp (<1 / 1-3 /3-5 / >5 yrs)

Author (country)	Outcome‡	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval		
Tseng 2012 [49]	NHL	insulin	no insulin	both	2.52	1.37	4.64	
Van Staa 2012 [50]	any excl nmsc	insulin only	metformin only	both	1.49 / 1.36 / 1.23 / 1.05 / 1.17	1.27 / 1.15 / 1.04 / 0.86 / 0.95	1.75 / 1.61 / 1.46 / 1.27 / 1.43	duration since start exp (<273 / 274-546 / 547-1001 / 1002-1547 / 1548+ days)
Yang 2010 [51]	any	insulin	no insulin	both	0.17	0.09	0.32	
Yang 2010 [51]	digestive+peritoneum	insulin	no insulin	both	0.19	0.08	0.46	

2) Case control studies (15 studies)

Author (country)	Outcome	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval		Dose/duration strata†
Bodmer 2010 [52]	breast	insulin	no insulin	women	1.74 / 1.30 / 1.51	0.95 / 0.62 / 0.76	3.21 / 2.70 / 3.01	number of prescriptions (1-9/10-29/30+ rx)
Bodmer 2011 [53]	ovarian	insulin	no insulin	women	4.67 / 1.17 / 1.46	1.07 / 0.43 / 0.54	20.42 / 3.14 / 3.98	number of prescriptions (1-9/10-29/30+ rx)
Bodmer 2012 [54]	colorectal	Insulin	no insulin	both	1.11 / 0.64 / 1.07 / 0.90	0.75 / 0.44 / 0.73 / 0.63	1.64 / 0.95 / 1.57 / 1.28	number of prescriptions (1-9/10-29/30-49/50+ rx)
Bodmer 2012 [55]	lung	Insulin	no insulin	both	1.64 / 1.16 / 1.53	1.20 / 0.84 / 1.18	2.24 / 1.59 / 1.99	number of prescriptions (1-14/10-39/40+ rx)
Bonelli 2003 [56]	pancreatic	insulin	oad	both	7.68	1.67	35.40	0.00
Chang 2012 [57]	liver	human short-acting	no use human short-acting	both	2.35	2.21	2.49	0.00
Chang 2012 [57]	colorectal	human short-acting	no use human short-acting	both	2.56	2.40	2.72	0.00
Chang 2012 [57]	lung	human short-acting	no use human short-acting	both	1.90	1.76	2.03	0.00
Chang 2012 [57]	bladder	human short-acting	no use human short-acting	both	1.11	0.96	1.28	0.00
Chang 2012 [58]	any	insulin	no insulin	both	1.97	1.85	2.09	0.00
Chang 2012 [58]	any	insulin	no insulin	both	1.03 / 1.32 / 9.94	0.95 / 1.18 / 8.93	1.12 / 1.49 / 11.08	time of use (past/recent/current)
Chang 2012 [58]	any	insulin	no insulin	both	2.23 / 1.93 / 1.73	2.05 / 1.77 / 1.57	2.43 / 2.11 / 1.90	cumulative dose (low/intermediate/high)
Chang 2012 [58]	any	insulin	no insulin	both	2.00 / 2.00 / 1.53	1.88 / 1.59 / 1.21	2.12 / 2.51 / 1.93	cumulative duration (<1/1-2/2+ years)
Chang 2012 [58]	colorectal	insulin	no insulin	both	2.67	2.29	3.12	0.00
Chang 2012 [58]	lung	insulin	no insulin	both	1.86	1.56	2.23	0.00
Chang 2012 [58]	breast	insulin	no insulin	both?	0.93	0.69	1.25	0.00
Chang 2012 [58]	prostate	insulin	no insulin	men	0.88	0.64	1.20	0.00
Chang 2012 [58]	stomach	insulin	no insulin	both	2.46	1.91	3.17	0.00
Chang 2012 [58]	pancreatic	insulin	no insulin	both	3.75	2.61	5.38	0.00
Chang 2012 [58]	liver	insulin	no insulin	both	1.98	1.71	2.31	0.00

