Mortality among people who inject drugs: a systematic review and meta-analysis

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Objective To systematically review cohort studies of mortality among people who inject drugs, examine mortality rates and causes of death in this group, and identify participant- and study-level variables associated with a higher risk of death.
Methods Tailored search strings were used to search EMBASE, Medline and PsycINFO. The grey literature was identified through online grey literature databases. Experts were consulted to obtain additional studies and data. Random effects meta-analyses were performed to estimate pooled crude mortality rates (CMRs) and standardized mortality ratios (SMRs).
Findings Sixty-seven cohorts of people who inject drugs were identified, 14 of them from low- and middle-income countries. The pooled CMR was 2.35 deaths per 100 person–years (95% confidence interval, CI: 2.12–2.58). SMRs were reported for 32 cohorts; the pooled SMR was 14.68 (95% CI: 13.01–16.35). Comparison of CMRs and the calculation of CMR ratios revealed mortality to be higher in low- and middle-income country cohorts, males and people who injected drugs that were positive for human immunodeficiency virus (HIV). It was also higher during off-treatment periods. Drug overdose and acquired immunodeficiency syndrome (AIDS) were the primary causes of death across cohorts.
Conclusion Compared with the general population, people who inject drugs have an elevated risk of death, although mortality rates vary across different settings. Any comprehensive approach to improving health outcomes in this group must include efforts to reduce HIV infection as well as other causes of death, particularly drug overdose.

Abstracts in عربي, 中文, Français, Русский and Español at the end of each article.

Introduction

People who use drugs, especially by injection, are at higher risk of dying from both acute and chronic diseases, many of which are related to their drug use, than people who do not use these drugs. Fatal overdose and infection with human immunodeficiency virus (HIV) and other blood-borne viruses transmitted through shared needles and syringes are the most common causes of death in this group.[1] Understanding causes of death is important when setting priorities for programmes designed to reduce deaths from the use of drugs. Longitudinal studies of people who inject drugs are critical for assessing the magnitude, nature and correlates of the risk of death in this population.

A systematic review conducted in 2004 identified 30 prospective studies published between 1967 and 2004 that dealt with "problematic drug users" or people who inject drugs.[2] These reviews have consistently shown that the practice of injecting drugs is associated with an elevated risk of death, particularly from the complications of HIV infection, drug overdose and suicide. Since these reviews were conducted, the number of studies examining mortality among cohorts of people who inject drugs has risen substantially. This has made it possible to perform fine-grained analyses that were not feasible in earlier reviews. Furthermore, those earlier reviews did not examine the potential impact of study-level variables, variation across countries, or of participant-level variables that could affect both mortality rates and differences in causes of death, yet study-level evidence suggests that males who inject drugs may be at higher risk of dying than females and that different types of drugs are associated with different risks of death.[3–5] Findings from other reviews have also suggested that rates of death among people who are dependent on opioids are different from the rates of death observed in people who are dependent on stimulants such as cocaine and amphetamine type stimulants.[3–5]

In recent years the number of studies reporting on mortality among people who inject drugs has increased. Hence, the objective of this review was to determine the following:

- overall crude mortality rates (CMRs) and excess deaths across cohorts of people who inject drugs, by sex;
- causes of death across studies, particularly from drug overdose and acquired immunodeficiency syndrome (AIDS); differences in mortality rates and causes of death among HIV-positive (HIV+) and HIV-negative (HIV–) people who inject drugs;
- differences in mortality rates across cohorts by geographical location and country income level;
- mortality rates by type of drug injected (e.g. opioids versus stimulants);
- mortality rates during in-treatment and off-treatment periods.

Methods

Identifying studies

A recent series of reviews identified cohort studies among opioid, amphetamine and cocaine users to examine mortality.[3–5] In these reviews tailored search strings were used to search three electronic databases for studies published between 1980 and

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(*Submitted: 31 May 2012 – Revised version received: 26 November 2012 – Accepted: 28 November 2012*)

2012: Medline, EMBASE and PsycINFO. The search strings contained keywords and database-specific terms (MeSH headings, EMTREE terms and explode terms; Box 1). All results were limited to human subjects. We identified grey literature sources reporting on mortality by searching online grey literature databases, library databases and the web sites listed in a published technical report.[6] To make sure that no relevant papers had been missed, we sent the draft lists of the papers identified through these searches to experts for their review.

For the current study we examined all papers found in the reviews of drug-related mortality but selected only cohorts composed of people who injected opioids and other drugs. We used the strategy outlined in the preceding paragraph to further search for these cohorts. We included in the analysis only studies of drug users that included mortality data disaggregated by participants' injecting drug use; studies were included only if more than 70% of the cohort was composed of people who injected drugs.

The searches yielded a total of 5981 studies of mortality related to the use of opioids, amphetamines and cocaine. We identified another 79 articles by searching the reference lists of reviews on mortality related to drug use. Experts provided additional studies for 16 cohorts. From these 5981 articles we excluded a total of 5762: 4999 did not focus on drug dependence or mortality, 118 did not include raw data, 292 were case series, and 600 had insufficient mortality data on people who inject drugs. In total, we selected 67 cohort studies for inclusion in the analyses (Fig. 1). These studies were further assessed using STROBE reporting guidelines.[7]

Data extraction

Once we had identified all studies, one of the authors (JL) extracted the data into an Excel database (Microsoft, Redmond, United States of America) and two others rechecked them (BM, CB). This yielded the basic data set for the statistical analyses. We extracted information on the location of each study, the period of recruitment and duration of follow-up, the number of people in the cohort, the percentage of people in the cohort who injected drugs, the number of person–years (PY) of follow-up and the number of deaths.

We extracted CMRs and standardized mortality ratios (SMRs). We ex-

Box 1. **Strategy for search of the peer-reviewed literature**

Database specific search terms were developed and combined using Boolean operators as follows:

(< opioids > **OR** < cocaine > **OR** < amphetamine type stimulants > **) AND** < drug use > **AND** < mortality > **AND** < longitudinal studies >

All results were limited to human subjects and publication years between 1980 and 2012. The full search strings used for each database were as follows:

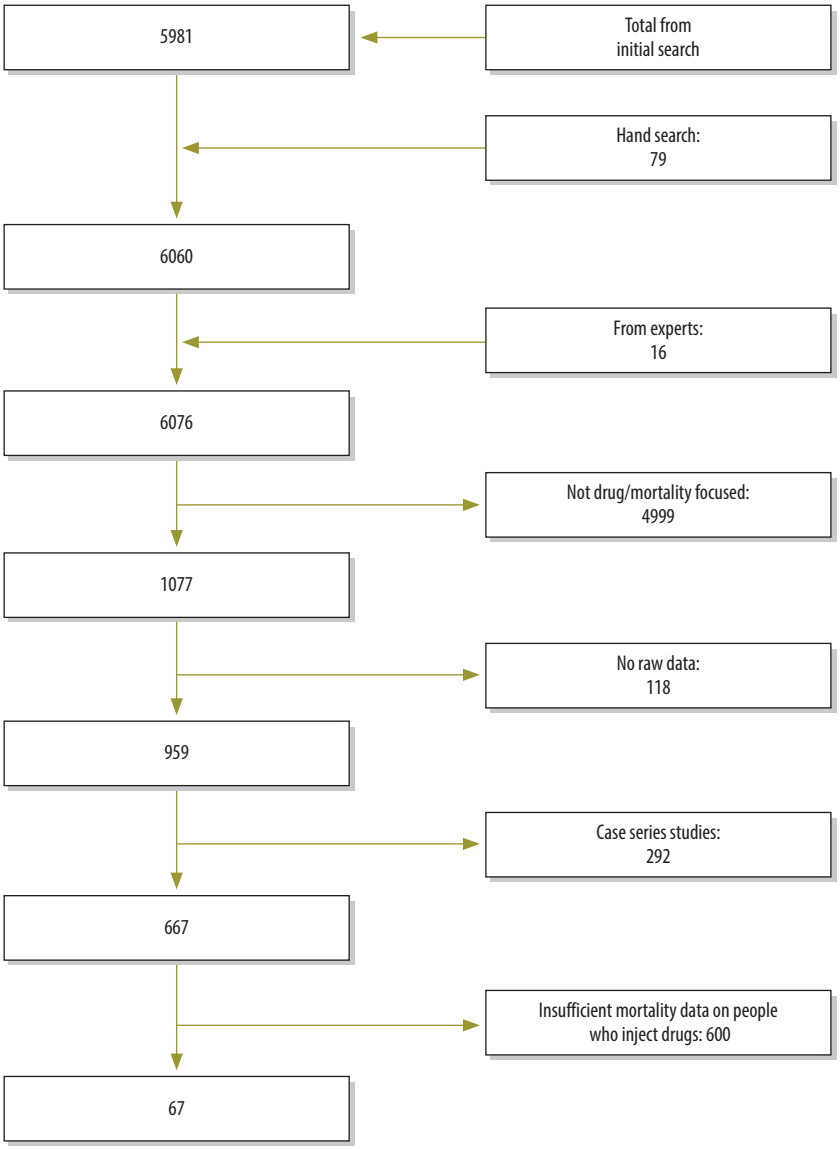
Medline: ((heroin or opiate$ OR opium OR opioid$ OR Exp Opium/ OR exp Narcotics/ OR exp Heroin Dependence/ OR exp Heroin/ OR exp Morphine/ OR exp Opioid-Related Disorders/ OR exp Opiate Alkaloids/ OR exp Methadone/ OR exp Analgesics, Opioid/) OR (Cocaine exp Cocaine-Related Disorders/ or exp Cocaine/ or exp Crack Cocaine/) OR (ATS OR amphetamine type stimulant$ OR amphetamine$ OR methamphetamine OR deoxyephedrine OR desoxyephedrine OR Desoxyn OR madrine OR metamfetamine OR methamphetamine hydrochloride OR methylamphetamine OR n-methylamphetamine OR d-amphetamine OR dextroamphetamine sulfate OR dexamphetamine OR dexedrine OR dextro-amphetamine sulfate OR dextroamphetamine sulfate OR d-amphetamine sulfate OR stimulant$ exp amphetamines/ or exp amphetamine/ or exp dextroamphetamine/ or exp p-chloroamphetamine/ or exp 2,5-dimethoxy-4-methylamphetamine/ or exp p-hydroxyamphetamine/ or exp iofetamine/ or exp methamphetamine/ or exp benzphetamine/ or exp phentermine/ or exp chlorphentermine/ or exp mephentermine/ or exp amphetamine-related disorders/)) AND (drug abuse$ OR drug use$ OR drug misuse$ OR drug dependenc$ OR substance abuse$ OR substance use$ OR substance misuse$ OR substance dependenc$ OR addict$ OR Exp Substance-related disorders/) AND (Mortal$ OR fatal$ OR death$ OR exp "death and dying"/ OR exp mortality/ OR exp hospitalization) AND ("cohort" OR "longitudinal" OR "incidence" OR "prospective" OR "follow-up" OR exp cohort studies/ OR exp longitudinal studies/ OR exp follow-up studies/ OR exp prospective studies/)

EMBASE: ((heroin OR opioid$ OR opiate$ OR opium OR exp Diamorphine/ OR exp Opiate/ OR exp Methadone treatment/ OR exp Methadone/) OR (Cocaine exp Cocaine-Related Disorders/ or exp Cocaine/ or exp Crack Cocaine/) OR (ATS OR amphetamine type stimulant$ OR amphetamine$ OR methamphetamine OR deoxyephedrine OR desoxyephedrine OR Desoxyn OR madrine OR metamfetamine OR methamphetamine hydrochloride OR methylamphetamine OR n-methylamphetamine OR d-amphetamine OR dextroamphetamine sulfate OR dexamphetamine OR dexedrine OR dextro-amphetamine sulfate OR dextroamphetamine sulfate OR d-amphetamine sulfate OR stimulant$ exp amphetamines/ or exp amphetamine/ or exp dextroamphetamine/ or exp p-chloroamphetamine/ or exp 2,5-dimethoxy-4-methylamphetamine/ or exp p-hydroxyamphetamine/ or exp iofetamine/ or exp methamphetamine/ or exp benzphetamine/ or exp phentermine/ or exp chlorphentermine/ or exp mephentermine/ or exp amphetamine-related disorders/)) AND (Drug abuse OR drug use$ OR drug misuse OR drug dependenc$ OR substance abuse OR substance use$ OR substance misuse OR substance dependenc$ OR addict$ OR exp substance abuse/ OR exp drug abuse/ OR exp analgesic agent abuse/ OR exp drug abuse pattern/ OR exp drug misuse/ OR exp drug traffic/ OR exp multiple drug abuse/ OR exp addiction/ OR exp drug dependence/ OR exp cocaine dependence/ OR narcotic dependence/ OR exp heroin dependence/ OR exp morphine addiction/ OR exp opiate addiction/) AND (Mortal$ OR fatal$ OR death$ OR exp death/ OR exp "cause of death"/ OR exp accidental death/ OR exp sudden death/ OR exp fatality/ OR exp mortality/ OR exp hospitalization/) AND ("cohort" OR "longitudinal" OR "incidence" OR "prospective" OR "follow-up" OR exp cohort analysis/ OR exp longitudinal study/ OR exp prospective study/ OR exp follow up/)

PsychINFO: (("heroin" OR "opium" OR "opiate$" OR "methadone" OR exp Opiates/ OR exp METHADONE/ OR exp HEROIN ADDICTION/ OR exp HEROIN) OR (Cocaine exp Cocaine-Related Disorders/ or exp Cocaine/ or exp Crack Cocaine/) OR (ATS OR amphetamine type stimulant$ OR amphetamine$ OR methamphetamine OR deoxyephedrine OR desoxyephedrine OR Desoxyn OR madrine OR metamfetamine OR methamphetamine hydrochloride OR methylamphetamine OR n-methylamphetamine OR d-amphetamine OR dextroamphetamine sulfate OR dexamphetamine OR dexedrine OR dextro-amphetamine sulfate OR dextroamphetamine sulfate OR d-amphetamine sulfate OR stimulant$ exp amphetamines/ or exp amphetamine/ or exp dextroamphetamine/ or exp p-chloroamphetamine/ or exp 2,5-dimethoxy-4-methylamphetamine/ or exp p-hydroxyamphetamine/ or exp iofetamine/ or exp methamphetamine/ or exp benzphetamine/ or exp phentermine/ or exp chlorphentermine/ or exp mephentermine/ or exp amphetamine-related disorders/)) AND (Drug abuse OR drug use$ OR drug misuse OR drug dependenc$ OR substance abuse OR substance use$ OR substance misuse OR substance dependenc$ OR addict$ OR Exp drug abuse/ OR exp drug addiction/ OR exp addiction/ OR exp drug usage) AND (Mortal$ OR fatal$ OR death$ OR exp "death and dying"/ OR exp mortality/ OR exp hospitalization) AND ("cohort" OR "longitudinal" OR "incidence" OR "prospective" OR "follow-up" OR Exp age differences/ OR exp cohort analysis/ OR exp human sex differences)

Note: $ indicates wildcard.

