

مرکز تحقیقات پیشگیری سوء مصرف مواد

پژوهشکده سلامت

مرور سیستماتیک و متاآنالیز

سطح سرب خون در بین

مصرف کنندگان اپیوم در ایران

دکتر برهان منصوری

استادیار دانشگاه علوم پزشکی

کرمانشاه

مقدمه

سرب □



- * یک فلز نرم و قابل انعطاف
- * از طریق جریان خون در بدن پخش و دفع از طریق ادرار و صفرا



- * نیمه عمر در حدود ۳۰ روز در بدن
- * اتصال سرب باقیمانده در بدن به گلبول های قرمز خون



- * تجمع در بافتهای نرم نظیر بافت استخوانی
- * زمان ماند تجمع ۲۰ تا ۳۰ سال

□ مسمومیت با سرب

تحت تاثیر قرار دادن:

- سیستمهای اعصاب مرکزی و محیطی
- عملکرد کلیه
- سیستم عروق
- و دستگاه گوارش

□ همچنین سبب:

- آنمی
- تخریب کلیه
- نوروپاتی محیطی
- و بیماریهای گوارشی



Sources of Lead Poisoning



Paint in Homes
Built Before 1978



Dirt



Lead Dust



Some Pottery



Take Home Lead
(Jobs or Hobbies)



Traditional Remedies, Make-up
and Powders



Some Candy



Some Jewelry



Some Toys

□ سرب و اپيوم

- شيوع مصرف ترياك و مشتقات آن در دنيا حدود ۱ تا ۲ درصد
- در ايران بسيار بيشتر از سطح جهاني بوده ۳/۳ درصد و در برخي از نواحی روستايی نزديک به ۲۲ درصد

□ قاچاقچيان:

- افزودن سرب به مواد مخدر طی فرآیند تولید، به منظور افزایش وزن آن و کسب منافع بيشتر



مقدمه

■ مطالعات متعددی در زمینه مقایسه سطح سرب در خون افراد اپیومی و مشتقات آن در ایران

□ هدف تحقیق:

❖ مرور سیستماتیک و متاآنالیز مسمومیت با سرب در بین مصرف کنندگان اپیوم در ایران



- No language restrictions in the search strategy
- Data was collected in accordance with the PRISMA guidelines which divides the selection into four main steps
- Databases: PubMed, Web of Science, Embase, Scopus, and Google Scholar.
- Case-control studies were conducted between January ۲۰۰۰ and January ۲۰۲۰.