Author (country)	Outcome	Exposure	Comparator	Gender	Risk estimate†	95% Confidence Interval		Dose/duration strata†
Chang 2012 [58]	liver	insulin	no insulin	both	1.11 / 1.74 / 10.28	0.92 / 1.32 / 7.68	1.35 / 2.31 / 13.74	time of use (past/recent/current)
Chang 2012 [58]	liver	insulin	no insulin	both	2.15 / 1.84 / 1.94	1.74 / 1.48 / 1.54	2.66 / 2.30 / 2.44	cumulative dose (low/intermediate/high)
Chang 2012 [58]	liver	insulin	no insulin	both	1.96 / 2.90 / 2.79	1.68 / 1.68 / 1.58	2.28 / 4.99 / 4.92	cumulative duration (<1/1-2/2+ years)
Cleveland 2012 [59]	breast	insulin	no insulin	women	1.15	0.40	3.40	0.00
Fortuny 2005 [60]	lymphoma	insulin	no insulin	both	0.73 / 0.36	0.23 / 0.07	2.33 / 1.79	lenght use (1-9/9+ years)
Kawaguchi 2010 [61]	hcc	Insulin	No insulin	both	2.97	1.29	6.82	0.00
Koro 2007 [62]	colon	insulin only	thiazolidinediones	both	4.46	1.05	19.00	0.00
Koro 2007 [62]	colon	insulin only	thiazolidinediones	both	1.25	0.68	2.32	0.00
Koro 2007 [62]	prostate	insulin only	thiazolidinediones	men	1.80	0.79	4.07	0.00
Koro 2007 [62]	prostate	insulin only	thiazolidinediones	men	1.09	0.61	1.95	0.00
Koro 2007 [62]	breast	insulin only	thiazolidinediones	women	1.27	0.61	2.67	0.00
Koro 2007 [62]	breast	insulin only	thiazolidinediones	women	1.00	0.56	1.77	0.00
Li 2011 [63]	pancreatic	insulin	no insulin	both	2.20	1.60	3.00	0.00
Li 2011 [63]	pancreatic	insulin	no insulin	both	2.4 / 1.2 / 0.5	1.6 / 0.7 / 0.3	3.7 / 1.9 / 0.9	lenght of use (≤3/3-9/10+ years)
Mizuno 2013 [64]	pancreatic	Insulin	No insulin	both	3.52	1.00	14.87	0.00
Mizuno 2013 [64]	pancreatic	Insulin	No insulin	both	4.77 / 2.47	1.09 / 0.71	22.34 / 9.91	lenght of use (<5/5+ years)
Mizuno 2013 [64]	pancreatic	Insulin	No insulin	both	3.50 / 2.63	0.89 / 0.72	15.15 / 10.81	cumulative dose (<30/30+ U/day)
Vinikoor 2009 [65]	rectal	insulin	no insulin	both	1.74	0.92	3.31	0.00
Vinikoor 2009 [65]	rectal	insulin	no insulin	both	2.11	1.05	4.23	0.00
Vinikoor 2009 [65]	rectal	insulin	no insulin	both	2.53	1.21	5.28	0.00
Yang 2004 [66]	colorectal	insulin	no insulin	both	1.4 / 2.9 / 4.7	0.6 / 1.1 / 1.3	2.9 / 7.7 / 16.7	cumulative duration (1-<3/3-<5/5+ years)
Yang 2004 [66]	colorectal	insulin	no insulin	both	1.21	1.03	1.42	incremental duration (1-year increment)

Supplementary Material 4: (Tables 1-14)

Presents estimates by 14 cancer sites examined in more than one study, sorted by type of exposure-comparator contrast (e.g. insulin vs. no insulin) and name of exposure. Only one risk estimate for each combination of cancer site and exposure contrast is included (chosen according to algorithm presented in article). These are the estimates preferred for inclusion in the pooled analyses, but note that pooled analyses were actually only performed for the 3 most frequently used exposure contrasts that were studied in several populations. See Supplementary Material 5 for cancer sites only examined in one study.
Abbreviations: ad, antidiabetic drug; excl, excluding; exp, exposure; Int-, intermediate-acting; ne, not estimable; niad, non-insulin antidiabetic drugs; oad, oral antidiabetic drug;

1) Any cancer (with or without exclusion of non-melanoma skin cancer)

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Yang 2010 [51]	insulin	no insulin	both	0.17	[0.09 , 0.32]
Carstensen 2012 [27]	insulin	no insulin	men	1.14	[1.08 , 1.20]
Carstensen 2013 [27]	insulin	no insulin	women	1.23	[1.16 , 1.30]
Chang 2012 [58]	insulin	no insulin	both	1.97	[1.85 , 2.09]
Insulin vs. niad:					
Currie 2009 [30]	insulin	metformin only	both	1.35	[1.19 , 1.54]
Hsieh 2012 [35]	insulin only	metformin only	both	1.78	[1.41 , 2.26]
Insulin A vs. B:					
Currie 2009 [30]	analog biphasic	glargine only	both	1.02	[0.76 , 1.37]
Fagot 2012 [31]	detemir	other int- / long-acting insulins	both	1.01	[0.89 , 1.13]
Ruiter 2012 [47]	glargine	human	both	0.77	[0.73 , 0.82]
Chang 2011 [28]	glargine	human int- / long-acting	both	0.86	[0.73 , 1.02]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	1.04	[0.93 , 1.16]
Blin 2012 [25]	glargine only	human only	both	0.59	[0.28 , 1.25]
Colhoun 2010 [29]	glargine only	non-glargine insulins only	both	1.64	[1.05 , 2.54]
Morden 2011 [42]	glargine only	non-glargine insulins only	both	0.94	[0.88 , 1.01]
Ljung 2011 [41]	glargine only	non-glargine insulins only	both	1.10	[0.96 , 1.26]
Currie 2009 [30]	human biphasic	glargine only	both	0.88	[0.66 , 1.19]
Fagot 2012 [31]	human int- / long-acting	other int- / long-acting insulins	both	0.91	[0.76 , 1.08]
Currie 2009 [30]	human long-acting only	glargine only	both	1.24	[0.90 , 1.70]
Ruiter 2012 [47]	non-glargine analogs only	human	both	0.85	[0.82 , 0.88]
Insulin A vs. B or no insulin:					
Hense 2011 [34]	insulin analogs	no use insulin analogs	both	0.89	[0.79 , 1.01]
Hense 2011 [34]	human only	no use human insulin	both	1.25	[1.17 , 1.33]