Fig. 1. **Flowchart showing study selection process for systematic review of studies on mortality in people who inject drugs**



pressed CMRs as the number of deaths per 100 PY of follow-up. We reported SMRs as calculated in the source papers. In several cases standard errors, confidence intervals (CIs) and CMRs were not reported, so we estimated them using standard calculations. We also put into the database CMRs and SMRs that were reported according to sex, HIV status, treatment status and type of drug injected, as well as data on deaths from drug overdose or AIDs-related causes.

We included in the analyses studies that specified treatment status if they classified the data by mutually exclusive treatment groups or periods. We only included studies in which the exact dates of entry into and exit from the study had been recorded and used to calculate the number of PYs, the number of deaths and mortality rates.

Statistical analysis

We performed meta-analyses to estimate pooled all-cause CMRs and all-cause SMRs, and pooled estimates of deaths from specific causes, as in previous reviews.[8] To perform the meta-analyses we used the "metan" command in STATA version 10.1 (StataCorp LP, College Station, USA). The "metan" command uses inverse-variance weighting to calculate random effects pooled summary estimates and their confidence limits, true effect differences between studies and study heterogeneity.[9,10] Random effects models allow for heterogeneity between and within studies. We expected high levels of heterogeneity between studies because of the marked differences between the samples of people injecting drugs; accordingly, we applied a random effects model to all analyses. The appropriateness of this a priori decision was confirmed by the resultant χ^2 and the I-squared statistic. To further investigate this heterogeneity, when the data permitted we divided the cohorts into subgroups and used CMR ratios to compare differences in mortality.[11] We made comparisons between subgroups as follows: sex (male versus female); primary drug injected at baseline (opioids versus stimulants); HIV status (HIV+ versus HIV−); and treatment for drug dependence (in-treatment period versus off-treatment period).

We examined the following as potential sources of heterogeneity in CMRs or SMRs using random effects univariate meta-regressions in STATA: geographic region, country income group (based on World Bank categories), percentage of sample that injected drugs, were male or were HIV+ at baseline; presence of opioid users in the cohort; and the year in which the follow-up period ended.[12,13]

Results

We included 67 cohorts in the analysis; 14 were from low- and middle-income countries (Table 1). Studies from Europe, North America and Australasia were the most common; nine studies were from Asia and one was from South America. The pooled CMR across the 65 cohorts for which a CMR was provided was 2.35 deaths per 100 PY (Fig. 2). Cohorts from Asia had the highest pooled CMRs (5.25), followed by the cohorts from North America (2.64) and western Europe (2.31); cohorts from Australasia had the lowest pooled CMR (0.71).

SMRs were reported for 31 cohorts; their pooled SMR was 14.68 (Fig. 3). Since the heterogeneities (I^2) of the pooled CMR and SMR were both very high (98.6% and 98.3%, respectively), we stratified estimates by subgroups.

Sex differences in mortality

Thirty-seven studies presented CMRs by sex.[14,17–19,21–24,26,28,30–32,34,36–38,43,45–50,52,54,57,58,62,66–72,74] The pooled CMR ratio for males versus females was 1.32 (Fig. 4), which suggests that crude mortality was higher among males. Nineteen studies reported SMRs by sex;[14,17,21,24,26,28,30,32,34,38,43,46,52,54,58,66,67,70,74] the pooled

Table 1. **Studies included in this systematic review of studies on mortality among people who inject drugs**

Study	Country	Country income	Sampling frame	*n*	People who inject drugs (%)	Males (%)	Drug(s) used	Recruitment period	End of follow-up period	PYs of follow-up	CMR	95% CI	SMR	95% CI
Antolini et al. (2006)[14]	Italy	High	DTS	4644	100	79.1	O, S	1975–1999	1999	39 667	2.01	1.80–2.16	13.01	12.11–13.91
Azim et al. (2008)[15]	Bangladesh	Low	DTS	552	100	100	O	2002–2004	2007	901.6	6.32	4.68–7.96	–	–
Azim et al. (2009)[16]	Bangladesh	Low	DTS	675	100	100	O	2005–2007	2007	1191.7	3.52	2.46–4.59	–	–
Bargagli et al. (2001)[17]	Italy	High	DTS	11 432	84	82.2	O	1980–1995	1997	80 787	2.15	2.05–2.25	17.3	16.5–18.2
Bauer et al. (2008)[18]	Austria	High	DTS	114	*99*[a]	58.8	O	1998–1999	2004	534.8	5.42	3.45–7.40	29.13	19.27–44.04
Brancato et al. (1995)[19]	Italy	High	DTS	138	100	76.8	O	1985	1994	1272	2.04	1.26–2.83	–	–
Cardoso et al. (2006)[20]	Brazil	Middle	NSP	478	100	78.7	S	2000–2001	2001	612	2.77	1.45–4.09	–	–
Ciccolallo et al. (2000)[21]	Italy	High	DTS	4260	100	78.0	–	1975–1995	1995	28 424	2.26	2.08–2.43	30.7	17.3–44.0
Clausen et al. (2008)[22]	Norway	High	DTS	3789	90–95	68.1	O	1997–2003	2003	10 934	1.95	1.7–2.23	–	–
Cornish et al. (2010)[23]	United Kingdom	High	HC	5577	≥ *70*[b]	69	O	1990–2005	2005	17 731.5	1.00	0.86–1.15	–	–
Copeland et al. (2004)[24]	United Kingdom	High	DTS	660	100	67.4	–	1980–2001	2001	6244	2.45	2.06–2.84	17.45	14.59–20.3
Davoli et al. (2007)[25]	Italy	High	DTS	10 454	72	80	O	1998–2001	2001	13 538.2	0.74	0.59–0.88	–	–
Degenhardt et al. (2009)[26]	Australia	High	DTS	42 676	≥ *70*[b]	–	O	1985–2006	2006	425 998	0.89	0.86–0.92	6.4	6.2–6.6
DiGiusto et al. (2004)[27]	Australia	High	DTS	1244	≥ *70*[b]	65.0	O	1998	2002	394	1.27	0.4–2.29	–	–
Eskild et al. (1993)[28]	Norway	High	T&C	1009	100	64.0	O, S	1985–1991	1991	3136.4	2.77	2.22–3.42	31	24.6–37.4
Esteban et al. (2003)[29]	Spain	High	DTS	1487	85	–	O	1990–1997	1997	4352	3.68	3.11–4.25	–	–
EMCDDA (2011)[30]	Bulgaria	Middle	DTS	652	> 80	81.6	O	1999	2008	6011	1.18	0.91–1.46	–	–
EMCDDA (2011)[30]	Croatia	Middle	DTS	3059	> 73	78.0	O	2000–2006	2007	15 968	1.09	0.93–1.25	10.3	8.9–12
EMCDDA (2011)[30]	Latvia	Middle	DTS	3644	> 98	80.0	O	2000–2009	2009	21 294	1.60	1.43–1.77	9.0	8.0–10.0
EMCDDA (2011)[30]	Romania	Middle	DTS	2707	> 94	30.8	O	2001–2006	2010	20 188	0.57	0.47–0.68	6.5	5.4–7.7
EMCDDA (2011)[30]	Sweden	High	DTS	678	> 72	–	O	1981–1988	2007	10 307	3.33	2.98–3.68	27.6	24.9–30.7
Evans (2012)[31]	USA	High	OR	644	100	68.3	O, S	1997–2007	2007	4167	0.91	0.62–1.20		
Ferri et al. (2007)[32]	Italy	High	DTS	10 376	72	85.6	O	1998–2001	2001	15 369	–	–	7.77	6.7–8.95
Fingerhood et al. (2006)[33]	USA	High	DTS	175	100		O, S	1994–1998	5 years[c]	742.5	7.14	5.22–9.06	–	–
Frischer et al. (1997)[34]	United Kingdom	High	DTS	459	100	99.4	O	1982–1993	1994	2547	2.08	1.52–2.64	22	16.5–28.8
Fugelstad et al. (1995)[35]	Sweden	High	DTS, other	472	100	–	O, S	1986–1990	1990	1793	3.85	2.94–4.76	–	–
Fugelstad et al. (1997)[36]	Sweden	High	DTS	1640	≥ 70[a]	69.2	O, S	1981–1988	1992	10 772	1.99	1.72–2.25	–	–
Fugelstad et al. (1998)[37]	Sweden	High	DTS	101	100	55.4	O	1986–1988	1993	515.3	7.76	5.54–10.58	–	–

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Study	Country	Country income	Sampling frame	*n*	People who inject drugs (%)	Males (%)	Drug(s) used	Recruitment period	End of follow-up period	PYs of follow-up	CMR	95% CI	SMR	95% CI
Galli & Musicco (1994)[38]	Italy	High	DTS	2432	100	78.3	O	1980–1998	1991	16 415	2.52	2.28–2.77	20.5	20.02–24.34
Goedert et al. (1995)[39]	Italy	High	DTS	4962	99[d]	–	O	1980–1990	1990	21 130	1.57	1.41–1.75	–	–
Goedert et al. (2001)[40]	USA	High	DTS	6570	100	66.0	–	1987–1991	1998	28 900.2	4.67	4.42–4.92	–	–
Golz et al. (2001)[41]	Germany	High	DTS	178	100	58.0	–	1996–2000	2000	805	4.22	2.80–5.64	–	–
Haarr & Nessa (2007)[42]	Norway	High	DTS	146	100	70.0	O	1997–2006	2006	574	1.92	0.95–3.44	–	–
Hickman et al. (2003)[43]	United Kingdom	High	DTS	881	76	74.5	O	1997–1999	2001	2075	1.59	1.13–2.23	–	–
Jafari et al. (2010)[44]	Islamic Republic of Iran	Middle	DTS	66	100	–	O	–	–	196	4.08	1.25–6.91	–	–
Jarrin et al. (2007)[45]	Spain	High	PR	6575	100	77.2	–	1987–1996	2004	73 901	2.02	1.92–2.12	–	–
Lejckova et al. (2007)[46]	Czech Republic	High	DTS	12 207	80	67.5	O, S	1997–2002	2002	38 131.2	0.84	0.75–0.93	8.15	7.28–9.09
Liu et al. (2011)[47]	China	Middle	DTS	860	95.2	96.1	O	2005–2011	2011	2192.9	6.85	5.79–7.98		
Lumbreras et al. (2006)[48]	Spain	High	DTS, other	3247	100	77.4	–	1990–1996	2002	26 826	2.18	2.00–2.36	–	–
Manfredi et al. (2006)[49]	Italy	High	DTS	1214	100	75.5	O	1977–1996	2002	13 280.3	2.04	1.8–2.3	–	–
McAnulty et al. (1995)[50]	USA	High	OR, HC	1769	100	73.3	–	1989–1991	1992	3149	1.05	0.69–1.41	8.3	5.71–11.66
Mezzelani et al. (1998)[51]	Italy	High	DTS	6248	100	–	–	1991	1991	6158.5	2.91	2.48–3.33	14.28	12.28–16.56
Miller et al. (2007)[52]	Canada	High	SIF	572	100	53.1	O, S	1966–2004	2004	1608	1.37	0.80–1.94	16.4	9.1–27.1
Moroni et al. (1991)[53]	Italy	High	DTS	2279	100	–	O	1981–1988	1989	13 069	2.43	2.16–2.69	–	–
Moskalewicz et al. (1996)[54]	Poland	Middle	DTS	656	100	74.2	O	1983–1992	1992	3594	2.28	1.81–2.83	12.06	9.6–15.0
Muga et al. (2007)[55]	Spain	High	DTS	1181	100	79.5	O	1987–2004	2004	10 116	3.74	3.38–4.14	–	–
Nyhlén (2011)[56]	Sweden	High	DTS	561	79	68	O, S	1970–1978	2006	15 203.1	1.30	1.12–1.48	5.94	5.5–6.8
O'Driscoll et al. (2001)[57]	USA	High	DTS, other	2849	100	63.9	O, S	1994–1997	1997	4591	1.59	1.22–1.96	–	–
Oppenheimer et al. (1994)[58]	United Kingdom	High	DTS	128	100	72.7	O	1969	1991	2349.7	1.83	1.28–2.38	11.9	8.64–16.09
Quan et al. (2007)[59]	Thailand	Middle	DTS	346	100	93.1	O, S	1999	2002	571.4	3.85	2.42–5.83	13.9	8.71–21.04
Quan et al. (2010)[60]	Viet Nam	Middle	DTS	894	100	100	O	2005	2007	710.1	6.30	4.60–8.50	13.4	11.4–15.3
Rahimi-Movaghar et al. (2009)[61]	Islamic Republic of Iran	Middle	DTS	79	100	–	O	2007	2007	20.7	4.83	0–14.30	–	–
Reece (2010)[62]	Australia	High	DTS	2773	100	72.8	O	2000–2007	2007	9362.4	0.50	0.36–0.65	–	–