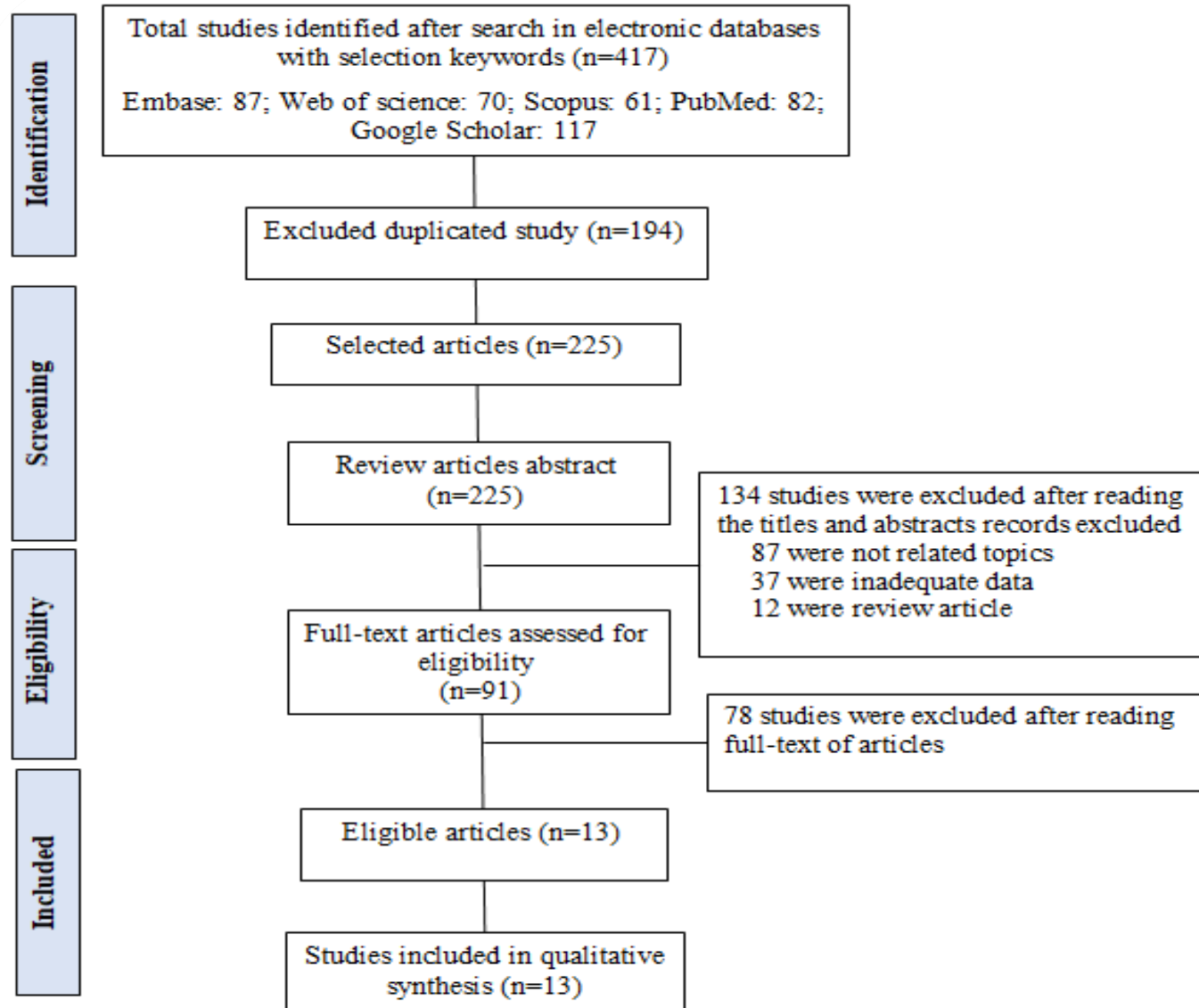


Figure 1. PRISMA flow diagram of study identification, inclusion, and exclusion

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□ search strategy

- **PubMed** was searched by keywords: ("Trace Elements"[Mesh]) OR "Lead"[Mesh]) AND "Poisoning"[Mesh]) OR "Lead Poisoning"[Mesh]) OR "Heavy Metal Poisoning"[Mesh]) OR "toxicity" [Subheading]) AND "Opium"[Mesh]);
- **Scopus** and **Google Scholar** were searched by keywords: (TITLE-ABS-KEY ("lead-contaminated opium") OR TITLE-ABS-KEY ("lead poisoning") OR TITLE-ABS-KEY ("Lead") OR TITLE-ABS-KEY ("Poisoning") OR TITLE-ABS-KEY ("lead toxicity") OR TITLE-ABS-KEY ("Heavy Metal Poisoning") OR TITLE-ABS-KEY ("Trace elements") AND TITLE-ABS-KEY ("Blood") AND TITLE-ABS-KEY ("opium") OR TITLE-ABS-KEY ("Opioid") OR TITLE-ABS-KEY ("Heroin") OR TITLE-ABS-KEY ("Methadone") AND TITLE-ABS-KEY ("Addict")));
- **ISI Web of Science** and **Embase** were searched by keywords: TS=(Trace Elements OR Lead) AND TS=(Poisoning OR lead toxicity OR Heavy Metal Poisoning OR toxicity OR lead-contaminated opium) AND TS=(Blood) AND TS=(Opium OR Opioid OR Heroin OR Methadone) AND TS=(Drug Users OR Addict) AND ('trace elements' OR 'lead') AND 'poisoning' OR 'lead toxicity' OR 'heavy metal poisoning' OR 'toxicity' OR 'lead contaminated opium') AND 'blood') AND 'opium' OR 'opioid') AND 'addict' AND 'article'/it AND 'cross-sectional study'/de.

□ Selection criteria

Inclusion criteria:

- opium use disorder
- no history of chronic physical and psychiatric disorders
- no LP before opium use disorder
- and multiple substance use history

Exclusion criteria:

- Letter to editor
- Conference
- review and meta-analysis articles

□ **Data extraction**

□ **Quality assessment**

Newcastle–Ottawa Scale (NOS)

□ **Publication bias**

Funnel plot asymmetry and Egger's test

□ *Statistical analysis*

□ effect size of each study

Standardized mean difference adjusted known as Hedge's g

$$g_w = \frac{\sum_{i=1}^k w_i g_i}{\sum_{i=1}^k w_i},$$

□ The heterogeneity using the Q statistic

$$Q = \sum_{i=1}^k w_i (g_i - g_w)^2$$

□ *Selection studies*

- Initially, ۴۱۷ articles were picked out from databases
- **Thirteen** articles were chosen for further analysis

□ *Systematic review*

- Studies were published between ۲۰۰۹ and ۲۰۱۹
- The sample size ranged from ۴۰ to ۱۳۱
- All studies were focused on **adults** with mean age ranged ۳۳/۵ to ۶۵/۱۵ years old
- Eight studies enrolled both **men and women**, four studies recruited only **men**, and the population study for one study was **unknown**.