2) Breast cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Neumann 2012 [43]	insulin	no insulin	women	0.86	[0.81 , 0.91]
Carstensen 2013 [27]	insulin	no insulin	men	2.59	[0.84 , 7.94]
Carstensen 2013 [27]	insulin	no insulin	women	0.96	[0.84 , 1.09]
Ferrara 2011 [32]	insulin	no insulin	women	1.00	[0.90 , 1.20]
Chang 2012 [58]	insulin	no insulin	both?	0.93	[0.69 , 1.25]
Cleveland 2012 [59]	insulin	no insulin	women	1.15	[0.40 , 3.40]
Redaniel 2012 [46]	insulin only	no ad drugs	women	0.72	[0.60 , 0.87]
Insulin vs. niad:					
Currie 2009 [30]	insulin	metformin only	women	1.07	[0.79 , 1.44]
Koro 2007 [62]	insulin only	thiazolidinediones	women	1.27	[0.61 , 2.67]
Hsieh 2012 [35]	insulin only	metformin only	women	1.63	[0.60 , 4.40]
Redaniel 2012 [46]	insulin only	sulfonylurea only	women	1.14	[0.54 , 2.39]
Insulin A vs. B:					
Kostev 2012 [36]	detemir	nph insulin	women	1.17	[0.66 , 2.06]
Fagot 2012 [31]	detemir	other int- / long-acting insulins	women	1.08	[0.72 , 1.62]
Ruiter 2012 [47]	glargine	human	women	1.39	[1.08 , 1.79]
Chang 2011 [28]	glargine	human int- / long-acting	women	0.53	[0.21 , 1.31]
Suissa 2012 [48]	glargine	non-glargine insulins only	women	0.80	[0.30 , 2.10]
Kostev 2012 [36]	glargine	nph insulin	women	0.93	[0.68 , 1.27]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	women	1.08	[0.72 , 1.62]
Currie 2009 [30]	glargine only	non-glargine insulin	women	0.86	[0.42 , 1.75]
Colhoun 2010 [29]	glargine only	non-glargine insulins only	women	3.65	[1.05 , 12.68]
Morden 2011 [42]	glargine only	non-glargine insulins only	women	1.03	[0.83 , 1.29]
Ljung 2011 [41]	glargine only	non-glargine insulins only	women	1.58	[1.09 , 2.29]
Fagot 2012 [31]	human int- / long-acting	other int- / long-acting insulins	women	1.03	[0.56 , 1.88]
Ruiter 2012 [47]	non-glargine analogs only	human	women	1.00	[0.93 , 1.09]
Insulin A vs. B or no insulin:					
Lind 2012 [40]	glargine	no glargine	women	1.54	[0.90 , 2.67]

3) Prostate cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Carstensen 2013 [27]	insulin	no insulin	men	0.79	[0.69 , 0.90]
Ferrara 2011 [32]	insulin	no insulin	men	0.80	[0.70 , 0.90]
Chang 2012 [58]	insulin	no insulin	men	0.88	[0.64 , 1.20]
Insulin vs. niad:					
Currie 2009 [30]	insulin	metformin only	men	1.10	[0.79 , 1.52]
Koro 2007 [62]	insulin only	thiazolidinediones	men	1.80	[0.79 , 4.07]
Hsieh 2012 [35]	insulin only	metformin only	men	0.89	[0.34 , 2.36]
Insulin A vs. B:					
Ruiter 2012 [47]	glargine	human	men	1.17	[0.84 , 1.62]
Chang 2011 [28]	glargine	human int- / long-acting	men	2.37	[0.94 , 6.01]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	men	1.01	[0.68 , 1.48]
Colhoun 2010 [29]	glargine only	non-glargine insulins only	men	1.16	[0.16 , 8.50]
Morden 2011 [42]	glargine only	non-glargine insulins only	men	1.12	[0.88 , 1.42]
Ljung 2011 [41]	glargine only	non-glargine insulins only	men	1.11	[0.81 , 1.52]
Ruiter 2012 [47]	non-glargine analogs only	human	men	0.82	[0.69 , 0.97]
Insulin A vs. B or no insulin:					
Lind 2012 [40]	glargine	no glargine	men	1.37	[0.78 , 2.39]