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Study	Country	Country income	Sampling frame	*n*	People who inject drugs (%)	Males (%)	Drug(s) used	Recruitment period	End of follow-up period	PYs of follow-up	CMR	95% CI	SMR	95% CI
Sánchez-Carbonell et al. (2000)[63]	Spain	High	DTS	135	88	71.0	O	1985	1995	1205.9	3.4	2.36–4.44	28.58	14.65–42.65
Seaman et al. (1998)[64]	United Kingdom	High	DTS	316	100	100	O	1983–1994	1994	1416.9	2.33	1.6–3.27	–	–
Solomon et al. (2009)[65]	India	Middle	DTS, other	1158	100	100	O	2005–2006	2008	1998	4.25	3.35–5.16	11.1	8.85–13.7
Sørensen et al. (2005)[66]	Denmark	High	DTS	101	100	67.3	O	1980–1984	1999	1232.3	3.49	2.44–4.53	15.75	11.4–21.2
Stenbacka et al. (2007)[67]	Sweden	High	Multiple	817	83	79.2	O, S	1967	2003	22 468.2	2.12	1.93–2.31	4.38	3.99–4.78
Stoov et al. (2008)[68]	Australia	High	OR, SB	220	100	56.4	O, S	1990–1995	2006	3151	0.83	0.56–1.21	–	–
Tait et al. (2008)[69]	Australia	High	DTS	894	≥ 70[b]	59.6	O	2001–2001	2005	4166.9	0.54	0.28–0.72	–	–
van Haastrecht et al. (1996)[70]	Netherlands	High	DTS, other	509	100	61.9	O, S	1985–1992	1993	2229	3.23	2.56–4.07	24.8	19.41–31.23
Vlahov et al. (2005)[71]	USA	High	OR, SB	3593	100	77.3	O, S	1988	2005	25 736	4.50	4.24–4.76	–	–
Vlahov et al. (2008)[72]	USA	High	OR, SB	2089	100	62.3	O, S	1997–1999	2002	8629.3	0.71	0.54–0.88	–	–
Zabranksy et al. (2011)[73]	Czech Republic	High	OR	151	100	43	O, S	1996–1998	2008	1659.7	0.48	0.15–0.81	14.4	9.31–19.49
Zaccarelli et al. (1994)[74]	Italy	High	DTS	2029	100	75.5	–	1985–1991	1991	7872.2	2.30	1.96–2.63	31.92	27.44–36.93
Zhang et al. (2005)[75]	China	Middle	DTS	376	100	82.8	O	2002	2003	382.4	7.73	4.87–10.6	47.62	31.63–68.71

CI, confidence interval, CMR, crude mortality rate; DTS, drug treatment service; HC, health clinic; NSP, needle and syringe programme; O, opioids; OR, outreach; PR, HIV prevention service; PY, person–years; S, stimulants; SB, snowballing; SIF, supervised injecting facility; SMR, standardized mortality ratio; T&C, HIV testing and counselling; USA, United States of America.

[a] Not explicitly stated, but implied in the paper.

[b] The proportion of subjects who injected drugs was not reported but was assumed to be at least 70% because of the predominance of injecting as a route of administration among opioid-dependent people in this country.

[c] Subjects were followed for 5 years after the date of enrolment.

[d] Data on history of drug use was available for 62% of the subjects, and of these, 99% had a history of injecting drugs.

Note: Some CMRs and PYs of follow-up were calculated (formulae available from the corresponding author).

Fig. 2. **Crude mortality rates for people who inject drugs, by region**

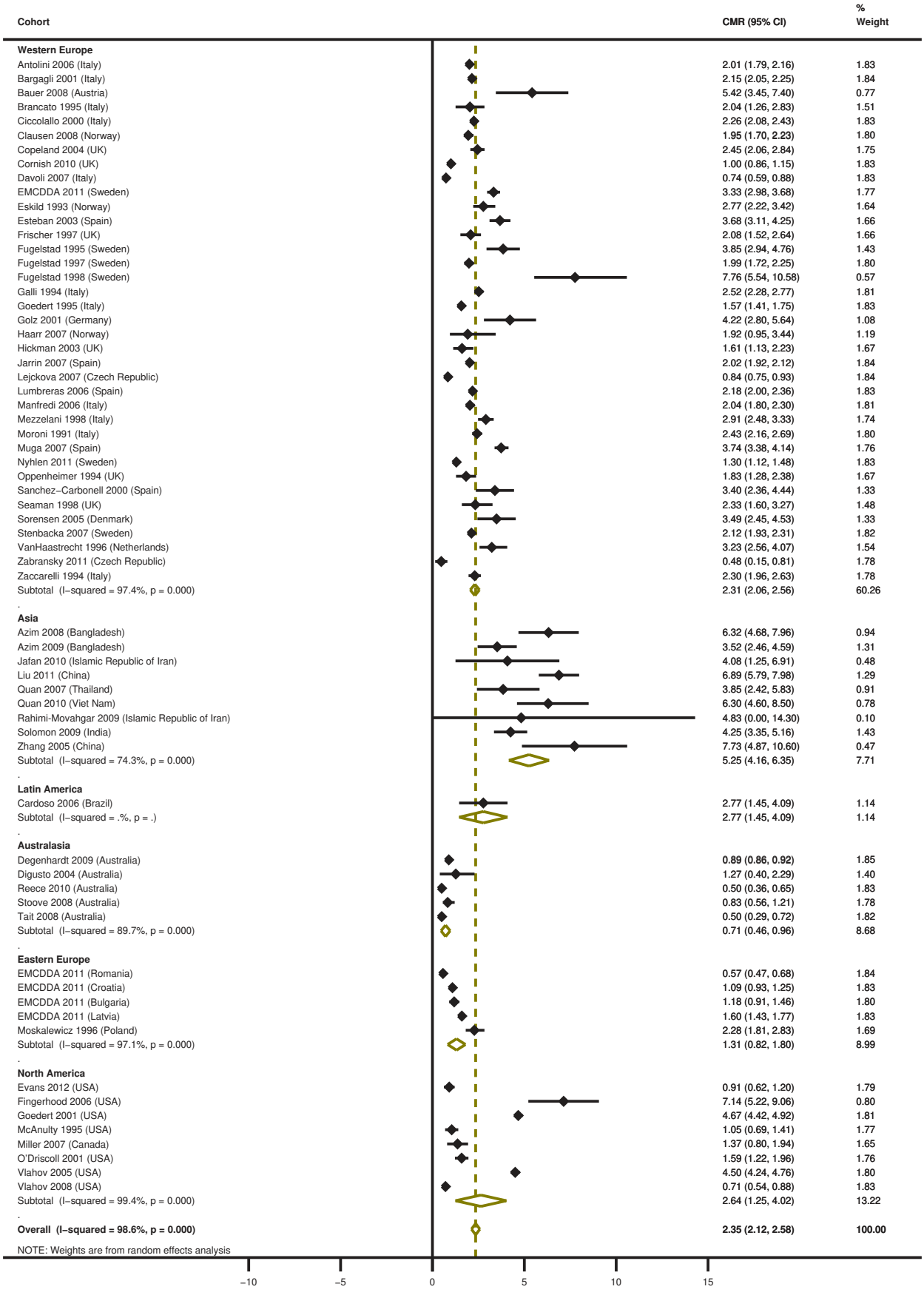

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; CMR, crude mortality rate.

Fig. 3. **Standardized mortality ratios for people who inject drugs, by region**

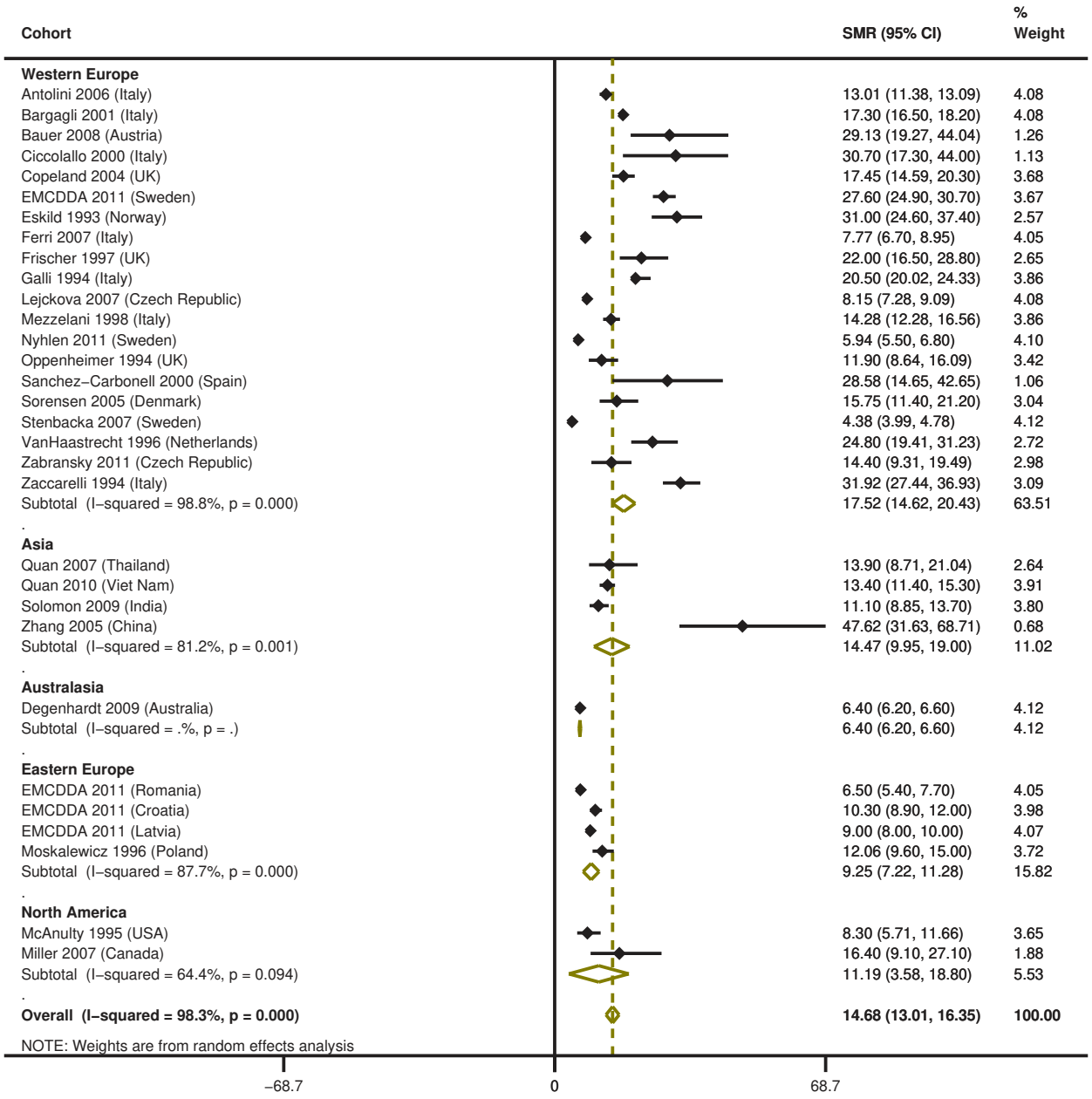

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; SMR, standardized mortality ratio.