❑ Differences in the Pb levels between opium and non-opium users

- The pooled effect size was $g_w = 2/48$ (95% CI: 1/58 – 3/39).
- Heterogeneity was 96/6% ($I^2 = 96.6$, $Q(17) = 50.4/31$, $p < 0.001$) indicating a high heterogeneity between true mean effects ($\tau^2 = 3.72$).
- All variability of the observed variance comes from real differences between studies.

□ *Meta-regression analysis*

- The **route of administration** was a significant predictor for the heterogeneity of effect sizes ($Q(2)=2/14$, $p=0/05$).
- The **duration of opium addiction** was not a significant predictor when all studies considered, $Q(1)=0/77$, $p=0/39$, but it was a significant predictor after excluding outliers, $Q(1)=4/24$, $p=0/041$.
- The **gender** revealed to be a significant predictor for effect sizes, $Q(1)=4/40$, $p=0/036$.
- No evidence of **time effect** when outliers studies removed from analysis ($Q = 0/18$, $df = 1$, $p = 0/675$).

□ **Quality assessment**

- The risk of bias assessment for each study included on the NOS scale. According to this result, ۱۳ studies had good quality.

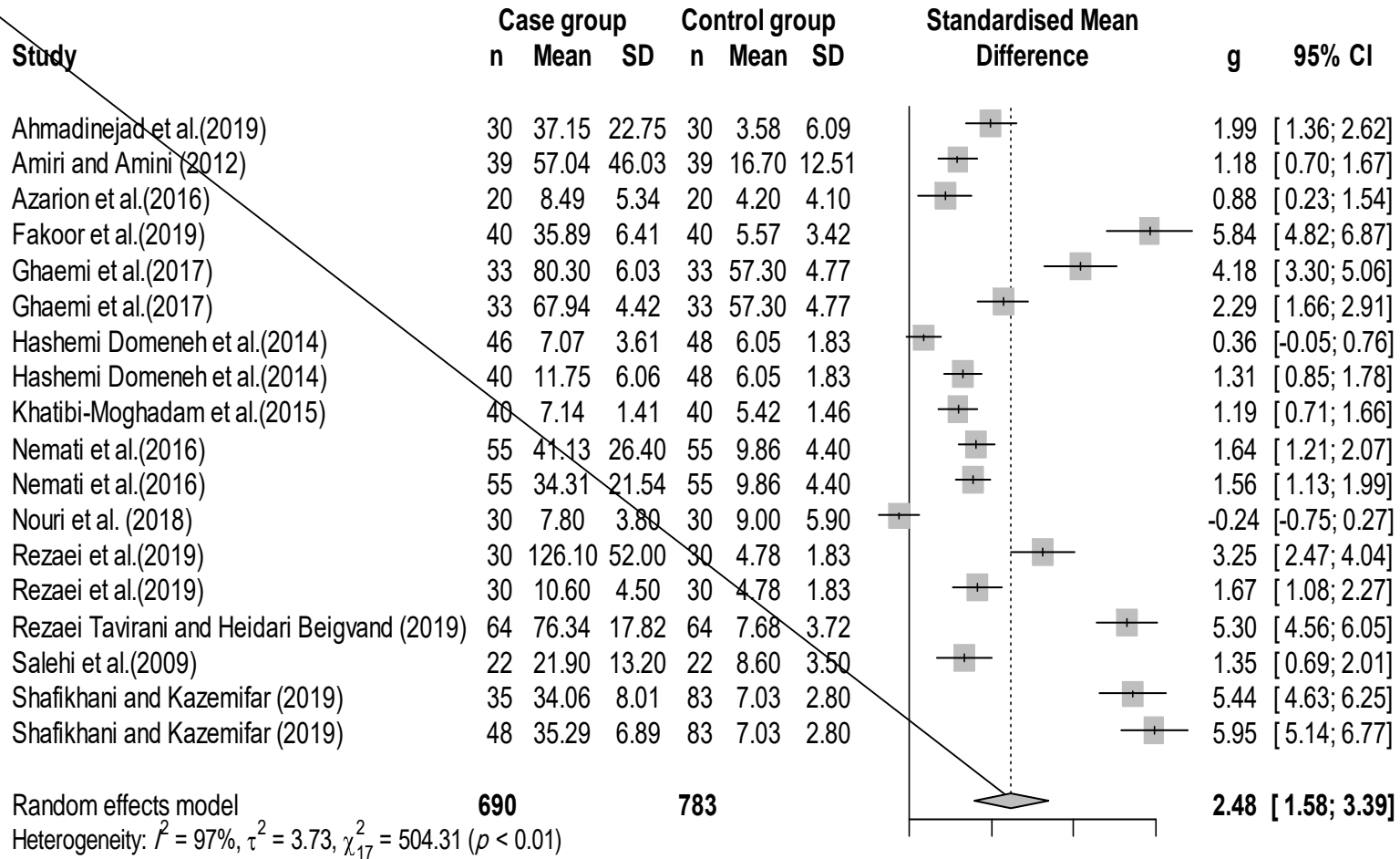


Figure ۲. The forest plots for the meta-analysis of all studies. For each study, the sample size, mean, and SD at the case and control group, and the Hedge's g effect size with corresponding 95% CI are presented. Heterogeneity indices, as well as a p-value for Cochran's Q-test of heterogeneity, are also presented.