4) Stomach cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Carstensen 2013 [27]	insulin	no insulin	men	1.23	[0.90 , 1.68]
Carstensen 2013 [27]	insulin	no insulin	women	1.43	[0.89 , 2.28]
Chang 2012 [58]	insulin	no insulin	both	2.46	[1.91 , 3.17]
Insulin vs. niad:					
Hsieh 2012 [35]	insulin only	metformin only	both	1.86	[0.78 , 4.42]
Insulin A vs. B:					
Chang 2011 [28]	glargine	human int- / long-acting	both	0.62	[0.27 , 1.42]

5) Pancreatic cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Lai 2012 [37]	insulin	no insulin	both	2.20	[1.40 , 3.45]
Carstensen 2013 [27]	insulin	no insulin	men	2.92	[2.49 , 3.42]
Carstensen 2013 [27]	insulin	no insulin	women	3.30	[2.77 , 3.93]
Ferrara 2011 [32]	insulin	no insulin	both	3.10	[2.40 , 4.00]
Chang 2012 [58]	insulin	no insulin	both	3.75	[2.61 , 5.38]
Li 2011 [63]	insulin	no insulin	both	2.20	[1.60 , 3.00]
Mizuno 2013 [64]	Insulin	No insulin	both	3.52	[1.00 , 14.87]
Oliveria 2008 [45]	insulin only	no insulin	both	0.64	[0.34 , 1.21]
Insulin vs. niad:					
Currie 2009 [30]	insulin	metformin only	both	4.63	[2.64 , 8.10]
Bonelli 2003 [56]	insulin	oad	both	7.68	[1.67 , 35.40]
Hsieh 2012 [35]	insulin only	metformin only	both	0.69	[0.09 , 5.55]
Insulin A vs. B:					
Chang 2011 [28]	glargine	human int- / long-acting	both	1.85	[1.06 , 3.22]
Morden 2011 [42]	glargine only	non-glargine insulins only	both	0.95	[0.67 , 1.35]
Ljung 2011 [41]	glargine only	non-glargine insulins only	both	1.52	[0.82 , 2.83]

6) Liver cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Lai 2012 [39]	insulin	no insulin	both	0.98	[0.74 , 1.28]
Carstensen 2013 [27]	insulin	no insulin	men	2.41	[1.93 , 3.00]
Carstensen 2013 [27]	insulin	no insulin	women	2.59	[1.58 , 4.23]
Chang 2012 [58]	insulin	no insulin	both	1.98	[1.71 , 2.31]
Kawaguchi 2010 [61]	Insulin	No insulin	both	2.97	[1.29 , 6.82]
Oliveria 2008 [45]	insulin only	no insulin	both	1.19	[0.54 , 2.65]
Insulin vs. niad:					
Hsieh 2012 [35]	insulin only	metformin only	both	1.82	[1.08 , 3.08]
Insulin A vs. B:					
Chang 2011 [28]	glargine	human int- / long-acting	both	0.76	[0.54 , 1.08]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	1.07	[0.72 , 1.59]
Insulin A vs. B or no insulin:					
Chang 2012 [57]	human short-acting	no use human short-acting	both	2.35	[2.21 , 2.49]

7) Colorectal cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Campbell 2010 [26]	insulin	no insulin	men	1.11	[0.82 , 1.51]
Campbell 2010 [26]	insulin	no insulin	women	0.94	[0.60 , 1.48]
Neumann 2012 [43]	insulin	no insulin	both	1.05	[1.01 , 1.11]
Carstensen 2013 [27]	insulin	no insulin	men	0.99	[0.86 , 1.14]
Carstensen 2013 [27]	insulin	no insulin	women	0.90	[0.75 , 1.09]
Chang 2012 [58]	insulin	no insulin	both	2.67	[2.29 , 3.12]
Oliveria 2008 [45]	insulin only	no insulin	both	0.99	[0.74 , 1.33]
Insulin vs. niad:					
Currie 2009 [30]	insulin	metformin only	both	1.69	[1.23 , 2.33]
Hsieh 2012 [35]	insulin only	metformin only	both	2.14	[1.23 , 3.72]
Insulin A vs. B:					
Chang 2011 [28]	glargine	human int- / long-acting	both	0.78	[0.49 , 1.26]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	0.98	[0.72 , 1.32]
Colhoun 2010 [29]	glargine only	non-glargine insulins only	both	1.43	[0.45 , 4.57]
Ljung 2011 [41]	glargine only	non-glargine insulins only	both	0.88	[0.61 , 1.28]
Insulin A vs. B or no insulin:					
Chang 2012 [57]	human short-acting	no use human short-acting	both	2.56	[2.40 , 2.72]