CMR ratio suggests that females had significantly greater excess mortality than males in similar age groups in the general population (Fig. 5). Only two of the nineteen studies presented SMRs for males that were greater than those for females.[30,74]

Causes of death

Several studies reported specific causes of death. The pooled CMR for death from drug overdose was 0.62 per 100 PY across 43 studies (Fig. 6). Eleven studies reported CMRs for death from drug overdose by sex: overall the CMR was 1.38 times higher (Fig. 7) among males than among females.[14,17,19,21,24,32,38,49,52,57,58]

In 20 studies CMRs were provided separately for people who inject drugs according to their HIV status.[15,16,18,28,34,36–40,45,48,49,55,57,60,65,70,72,74] All-cause mortality was three times higher among HIV+ than among HIV– subjects (CMR ratio: 3.15) (Fig. 8). Much of this elevated mortality appeared to result from AIDS deaths among HIV+ users of injecting drugs. The pooled estimate of AIDS-related mortality for the 16 studies for which data were available was 2.55 per 100 PY (Fig. 9).[28,33–36,38–41,48,49,60,65,70,72,74] When we examined mortality from causes other than AIDS, we found it to be 1.63 times higher among HIV+ than among HIV– people who inject drugs (Fig. 10).[28,34,36,38–40,48,49,60,65,70,72,74]

Mortality from drug overdose was presented by HIV status in 9 studies.[28,34,36,38,39,49,65,70,74] Pooled estimates showed mortality to be twice as high among HIV+ than among HIV– people who inject drugs (CMR ratio: 1.99) (Fig. 11). Further analyses across 13 studies conducted on HIV+ people who inject drugs showed no significant

Fig. 4. **Ratios of crude mortality rates in males versus females who inject drugs**

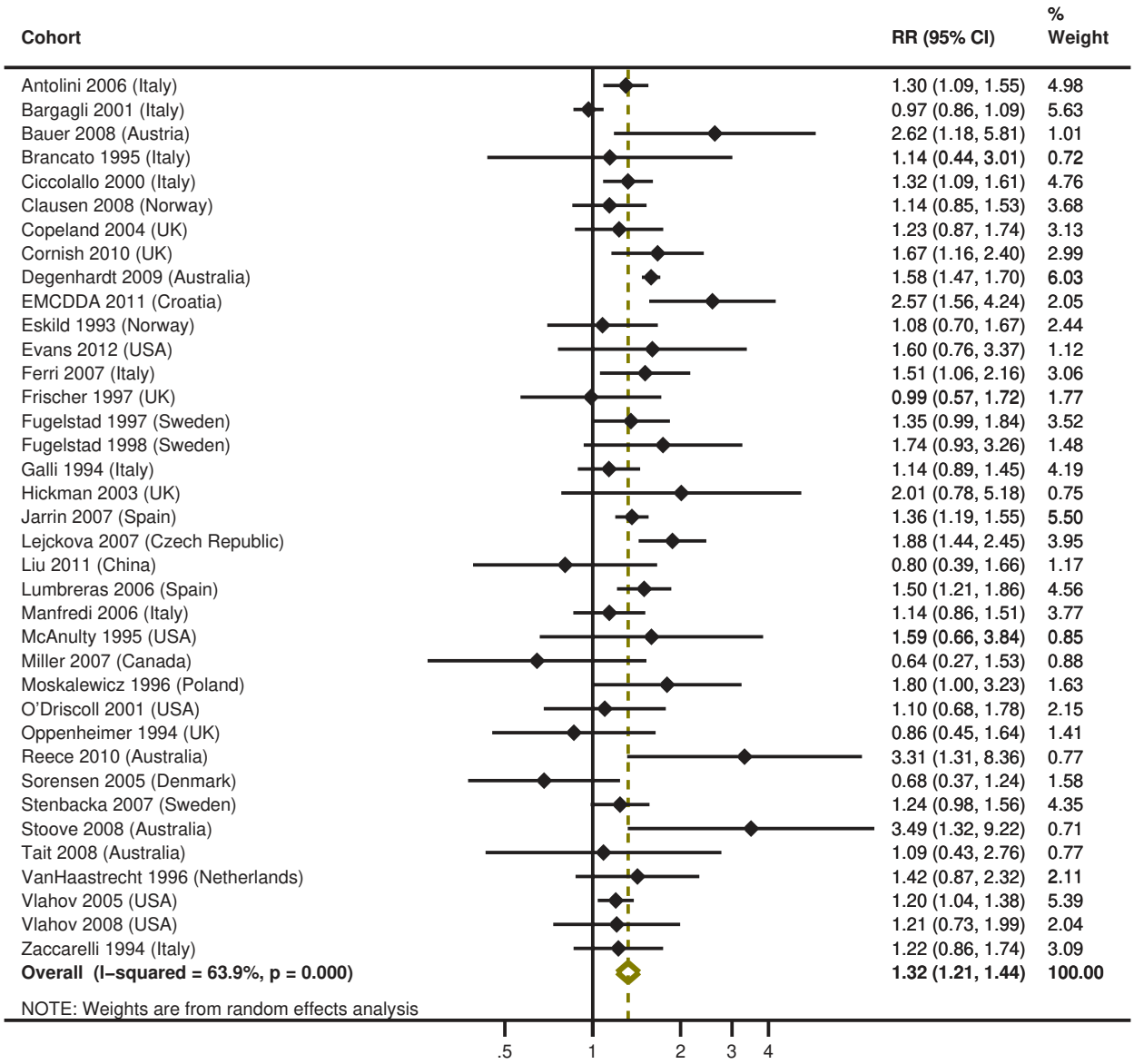

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; RR, relative risk.

difference in deaths from drug overdose and from AIDS in this group (CMR ratio: 1.35; $P = 0.554$) (Fig. 12).[28,33–36,38,39,41,49,65,70,71,74]

Only four studies presented data by sex and HIV status.[37,47,49,74] They showed no significant difference in CMRs between HIV+ males and HIV+ females who inject drugs (CMR ratio: 1.13; Fig. 13), but HIV– males had a pooled CMR 1.81 times greater than that of HIV– females who inject drugs (Fig. 14).

Mortality by primary drug injected at baseline

Five studies estimated mortality by primary drug injected (opioids versus stimulants) (Table 2). Pooled estimates of all-cause mortality by primary type of drug injected showed no overall difference across studies (CMR ratio: 1.25; 95% CI: 0.60–2.61; $P = 0.553$).[36,46,57,70,71] The same was true of studies of mortality resulting from drug overdose (CMR ratio: 1.85; 95% CI: 0.75–4.56; $P = 0.18$). In three of the four studies mortality associated with drug overdose was higher among people injecting opioids than among those injecting stimulants.[36,46,71] In the fourth study, people who injected primarily stimulants had higher rates of drug overdose; however, the deaths from overdose in this group were later shown to have been caused by opioid use.[57]

Mortality according to treatment

Six studies provided information on mortality during in-treatment and off-treatment periods at follow-up: the meta-analysis suggested that mortality was 2.52 times higher during off-treatment periods than during in-treatment periods (Fig. 15).[22,23,25,26,35,37]

Heterogeneity in mortality

We performed univariate analyses to determine if the heterogeneity in overall CMRs and SMRs could be explained by participant characteristics and methodological variables. The results showed that high-income countries had lower

Fig. 5. **Ratios of standardized mortality ratios for males versus females who inject drugs**

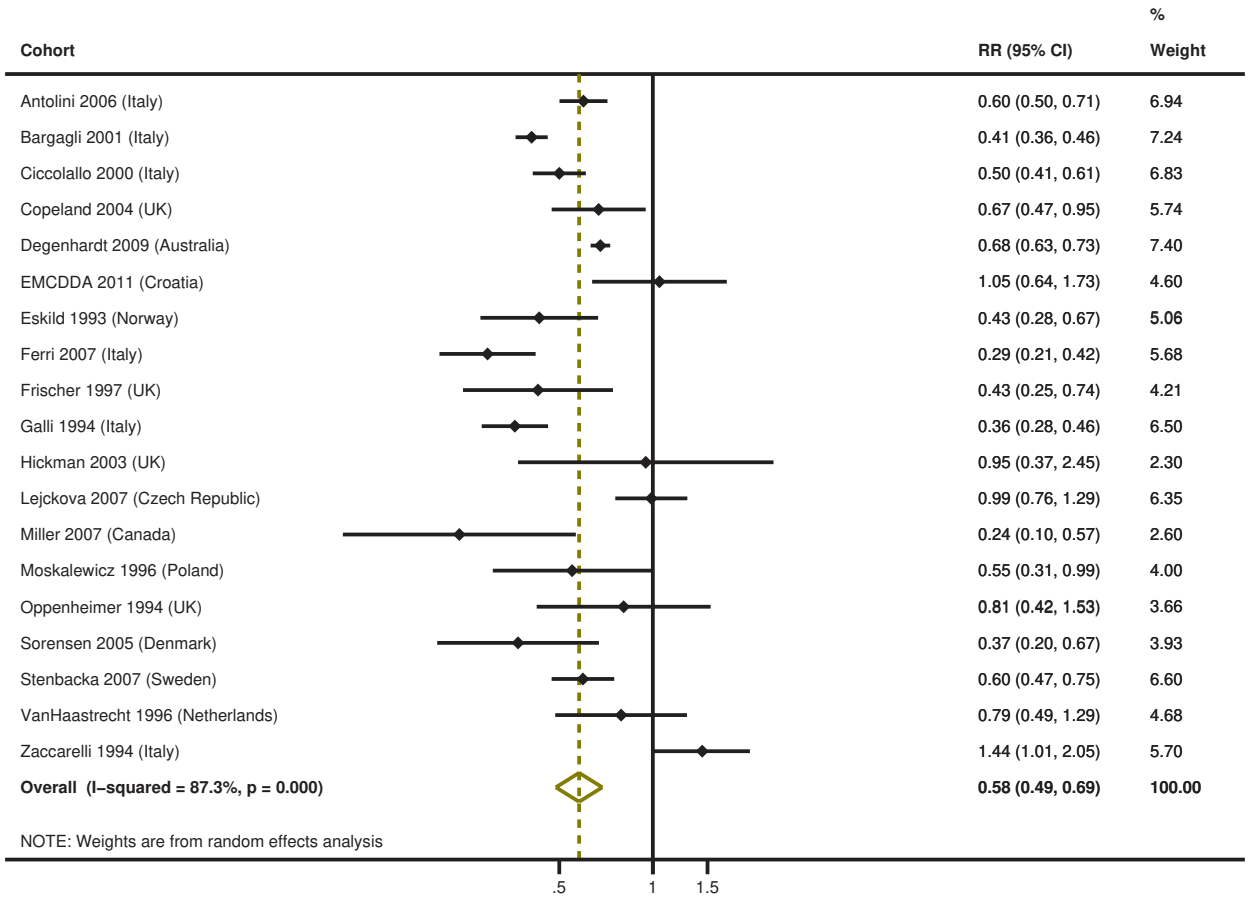

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; RR, relative risk.

CMRs than low- and middle-income countries (Fig. 16). Cohorts with greater proportions of males and HIV+ participants at baseline also had higher CMRs. Cohorts whose follow-up periods ended in more recent years had lower SMRs (Table 3). Study data were not sufficient to allow for multivariate analyses.

Discussion

Although previous reviews have examined mortality among people who inject drugs, to our knowledge this is the most comprehensive systematic review of the topic and the first to employ novel approaches to search for the available evidence. These approaches ranged from standard searches of the peer-reviewed literature to comprehensive searches of the non-peer reviewed literature and multiple expert consultations, as well as examination of both participant- and study-level factors potentially associated with the risk of death.

The pooled CMR of 2.35 deaths per 100 PY provides evidence of the high mortality associated with injecting drug use. The pooled SMR of 14.68 also shows that mortality is much higher in those who inject drugs than in the general population. Differences by sex were evident: across all studies that reported mortality by sex, males had higher CMRs, yet females who inject drugs had a much higher elevation in mortality relative to their age-matched peers in the general population than did males who inject drugs.