8) Colon cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Campbell 2010 [26]	insulin	no insulin	men	1.13	[0.79 , 1.61]
Campbell 2010 [26]	insulin	no insulin	women	1.04	[0.62 , 1.73]
Carstensen 2013 [27]	insulin	no insulin	men	1.00	[0.84 , 1.19]
Carstensen 2013 [27]	insulin	no insulin	women	0.90	[0.73 , 1.12]
Ferrara 2011 [32]	insulin	no insulin	both	1.10	[0.90 , 1.30]
Insulin vs. niad:					
Koro 2007 [62]	insulin only	thiazolidinediones	both	4.46	[1.05 , 19.00]
Insulin A vs. B:					
Ruiter 2012 [47]	glargine	human	both	0.61	[0.43 , 0.88]
Morden 2011 [42]	glargine only	non-glargine insulins only	both	0.79	[0.60 , 1.05]
Ruiter 2012 [47]	non-glargine analogs only	human	both	0.87	[0.78 , 0.97]

9) Rectal cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Campbell 2010 [26]	insulin	no insulin	men	1.05	[0.58 , 1.90]
Campbell 2010 [26]	insulin	no insulin	women	0.65	[0.24 , 1.75]
Carstensen 2013 [27]	insulin	no insulin	men	0.98	[0.77 , 1.24]
Carstensen 2013 [27]	insulin	no insulin	women	0.91	[0.62 , 1.32]
Ferrara 2011 [32]	insulin	no insulin	both	1.00	[0.70 , 1.40]
Vinikoor 2009 [65]	insulin	no insulin	both	1.74	[0.92 , 3.31]

10) Respiratory cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Lai 2012 [38]	insulin	no insulin	both	1.00	[0.68 , 1.45]
Neumann 2012 [43]	insulin	no insulin	both	1.23	[1.17 , 1.29]
Carstensen 2013 [27]	insulin	no insulin	men	1.28	[1.13 , 1.45]
Carstensen 2013 [27]	insulin	no insulin	women	1.31	[1.11 , 1.54]
Ferrara 2011 [32]	insulin	no insulin	both	1.10	[0.90 , 1.30]
Chang 2012 [58]	insulin	no insulin	both	1.86	[1.56 , 2.23]
Insulin vs. niad:					
Hsieh 2012 [35]	insulin only	metformin only	both	1.06	[0.51 , 2.18]
Insulin A vs. B:					
Ruiter 2012 [47]	glargine	human	both	0.92	[0.74 , 1.16]
Chang 2011 [28]	glargine	human int- / long-acting	both	1.01	[0.59 , 1.71]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	1.10	[0.78 , 1.57]
Colhoun 2010 [29]	glargine only	non-glargine insulins only	both	1.43	[0.53 , 3.88]
Ruiter 2012 [47]	non-glargine analogs only	human	both	0.70	[0.62 , 0.78]
Insulin A vs. B or no insulin:					
Chang 2012 [57]	human short-acting	no use human short-acting	both	1.90	[1.76 , 2.03]

11) Bladder cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Neumann 2012 [43]	insulin	no insulin	both	1.08	[0.97 , 1.21]
Carstensen 2013 [27]	insulin	no insulin	men	0.91	[0.75 , 1.10]
Carstensen 2013 [27]	insulin	no insulin	women	1.13	[0.77 , 1.64]
Newton 2012 [44]	insulin	no insulin	both	1.70	[1.13 , 2.54]
Oliveria 2008 [45]	insulin only	no insulin	both	1.09	[0.72 , 1.64]
Insulin A vs. B:					
Ruiter 2012 [47]	glargine	human	both	1.77	[1.04 , 3.00]
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	1.06	[0.67 , 1.66]
Ruiter 2012 [47]	non-glargine analogs only	human	both	0.69	[0.57 , 0.84]
Insulin A vs. B or no insulin:					
Chang 2012 [57]	human short-acting	no use human short-acting	both	1.11	[0.96 , 1.28]

12) Kidney cancer

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Neumann 2012 [43]	insulin	no insulin	both	1.09	[1.00 , 1.20]
Carstensen 2013 [27]	insulin	no insulin	men	1.39	[1.06 , 1.83]
Carstensen 2013 [27]	insulin	no insulin	women	2.04	[1.45 , 2.86]
Ferrara 2011 [32]	insulin	no insulin	both	1.30	[0.90 , 1.70]
Insulin A vs. B:					
Fagot 2012 [31]	glargine	other int- / long-acting insulins	both	1.11	[0.54 , 2.26]

13) Melanoma

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Carstensen 2013 [27]	insulin	no insulin	men	0.80	[0.57 , 1.12]
Carstensen 2013 [27]	insulin	no insulin	women	1.10	[0.76 , 1.60]
Ferrara 2011 [32]	insulin	no insulin	both	1.10	[0.80 , 1.50]

14) Non-Hodgkin's lymphoma (NHL)

Author (country)	Exposure	Comparator	Gender	Risk	[95% CI]
Insulin vs. no insulin:					
Carstensen 2013 [27]	insulin	no insulin	men	0.85	[0.60 , 1.19]
Carstensen 2013 [27]	insulin	no insulin	women	1.18	[0.81 , 1.73]
Tseng 2012 [49]	insulin	no insulin	both	2.52	[1.37 , 4.64]
Ferrara 2011 [32]	insulin	no insulin	both	1.00	[0.80 , 1.30]

Supplementary Material 5

Presents results for the cancer sites that were only examined in one study per exposure contrast, i.e. no pooled analyses could be performed for these cancer sites.
In addition to these cancer sites, lymphoma was examined in only one study and risk by strata of duration of exposure is presented in Appendix 6 (Fortuny 2005 [60]).
Abbreviations: HL, Hodgkin's lymphoma; Int-, intermediate-acting;

Author (country)	Outcome	Exposure	Comparator	Gender	Risk	[95% CI]
Carstensen 2013 [27]	leukaemia	insulin	no insulin	men	1.01	[0.72 , 1.43]
Carstensen 2013 [27]	leukaemia	insulin	no insulin	women	1.08	[0.70 , 1.66]
Carstensen 2013 [27]	HL	insulin	no insulin	men	1.07	[0.50 , 2.29]
Carstensen 2013 [27]	HL	insulin	no insulin	women	0.52	[0.12 , 2.22]
Carstensen 2013 [27]	multiple myeloma	insulin	no insulin	men	0.92	[0.57 , 1.49]
Carstensen 2013 [27]	multiple myeloma	insulin	no insulin	women	0.74	[0.36 , 1.52]
Carstensen 2013 [27]	brain	insulin	no insulin	men	1.00	[0.69 , 1.44]
Carstensen 2013 [27]	brain	insulin	no insulin	women	1.47	[1.00 , 2.18]
Neumann 2012 [43]	head+neck	insulin	no insulin	both	1.24	[1.14 , 1.36]
Fagot 2012 [31]	head+neck	glargine	other int- / long-acting insulins	both	0.91	[0.48 , 1.72]
Chang 2011 [28]	skin	glargine	human int- / long-acting	both	1.08	[0.48 , 2.46]
Carstensen 2013 [27]	testis	insulin	no insulin	men	0.57	[0.25 , 1.28]
Carstensen 2013 [27]	ovarian	insulin	no insulin	women	1.07	[0.76 , 1.50]
Carstensen 2013 [27]	uterus	insulin	no insulin	women	1.05	[0.82 , 1.36]
Ferrara 2011 [32]	uterus	insulin	no insulin	women	1.00	[0.80 , 1.30]
Carstensen 2013 [27]	cervical	insulin	no insulin	women	1.37	[0.89 , 2.09]
Carstensen 2013 [27]	thyroid	insulin	no insulin	men	1.38	[0.57 , 3.35]
Carstensen 2013 [27]	thyroid	insulin	no insulin	women	2.05	[1.07 , 3.90]
Carstensen 2013 [27]	oesophagus	insulin	no insulin	men	0.98	[0.67 , 1.43]
Carstensen 2013 [27]	oesophagus	insulin	no insulin	women	1.19	[0.57 , 2.49]
Ljung 2011 [41]	gastrointestinal	glargine only	non-glargine insulins only	both	0.86	[0.61 , 1.23]
Yang 2010 [51]	digestive+peritoneum	insulin	no insulin	both	0.19	[0.08 , 0.46]

Supplementary Material 6

Presents estimates for strata of dose or duration of insulin exposure for all cancer sites and exposure contrasts.
Abbreviations: ad, antidiabetic drug; excl, excluding; exp, exposure; Int-, intermediate-acting; ne, not estimable; niad, non-insulin antidiabetic drugs; nmsc, non-melanoma skin cancer; rx, prescription.
† Numbers separated by " / " are estimates by different strata of dose or duration. Note that the same study may have several dose and / or duration analyses for the same cancer site and exposure contrast.