Most of the cohorts identified were from 14 high-income countries; together these 14 counties represent 78% of the total estimated population of people who inject drugs in such countries.[76] Studies from only 11 low or middle income countries were identified; these countries account for only 40% of the estimated number of people injecting drugs in low- or middle-income countries.[76]

Although pooled CMRs were higher among people injecting drugs in low- and middle-income countries rather than high-income countries, we observed no significant difference in pooled SMRs. This suggests that the higher CMRs may reflect higher overall mortality in the general population in low- and middle-income countries than in high-income countries. The lowest and highest mortality rates were documented in cohorts in Australasia and Asia, respectively. Differences across high-income countries probably reflect differences in HIV infection prevalence, coverage of HIV prevention and coverage of opioid agonist maintenance treatment.[76,77]

Drug overdose and AIDS-related mortality were by far the most common causes of death. The pooled CMR for death from drug overdose was 0.62 per 100 PY, higher among males than females who inject drugs, and higher among HIV+ people who inject drugs than among those who were HIV−. In three of the four studies comparing drug overdose among people injecting opioids compared to those injecting stimulants, CMRs were higher among the former group, as expected.[36,46,71] In

Fig. 6. **Crude mortality rates for death from drug overdose in people who inject drugs**

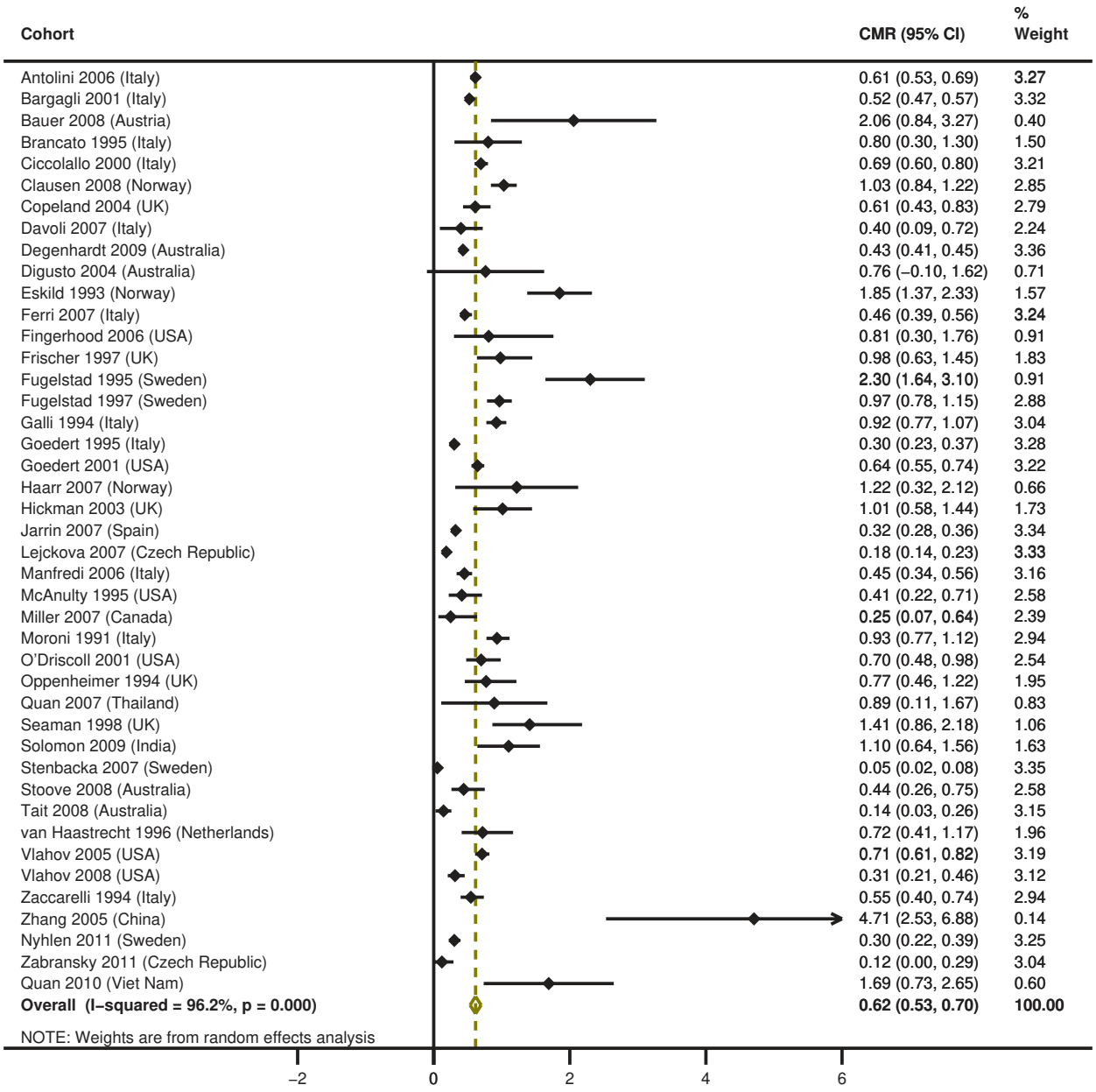

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; CMR, crude mortality rate.

a fourth study, however, drug overdose was higher among people who injected stimulants,[57] although further investigation revealed that the deaths from overdose in this group were more often linked to the injection of opioids than to the injection of stimulants. This finding highlights the fact that people who inject drugs often use more than one drug type, even if they have a particular drug of choice.

The prevalence of HIV infection varied widely. As expected, overall mortality was much higher among HIV+ than among HIV– people who inject drugs (pooled CMR ratio: 3.15), but mortality from causes other than AIDS was also higher among those who were HIV+. Overdose-related mortality was also higher among HIV+ people who inject drugs in many cohorts. These differences in mortality may reflect differences in risky behaviour, physical health and social disadvantage.

The observational evidence examined in this review is consistent with the evidence from randomized controlled trials that opioid agonist maintenance treatment is associated with a reduced risk of death.[78] Among cohorts for which in-treatment and off-treatment periods were carefully tracked, mortality rates were around 2.5 times higher in off-treatment periods than in in-treatment periods. Variation in exposure to treatment could also explain differences between cohorts in mortality from drug overdose, although this variation was not explicitly measured across cohorts.

The prevention of HIV transmission among people who inject drugs is clearly a public health priority.[79,80] There is growing evidence that opioid agonist maintenance treatment, antiretroviral treatment and needle and syringe programmes reduce HIV transmission.[81–83] These interventions have been implemented in many countries, but

often on a limited scale only.[77] Clearly, however, AIDS is only one of several common causes of death in this group: a comprehensive approach to improving health outcomes among people who inject drugs must also include efforts to reduce other causes of death frequently found among them, particularly drug overdose.[84]

Limitations of the evidence

Evidence on mortality rates among users of injecting drugs is still predominantly from high-income countries, particularly in western Europe. Interestingly, however, this review has shown that despite marked differences in CMRs across countries, the extent to which this mortality exceeds that of the general population may show less pronounced differences. It would be inappropriate to assume that mortality is equally high among all people who inject drugs. New research in this area is needed, especially

Fig. 7. **Ratios of crude mortality rates for death from drug overdose in males versus females who inject drugs**

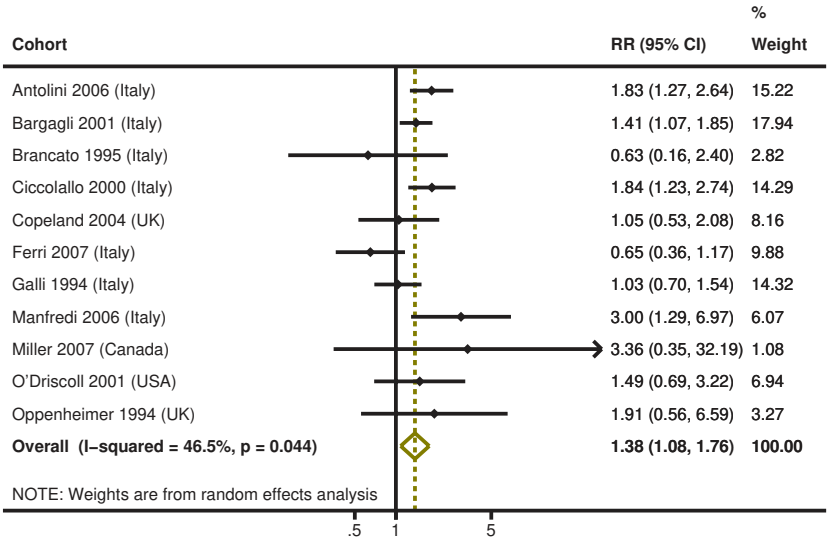

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval, RR, relative risk.

Fig. 8. **Ratios of crude mortality rates in HIV-positive versus HIV-negative people who inject drugs**

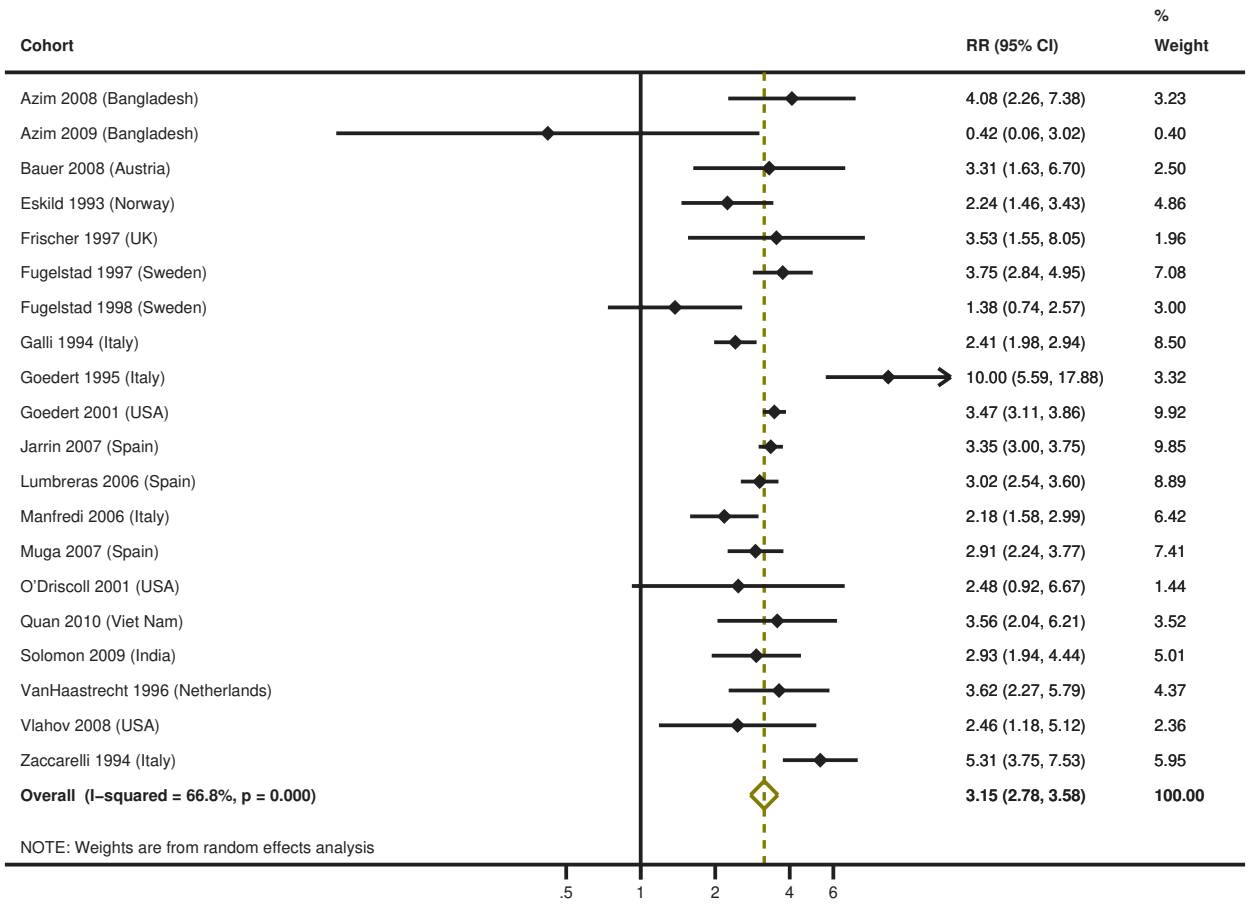

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

Fig. 9. **Crude mortality rates for AIDS-related deaths in people injecting drugs who were HIV-positive at baseline**

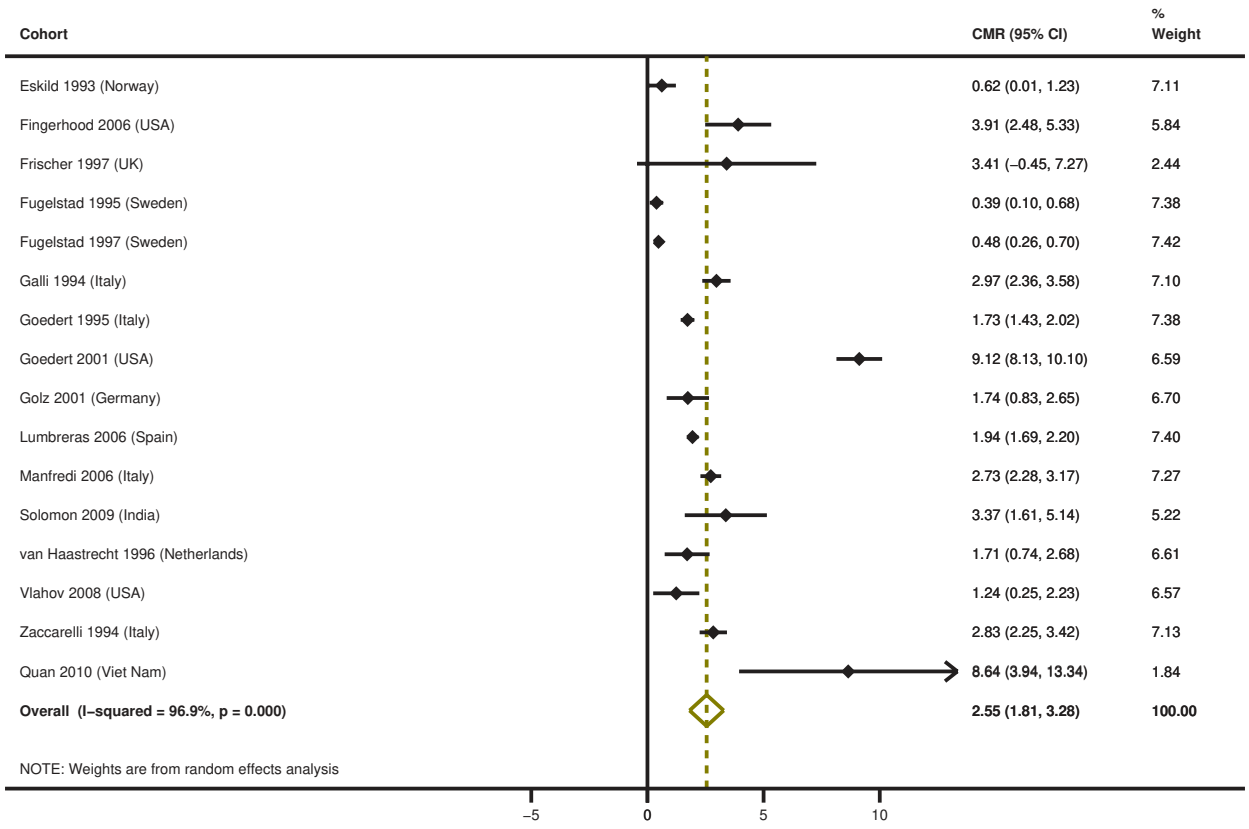

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
AIDS, acquired immunodeficiency syndrome; CI, confidence interval; CMR, crude mortality rate; HIV, human immunodeficiency virus.

Fig. 10. **Ratios of crude mortality rates for non-AIDS-related deaths in HIV-positive versus HIV-negative people who inject drugs**

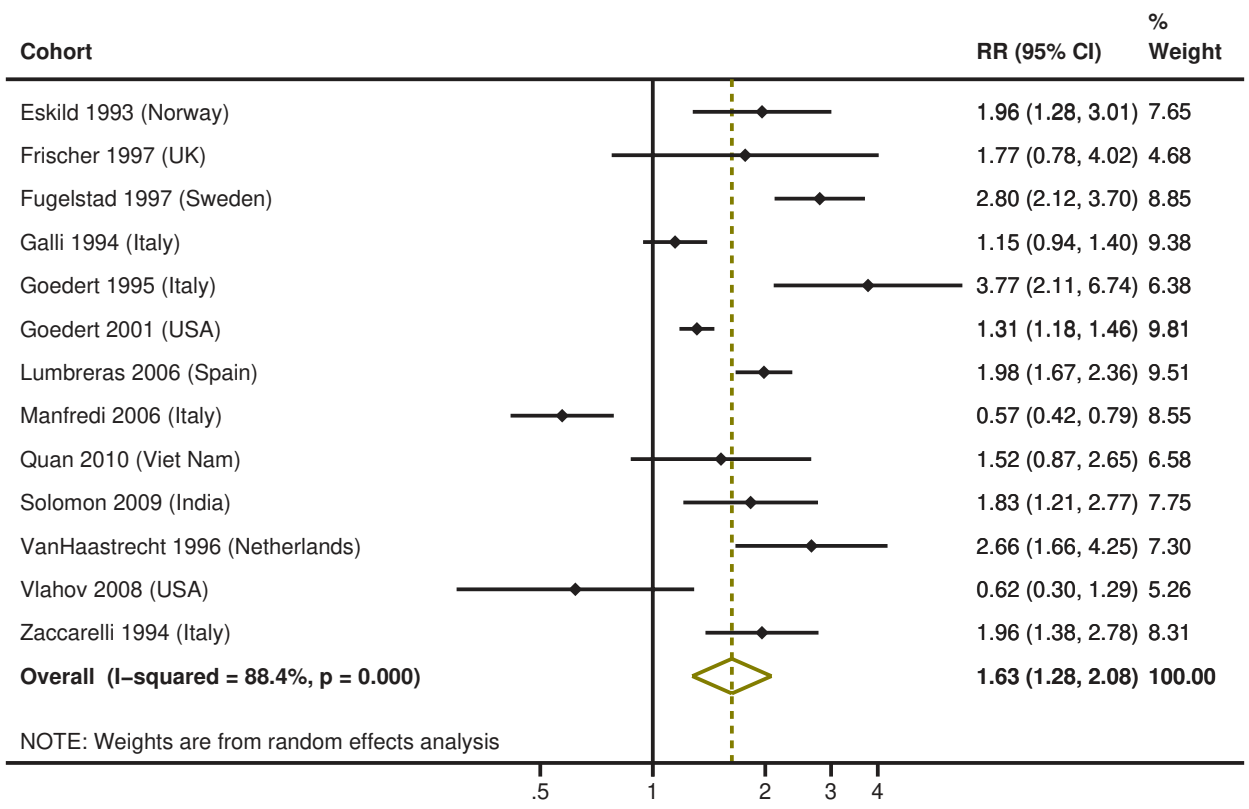

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
AIDS, acquired immunodeficiency syndrome; CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

Fig. 11. **Ratios of crude mortality rates for death from drug overdose in HIV-positive versus HIV-negative people who inject drugs**

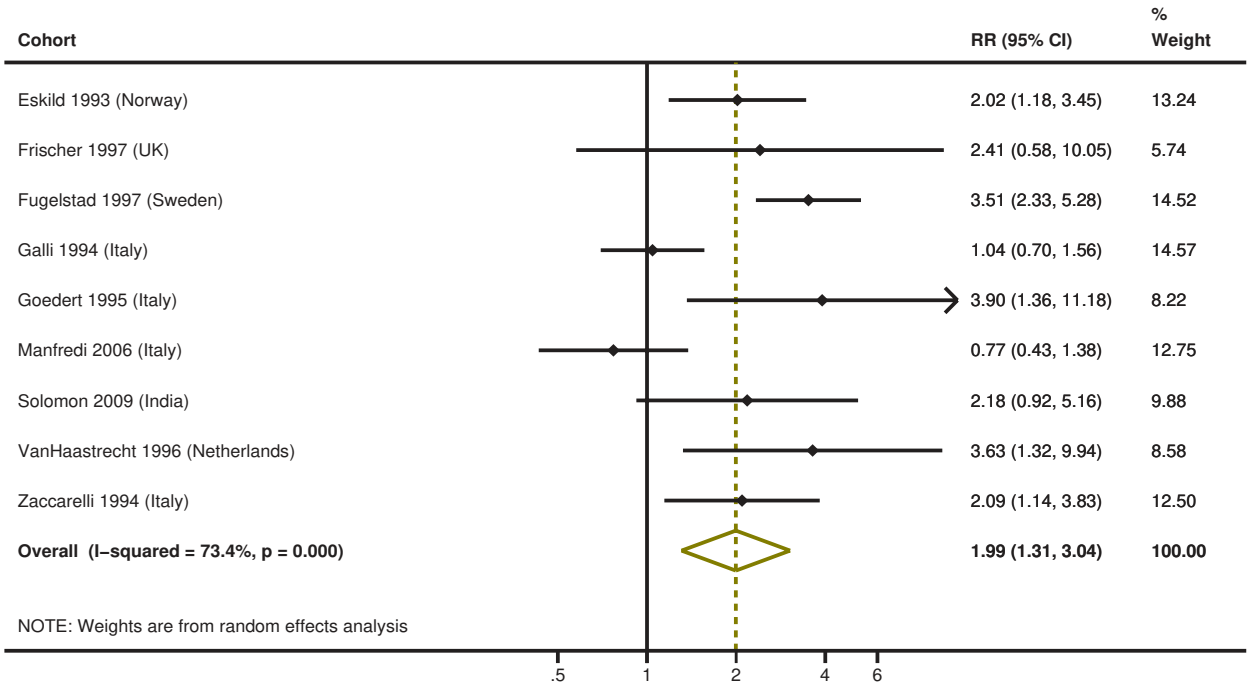

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

Fig. 12. **Ratios of crude mortality rates for AIDS-related death versus death from drug overdose in HIV-positive people who inject drugs**

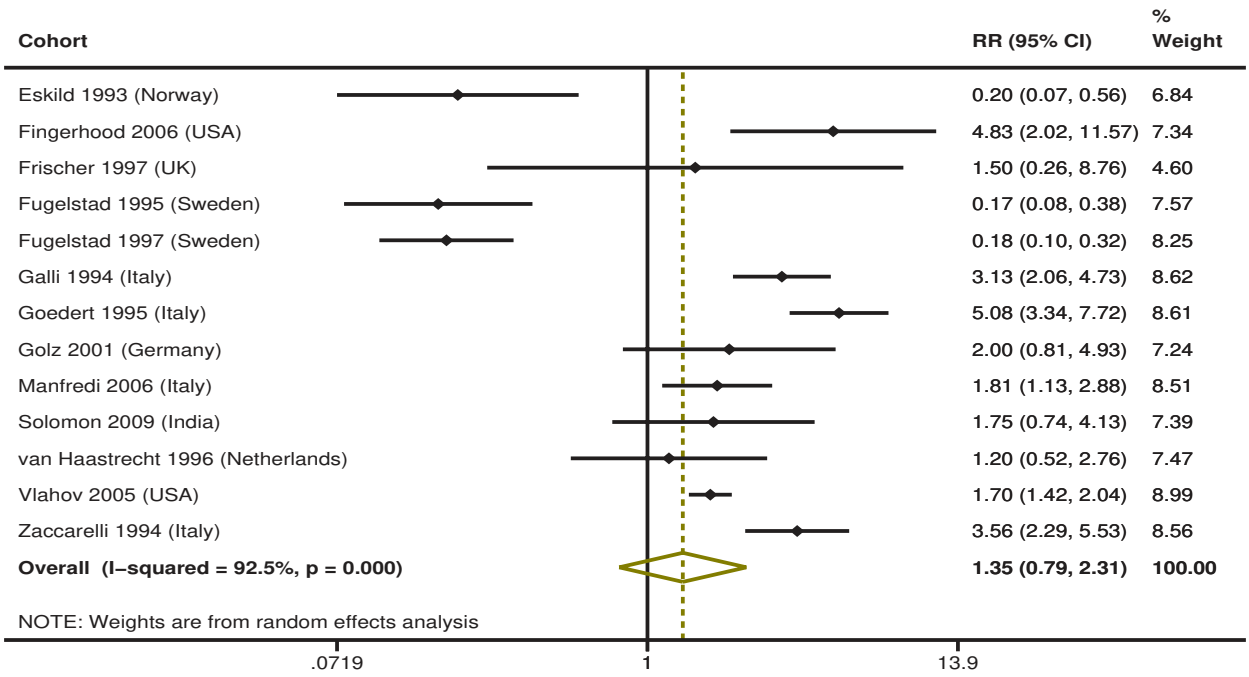

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
AIDS, acquired immunodeficiency syndrome; CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

Fig. 13. **Ratios of crude mortality rates in HIV-positive males versus HIV-positive females who inject drugs**

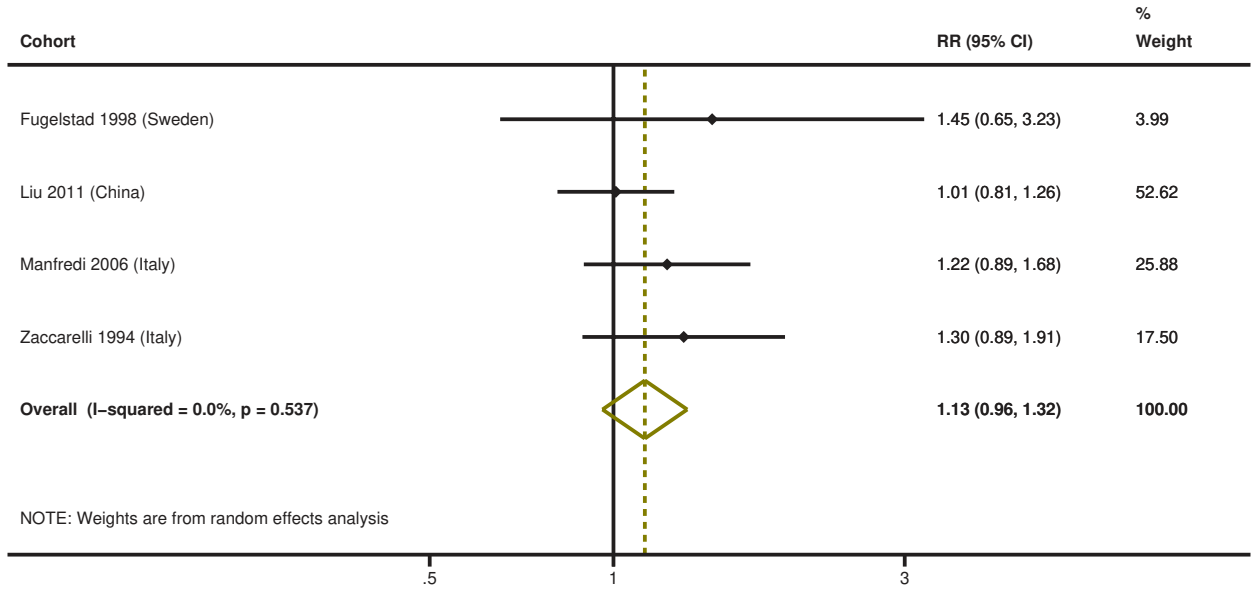

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

Fig. 14. **Ratios of crude mortality rates in HIV-negative males versus HIV-negative females who inject drugs**

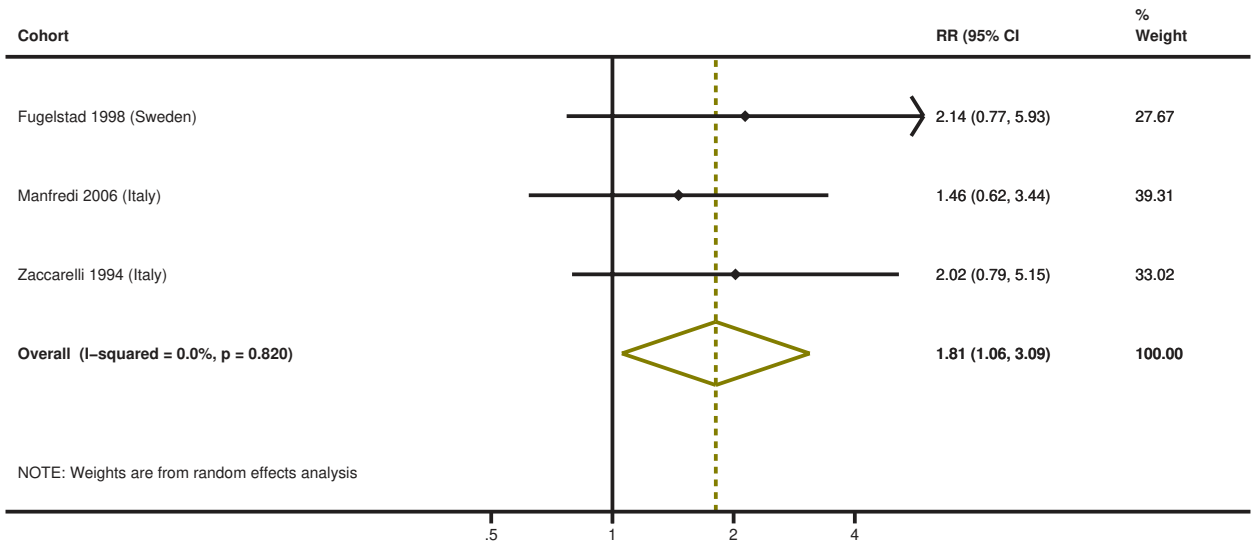

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; HIV, human immunodeficiency virus; RR, relative risk.

in countries where drug injecting is taking place but little research has been conducted about it.