Author (country)	Outcome‡	Exposure	Comparator	Dose / duration strata†	Risk estimates†	95% Confidence Interval (CI)		Gender	diabetes type
Chang 2012 [58]	any	insulin	no insulin	time of use (past / recent / current)	1.03 / 1.32 / 9.94	0.95 / 1.18 / 8.93	1.12 / 1.49 / 11.08	both	DM2
Chang 2012 [58]	any	insulin	no insulin	cumulative dose (low / intermediate / high)	2.23 / 1.93 / 1.73	2.05 / 1.77 / 1.57	2.43 / 2.11 / 1.90	both	DM2
Chang 2012 [58]	any	insulin	no insulin	cumulative duration (<1 / 1-2 / 2+ years)	2.00 / 2.00 / 1.53	1.88 / 1.59 / 1.21	2.12 / 2.51 / 1.93	both	DM2
Van Staa 2012 [50]	any excl nmsc	insulin only	metformin only	duration since start exp (<273 / 274-546 / 547-1001 / 1002-1547 / 1548+ days)	1.49 / 1.36 / 1.23 / 1.05 / 1.17	1.27 / 1.15 / 1.04 / 0.86 / 0.95	1.75 / 1.61 / 1.46 / 1.27 / 1.43	both	DM2
hemkens 2009 [33]	any	aspartat only	human only	mean daily dose (10 / 30 / 50 IU mean daily dose)	1.00 / 1.02 / 1.04	0.82 / 0.85 / 0.87	1.21 / 1.22 / 1.24	both	Unspecified
hemkens 2009 [33]	any	lispro only	human only	mean daily dose (10 / 30 / 50 IU mean daily dose)	0.99 / 0.98 / 0.98	0.82 / 0.83 / 0.83	1.19 / 1.16 / 1.16	both	Unspecified
hemkens 2009 [33]	any	glargine only	human only	mean daily dose (10 / 30 / 50 IU mean daily dose)	1.09 / 1.19 / 1.31	1.00 / 1.10 / 1.20	1.19 / 1.30 / 1.42	both	Unspecified
Chang 2011 [28]	any	glargine	human int- / long-acting	cumulative dose (<50 / 50-135 / 135-300 / >300 DDD)	0.81 / 0.75 / 0.79 / 1.18	0.6 / 0.5 / 0.54 / 0.83	1.07 / 1.11 / 1.16 / 1.67	both	DM2
Chang 2011 [28]	any	glargine	human int- / long-acting	mean daily dose (<0.5 / ≥0.5 DDD / day)	0.68 / 1.05	0.52 / 0.84	0.89 / 1.32	both	DM2
Chang 2011 [28]	any	glargine	human int- / long-acting	cumulative duration (<1 / ≥1 year)	0.83 / 0.91	0.69 / 0.61	1.01 / 1.36	both	DM2
Fagot 2012 [31]	any	glargine	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	1.04 / 1.01 / 1.06	0.91 / 0.88 / 0.91	1.18 / 1.16 / 1.24	both	DM2
Fagot 2012 [31]	any	detemir	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	1.05 / 0.91 / 1.06	0.88 / 0.73 / 0.85	1.23 / 1.12 / 1.32	both	DM2
Fagot 2012 [31]	any	human int- / long-acting	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	0.93 / 0.89 / 0.89	0.73 / 0.65 / 0.63	1.18 / 1.21 / 1.24	both	DM2
Bodmer 2010 [52]	breast	insulin	no insulin	number of prescriptions (1-9 / 10-29 / 30+ rx)	1.74 / 1.30 / 1.51	0.95 / 0.62 / 0.76	3.21 / 2.70 / 3.01	women	DM2
Redaniel 2012 [46]	breast	insulin only	sulfonylurea only	duration since start exp (<1 / 1-5 / >5 years)	1.01 / 0.54 / 2.25	0.11 / 0.18 / 0.72	8.97 / 1.68 / 6.99	women	DM2
Fagot 2012 [31]	breast	detemir	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	1.13 / 1.02 / 1.04	0.66 / 0.51 / 0.48	1.96 / 2.03 / 2.26	women	DM2
Fagot 2012 [31]	breast	human int- / long-acting	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	1.21 / 1.51 / -	0.56 / 0.61 / -	2.60 / 3.72 / -	women	DM2
Fagot 2012 [31]	breast	glargine	other int- / long-acting insulins	cumulative dose (<14000 / 14000-27000 / 27000+ IU)	0.88 / 1.02 / 1.49	0.54 / 0.62 / 0.91	1.45 / 1.67 / 2.45	women	DM2
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	duration since start exp (<1 / 1-3 / 3-5 / >5 yrs)	1.0 / 0.9 / 0.8 / ne	0.3 / 0.3 / 0.2 / ne	3.1 / 2.7 / 3.1 / ne	women	DM2
Suissa 2012 [48]	breast	glargine	non-glargine insulins only	duration since start exp (<1 / 1-3 / 3-5 / >5 yrs)	0.9 / 1.0 / 0.8 / 1.8	0.5 / 0.6 / 0.5 / 0.8	1.5 / 1.7 / 1.6 / 4.0	women	DM2

Author (country)	Outcome‡	Exposure	Comparator	Dose / duration strata†	Risk estimates†	95% Confidence Interval (CI)		Gender	diabetes type
Chang 2011 [28]	pancreatic	glargine	human int- / long-acting	cumulative dose (<50 / 50-135 / 135-300 / >300 DDD)	1.23 / 1.19 / 1.15 / 7.90	0.53 / 0.34 / 0.27 / 2.64	2.84 / 4.17 / 5.00 / 23.71	both	DM2
Chang 2011 [28]	pancreatic	glargine	human int- / long-acting	cumulative duration (<1 / ≥1 year)	1.75 / 2.58	0.98 / 0.50	3.12 / 13.23	both	DM2
Chang 2011 [28]	pancreatic	glargine	human int- / long-acting	mean daily dose (<0.5 / ≥0.5 DDD / day)	1.92 / 1.84	0.85 / 0.86	4.32 / 3.95	both	DM2
Li 2011 [63]	pancreatic	insulin	no insulin	lenght of use (≤3 / 3-9 / 10+ years)	2.4 / 1.2 / 0.5	1.6 / 0.7 / 0.3	3.7 / 1.9 / 0.9	both	Unspecified
Mizuno 2013 [64]	pancreatic	Insulin	No insulin	lenght of use (<5 / 5+ years)	4.77 / 2.47	1.09 / 0.71	22.34 / 9.91	both	unspecified
Mizuno 2013 [64]	pancreatic	Insulin	No insulin	cumulative dose (<30 / 30+ U / day)	3.50 / 2.63	0.89 / 0.72	15.15 / 10.81	both	unspecified
Chang 2011 [28]	prostate	glargine	human int- / long-acting	cumulative dose (<50 / 50-135 / 135-300 / >300 DDD)	1.88 / 2.06 / 5.37 / 2.16	0.30 / 0.29 / 0.71 / 0.33	11.63 / 14.7 / 40.85 / 14.10	men	DM2
Chang 2011 [28]	prostate	glargine	human int- / long-acting	cumulative duration (<1 / ≥1 year)	2.52 / 1.79	0.87 / 0.26	7.25 / 12.33	men	DM2
Chang 2011 [28]	prostate	glargine	human int- / long-acting	mean daily dose (<0.5 / ≥0.5 DDD / day)	2.95 / 1.98	0.83 / 0.47	10.43 / 8.40	men	DM2
Chang 2012 [58]	liver	insulin	no insulin	time of use (past / recent / current)	1.11 / 1.74 / 10.28	0.92 / 1.32 / 7.68	1.35 / 2.31 / 13.74	both	DM2
Chang 2012 [58]	liver	insulin	no insulin	cumulative dose (low / intermediate / high)	2.15 / 1.84 / 1.94	1.74 / 1.48 / 1.54	2.66 / 2.30 / 2.44	both	DM2
Chang 2012 [58]	liver	insulin	no insulin	cumulative duration (<1 / 1-2 / 2+ years)	1.96 / 2.90 / 2.79	1.68 / 1.68 / 1.58	2.28 / 4.99 / 4.92	both	DM2
Yang 2004 [66]	colorectal	insulin	no insulin	cumulative duration (1-<3 / 3-<5 / 5+ years)	1.4 / 2.9 / 4.7	0.6 / 1.1 / 1.3	2.9 / 7.7 / 16.7	both	DM2
Bodmer 2012 [54]	colorectal	Insulin	no insulin	number of prescriptions (1-9 / 10-29 / 30-49 / 50+ rx)	1.11 / 0.64 / 1.07 / 0.90	0.75 / 0.44 / 0.73 / 0.63	1.64 / 0.95 / 1.57 / 1.28	both	Unspecified
Oliveria 2008 [45]	colorectal	insulin only	other ad drug	time of use (past / current)	1.48 / 1.24	0.58 / 0.57	3.78 / 2.68	both	Unspecified
Bodmer 2011 [53]	ovarian	insulin	no insulin	number of prescriptions (1-9 / 10-29 / 30+ rx)	4.67 / 1.17 / 1.46	1.07 / 0.43 / 0.54	20.42 / 3.14 / 3.98	women	Unspecified
Bodmer 2012 [55]	lung	Insulin	no insulin	number of prescriptions (1-14 / 10-39 / 40+ rx)	1.64 / 1.16 / 1.53	1.20 / 0.84 / 1.18	2.24 / 1.59 / 1.99	both	Unspecified
Fortuny 2005 [60]	lymphoma	insulin	no insulin	lenght use (1-9 / 9+ years)	0.73 / 0.36	0.23 / 0.07	2.33 / 1.79	both	DM2

Supplementary Material 7

List of records excluded because of using same data as one of the records included in the review and study the same cancer site and exposure.

‡ Mannucci study [80] was in final analysis excluded because of ambiguous or insufficient reporting of the comprator group.

Excluded study	Included study
Blin 2012 [67]	Blin 2012 [25]
Li 2009 [68]	Li 2011 [63]
Silverman 1999 [69]	Li 2011 [63]
Jonasson 2009 [70]	Ljung 2011 [41]
Ljung 2012 [71]	Ljung 2011 [41]
Liao 2012 [72]	Lai 2012 [37]
Liao 2012 [73]	Chang 2012 [58]
Monami 2008 [74]	Mannucci 2010 [80] ‡
Monami 2009 [75]	Mannucci 2010 [80] ‡