In this review we found no significant differences in the risk of death by type of primary drug injected. This contrasts with the findings of other reviews of people dependent on different drug types, which, despite their own limitations, have suggested differences in mortality among opioid-, amphetamine- and cocaine-dependent persons.[3–5] An explanation for this discrepancy might lie in the extent of drug injection among the groups examined, whether people used multiple drugs (polydrug use being the norm), or the possibility, seldom examined, that some people in the cohorts switched from one primary drug to another during the follow-up period. All of these factors would have reduced our capacity to detect any differences in mortality among people injecting different types of drugs.

The ability to detect differences in mortality in cohort studies according to HIV status is subject to limitations. HIV status was typically measured at baseline only, and some subjects who contracted HIV infection during follow-up would remain assigned to the HIV– group for the entire follow-up period. Nonetheless, this would only serve to underestimate the relative differences in mortality between HIV+ and HIV– people who inject drugs. The markedly higher all-

Table 2. **Comparison of risk of dying from all causes and from drug overdose among people injecting opioids and those injecting stimulants**

Study	Users of opioids					Users of stimulants					All-cause CMR ratio		Overdose CMR ratio		Opioid use definition	Stimulant use definition
	PY	All-cause deaths (No.)	All-cause CMR[a]	Deaths from OD (No.)	OD CMR[a]	PY	All-cause deaths (No.)	All-cause CMR[a]	Deaths from OD (No.)	OD CMR[a]	Ratio[b]	95% CI	Ratio[b]	95% CI		
Fugelstad et al. (1997)[36]	*3022.7*	133	*4.40*	72	*1.67*	*3938*	39	*0.99*	15	*0.38*	4.44	3.12–6.33	4.39	3.46–5.53	Hospital records – at least once had a diagnosis of heroin dependence –opioid user	Hospital records – if had no heroin dependence diagnosis and at least once had a diagnosis of ATS dependence
Lejckova et al. (2007)[46]	13 323.9	114	0.86	36	*0.27*	9748.4	48	0.49	8	*0.08*	1.74	1.24–2.44	3.29	2.35–4.61	ICD-10 code F11 opioid dependence	ICD-10 code F15 – stimulant dependence
O'Driscoll et al. (2001)[57]	2984.9	40	1.34	19	*0.64*	544.6	14	2.57	7	*1.29*	0.52	0.29–0.95	0.50	0.20–1.24	Primary drug – heroin	Primary drug – cocaine or speed
van Haastrecht et al. (1996)[70]	268	9	3.36	–	–	326	15	4.60	–	–	0.73	0.33–1.64	–	–	Main drug injected – heroin	Main drug injected – cocaine or ATS
Vlahov et al. (2005)[71]	2047	85	*4.15*	16	*0.78*	3727	175	*4.70*	20	*0.54*	0.88	0.69–1.14	1.44	1.12–1.86	Heroin	Any cocaine or crack
Pooled estimate	–	–	–	–	–	–	–	–	–	–	**1.25[c]**	**0.60–2.61**	**1.85[d]**	**0.75–4.56**	–	–

CI, confidence interval; CMR, crude mortality rate; ICD-10, International Classification of Diseases; OD, overdose; PY, person–years; S, stimulant.

[a] Deaths per 100 PY of follow-up.

[b] Represents the CMR ratio for people injecting opioids (numerator) versus people injecting stimulants (denominator).

[c] Meta-analysis of all-cause CMR ratio: Test of estimate = 1; $P = 0.553$; heterogeneity (χ^2) = 67.99; $P < 0.0005$; $I^2 = 94.1\%$.

[d] Meta-analysis of overdose CMR ratio: Test of estimate = 1: $P = 0.18$; heterogeneity (χ^2) = 20.10; $P < 0.0005$; $I^2 = 85.1\%$.

Note: Values reported in papers appear in plain text; *italicized* values were derived from other available data.

Fig. 15. **Ratios of crude mortality rates in people who inject drugs during in-treatment period versus off-treatment period**

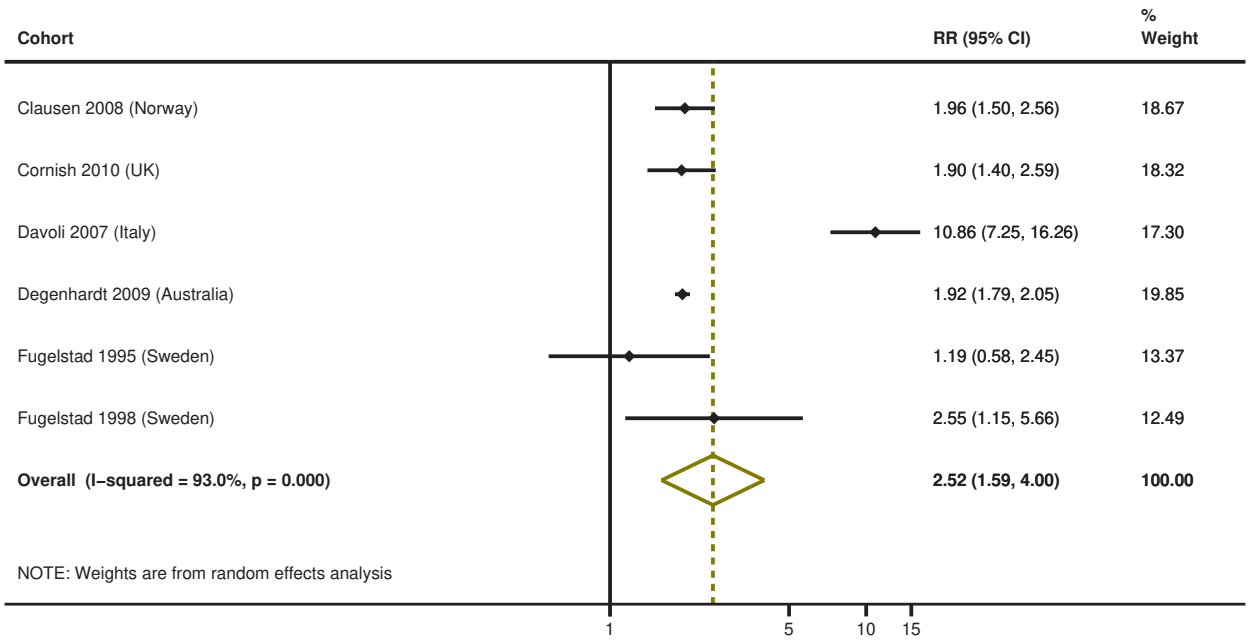

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; RR, relative risk.

Table 3. **Univariate associations between study-level variables and all-cause crude mortality rates (CMRs) and standardized mortality ratios (SMRs)**

Characteristic	CMR			SMR		
	n	*t*	*P*	*n*	*t*	*P*
Geographic region	53	−1.05	0.298	23	0.74	0.466
Country income	67	3.03	0.004	33	0.65	0.519
Percentage of cohort who inject drugs	60	1.49	0.141	26	2.04	0.052
Percentage of males	57	3.40	0.001	31	0.29	0.771
Percentage of cohort HIV+ at baseline	30	2.42	0.022	9	1.00	0.349
Presence of people using opioids (alone or with other drugs) in cohort	67	−0.07	0.945	33	−1.28	0.209
Year in which follow-up ceased	59	0.26	0.795	32	−2.80	0.009

cause mortality that we observed among HIV+ people who inject drugs is therefore probably a conservative estimate of the elevation in mortality in that group. Misattribution of cause of death as either AIDS- or non-AIDS-related could have occurred as well.

Treatment for HIV infection has improved greatly and has become more widely available. In some cohorts, mortality was examined for the periods before and after highly active antiretroviral therapy (HAART) was introduced. The findings suggest that mortality among HIV+ people who inject drugs decreased after the widespread introduction of HAART.[55] Unfortunately, we were unable to examine the impact of treatment for HIV infection across studies because mortality was rarely reported separately for the periods before and after the introduction of HAART.[77] However, the observed association between cohorts with more recent follow-up periods and lower SMRs might have to do with the greater availability in recent years of effective interventions for the prevention and treatment of HIV infection.

Reporting quality was poor. Few studies met criteria in consensus statements for the reporting of observational studies.[7] Mortality estimates were reported in various forms, including odds ratios, relative risks, hazard ratios and CMRs. Most studies did not report SMRs and many failed to report standard parameters such as PY, or were seldom easy to calculate, particularly for disaggregated mortality estimates. As a result, only a subset of studies could be included in many of the analyses.

Causes of death were not uniformly or consistently coded. Deaths from drug overdose might have been missed in countries with limited capacity to conduct toxicological tests or where recording a death as being from a drug overdose is surrounded by stigma. As a result, we may have underestimated CMRs and SMRs for death from drug overdose. Misattribution of deaths by HIV status may have occurred, since most cohorts were assessed for HIV status at the beginning of the study only and people infected during follow-up could have been missed. Again, this may have resulted in conservative estimates of mortality among HIV+ people who inject drugs and in lower effect sizes. In future research, assessing individuals' HIV status at several time points during the follow-up period would allow a more accurate measurement of mortality in relation to HIV status.

Fig. 16. **Crude mortality rates for people who inject drugs, by country income group**

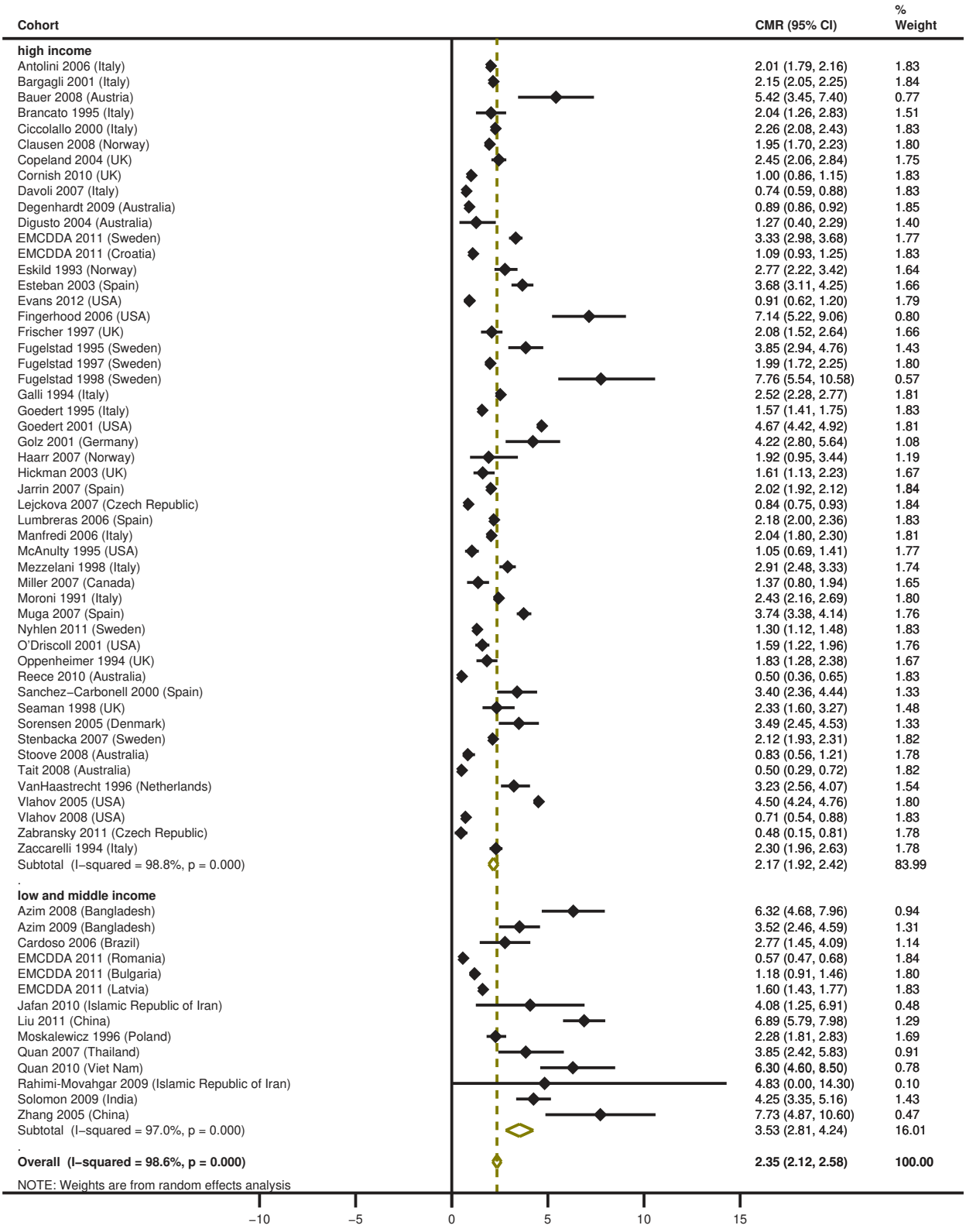

Image produced using Stata (StataCorp. LP, College Station, TX, United States of America).
CI, confidence interval; CMR, crude mortality rate.

Limitations of the review and meta-analysis

Our review has limitations. The lag time between the date when the studies were conducted and when they were published in peer-reviewed journals was generally long. In light of this we used several methods to search for published and unpublished studies. We reviewed primarily English-language papers, although we also reviewed the abstracts of non-English-language peer-reviewed articles when they were available in English. When studies seemed relevant, we had them translated; we engaged experts from a range of different countries and language groups to review these reference lists. Meta-analytical methods were originally developed to aggregate the findings of randomized controlled trials,[85] which have the advantage of allowing for control or adjustment of pre-conditions and sample-related factors that could influence the outcomes of interest. Controlling for such factors is not possible in observational studies, like the ones included in our review.

Conclusion

People who inject drugs have a much higher risk of death than those who do not. Major causes of death in this group are often poorly specified, but death from drug overdose is common, as is AIDS-related mortality in settings with a high prevalence of HIV infection. HIV+ people who inject drugs have higher mortality not just from HIV-related causes but also from drug overdose. Mortality varies by participant- and study-level characteristics, which suggests that multiple factors contribute to the higher risk of death observed in people who inject drugs. Many of these factors are probably modifiable, since certain predominant causes of death account for most of the mortality observed in this group. ■

Competing interests: None declared.

ملخص

معدل الوفيات بين الأشخاص الذين يتعاطون المخدرات عن طريق الحقن: استعراض منهجي وتحليل وصفي

الغرض استعراض الدراسات الأترابية المعنية بمعدل الوفيات بين الأشخاص الذين يتعاطون المخدرات عن طريق الحقن على نحو منهجي، ودراسة معدلات الوفيات وأسباب الوفاة في هذه الفئة، وتحديد متغيرات مستوى المشاركين والدراسة المرتبطة بارتفاع خطر الوفاة.

الطريقة تم استخدام عبارات بحث مخصصة للبحث في قواعد بيانات EMBASE وMedline وPsycINFO. وتم تحديد الكتابات غير الرسمية من خلال قواعد بيانات الكتابات غير الرسمية على شبكة الإنترنت. وتم استشارة الخبراء للحصول على دراسات وبيانات إضافية. وتم إجراء التحليلات الوصفية للتأثيرات العشوائية لتقييم معدلات الوفيات الأولية المجمعة (CMRs) ونسب الوفيات الموحدة (SMRs).

النتائج تم تحديد سبع وستين مجموعة من الأشخاص الذين يتعاطون المخدرات عن طريق الحقن، أربع عشرة منها من البلدان المنخفضة والمتوسطة الدخل. وكان معدل الوفيات الأولي المجمع 2.35 وفاة لكل 100 شخص-سنة (فاصل الثقة 95 ٪، فاصل الثقة: 2.12 إلى 2.58). وتم الإبلاغ عن نسب الوفيات الموحدة لاثنتين وثلاثين مجموعة؛ وكانت نسبة الوفيات الموحدة 14.68 (فاصل الثقة 95 ٪: 13.01 إلى 16.35). وأظهرت مقارنة معدلات الوفيات الأولية وحساب نسب معدلات الوفيات الأولية ارتفاع معدل الوفيات في البلدان المنخفضة والمتوسطة الدخل بين المجموعات والذكور والأشخاص الإيجابيين لفيروس العوز المناعي البشري (HIV) الذين تعاطوا المخدرات عن طريق الحقن. وكان المعدل مرتفعاً كذلك خلال فترات وقف العلاج. وكان فرط جرعة المخدرات ومتلازمة العوز المناعي المكتسب (الأيدز) السببين الرئيسيين للوفاة بين المجموعات.

الاستنتاج مقارنة بعامة السكان، يتعرض الأشخاص الذين يتعاطون المخدرات عن طريق الحقن لخطر وفاة مرتفع، على الرغم من تفاوت معدلات الوفيات بين البيئات المختلفة. ويجب أن يتضمن أي نهج شامل لتحسين حصائل الصحة في هذه الفئة جهوداً لخفض عدوى الإصابة بفيروس العوز المناعي البشري بالإضافة إلى غيرها من أسباب الوفاة، ولاسيما فرط جرعة المخدرات.

摘要

药物注射人群的死亡率：系统回顾和荟萃分析

目的 系统回顾药物注射人群死亡率的队列研究，检查该群体的死亡率和死亡原因，并确定与较高死亡风险相关的参与水平和研究水平变量。

方法 使用定制的搜索字符串搜索EMBASE、Medline和PsycINFO。通过网上灰色文献数据库识别灰色文献。咨询专家以获取更多的研究和数据。执行随机效果荟萃分析来估计汇集的粗死亡率（CMR）和标准化死亡率（SMR）。

结果 确定67 个药物注射人群队列，其中14 个来自中低收入国家。汇集的CMR为每100 人年2.35 例死亡（95%置信区间，CI：2.12-2.58）。报告32 个队列的SMR；汇集的SMR为14.68（95% CI：13.01-16.35）。CMR的比较和CMR比率的计算表明，中低收入国家的队列、男性以及艾滋病毒（HIV）呈阳性的药物注射人群中的死亡率较高。治疗结束期间死亡率也较高。药物过量和艾滋病（AIDS）是各个队列的主要死亡原因。

结论 尽管不同环境中的死亡率各异，与普通人群相比，药物注射人群的死亡风险更高。任何改善该群体的健康疗效的综合方案都必须包括减少艾滋病毒感染以及其他死亡致因（尤其是药物过量）的努力。

Résumé

Mortalité chez les personnes qui s'injectent des drogues : revue systématique et méta-analyse

Objectif Examiner systématiquement les études de cohortes de la mortalité chez les toxicomanes par injection, étudier les taux de mortalité et les causes de décès dans ce groupe, et identifier les variables, au niveau des participants et des études, associées à un risque accru de décès.

Méthodes Des critères de recherche spécifiquement adaptés ont été utilisés pour les recherches réalisées sur EMBASE, Medline et PsycINFO. La littérature grise a été identifiée par le biais de bases de données de littérature grise disponibles en ligne. Des experts ont été consultés pour obtenir des données et des études supplémentaires. Des méta-analyses des effets aléatoires ont été réalisées afin d'estimer les taux bruts de mortalité (TBM) groupés et les taux de mortalité standardisés (TMS).

Résultats Soixante-sept cohortes de personnes qui s'injectent des drogues ont été identifiées, dont 14 appartenant à des pays à revenu faible et intermédiaire. Le TBM groupé était de 2,35 décès pour 100 personnes-années (intervalle de confiance de 95%, IC: 2,12 – 2,58). Les TMS étaient indiqués pour 32 cohortes, avec un TMS groupé de 14,68 (IC de 95%: 13,01 – 16,35). La comparaison des TBM et le calcul des taux de TMS ont révélé une mortalité plus élevée parmi les cohortes des pays à revenu faible et intermédiaire, les sujets masculins et les toxicomanes par injection séropositifs. Elle était également plus élevée pendant les périodes d'interruption thérapeutique. L'overdose et le syndrome d'immunodéficience acquise (SIDA) étaient les causes principales des décès parmi ces cohortes.

Conclusion Si l'on compare avec la population globale, les personnes qui s'injectent des drogues ont un risque élevé de décès, bien que les taux de mortalité varient selon les contextes. Toute approche exhaustive visant à améliorer les résultats de ce groupe en matière de santé doit comprendre des efforts en vue de diminuer l'infection par le VIH, ainsi que d'autres causes de décès, notamment l'overdose.

Резюме

Смертность среди лиц, вводящих наркотики внутривенно: систематический обзор и мета-анализ

Цель Провести систематический обзор когортных исследований смертности среди лиц, вводящих наркотики внутривенно, изучить уровни смертности и причины смерти в данной группе и определить переменные на уровне участников и исследований, связанные с высоким риском смерти.

Методы Поиск исследований осуществлялся по базам данных EMBASE, Medline и PsycINFO по специализированным критериям поиска. Поиск литературы для служебного пользования осуществлялся по онлайновым базам данных литературы для служебного пользования. С целью получения дополнительных данных и исследований проводились консультации с экспертами. Для определения суммарных общих показателей смертности (ОПС) и стандартизированных коэффициентов смертности (СКС) выполнялся мета-анализ случайных эффектов.

Результаты Были выявлены шестьдесят семь когорт лиц, вводящих наркотики внутривенно, 14 из которых относятся к странам с низким и средним уровнями доходов. Суммарный ОПС составлял 2,35 смертей на 100 человеко-лет (95% доверительный интервал, ДИ: 2,12–2,58). СКС фиксировался для 32 когорт; суммарный СКС составлял 14,68 (95% ДИ: 13,01-16,35). Сравнение ОПС и расчет коэффициентов ОПС выявил высокий уровень смертности в когортах, относящихся к странам с низким и средним уровнями доходов, среди мужчин и лиц, вводивших наркотики внутривенно, которые имели положительные результаты на вирус иммунодефицита человека (ВИЧ). Высокий уровень также отмечен вне периодов лечения. Передозировка наркотиков и синдром приобретенного иммунодефицита (СПИД) являлись основными причинами смерти в когортах.

Вывод По сравнению с населением в целом, лица, вводящие наркотики внутривенно, подвержены повышенному риску смерти несмотря на то, что уровни смертности варьируются в зависимости от условий. Любой комплексный подход к улучшению результатов мероприятий по охране здоровья в данной группе должен включать в себя меры по сокращению уровня ВИЧ-инфекции, а также других причин смерти, в особенности, передозировки наркотиков.

Resumen

La mortalidad entre consumidores de drogas inyectables: una revisión sistemática y meta-análisis

Objetivo Revisar de forma sistemática los estudios de cohortes sobre la mortalidad entre los consumidores de drogas inyectables, examinar las tasas de mortalidad y las causas de muerte en este grupo e identificar las variables relacionadas con el estudio y los participantes asociadas a un mayor riesgo de muerte.

Métodos Se emplearon cadenas de búsqueda adaptadas para registrar EMBASE, Medline y PsycINFO. La literatura gris se identificó por medio de bases de datos de literatura gris en línea. Se consultaron expertos a fin de obtener datos y estudios adicionales y se llevaron a cabo metaanálisis de efectos aleatorios para calcular las tasas brutas combinadas de mortalidad y las tasas de mortalidad estandarizadas.

Resultados Se identificaron diecisiete cohortes de consumidores de drogas inyectables, 14 de las cuales en países con ingresos bajos y medios. La tasa bruta combinada de mortalidad fue de 2,35 fallecimientos por cada 100 años-persona (intervalo de confianza del 95%, IC: 2,12-2,58). Se declararon las tasas de mortalidad estandarizadas para 32 cohortes; la tasa bruta combinada de mortalidad fue de 14,68 (IC 95%: 13,01-16,35). La comparación de las tasas brutas combinadas de mortalidad y el cálculo de las proporciones de la mortalidad bruta combinada revelaron que la mortalidad fue superior en las cohortes de países con ingresos bajos y medios, en varones y entre consumidores de drogas inyectables que dieron positivo para el virus de la inmunodeficiencia humana (VIH), así como durante los periodos sin tratamiento. Las sobredosis y el síndrome de la inmunodeficiencia adquirida (SIDA) fueron las causas principales de muerte en las cohortes.

Conclusión En comparación con la población general, los consumidores de drogas inyectables presentan un riesgo elevado de muerte, si bien las tasas de mortalidad varían en los distintos lugares. Cualquier enfoque completo para mejorar los resultados sanitarios en este grupo deberá esforzarse por reducir la infección por VIH, así como las otras causas de muerte, en especial, la sobredosis.

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