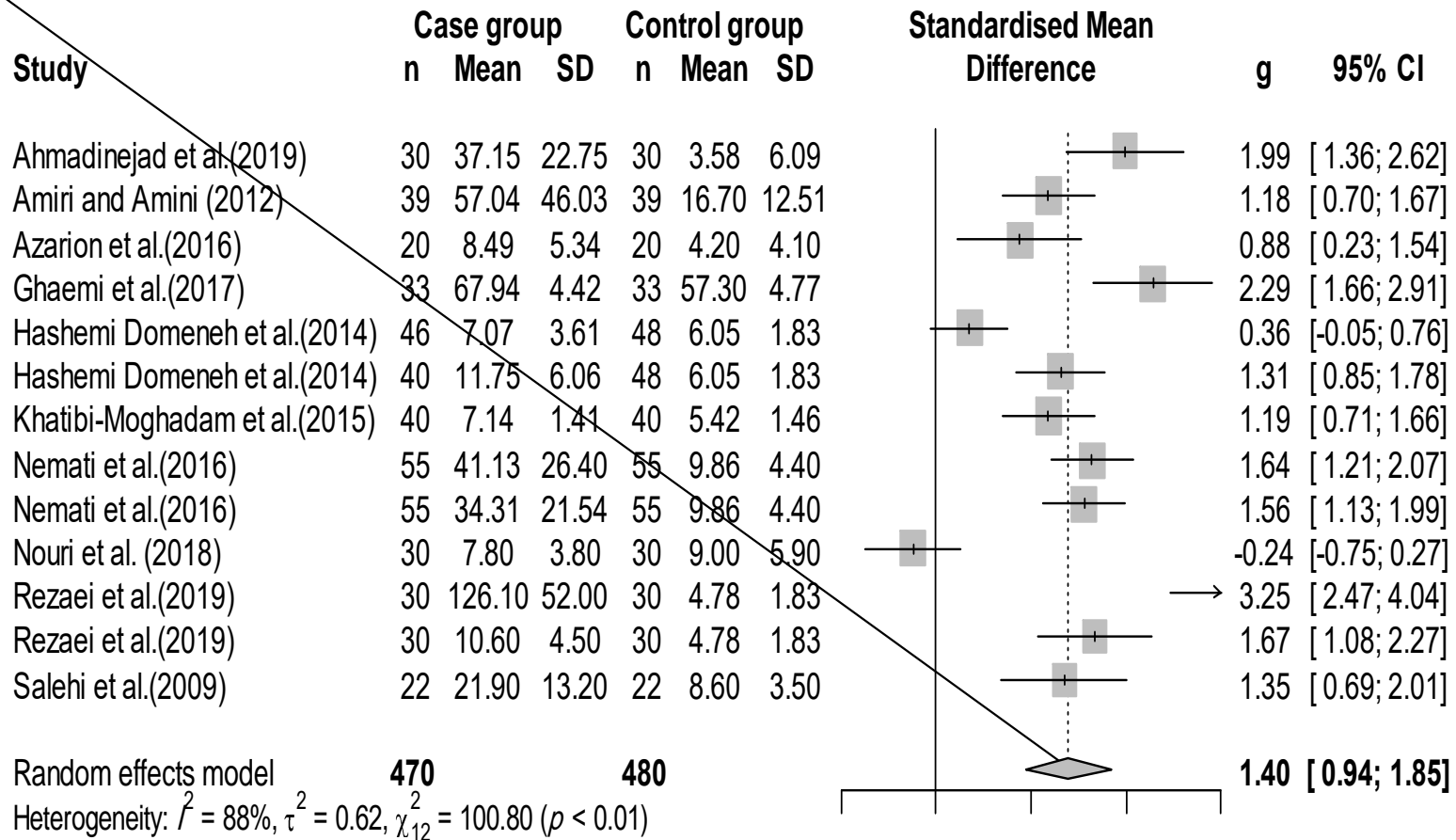


Figure ۳. The forest plots for the meta-analysis of the reduced studies after excluding outlier studies with large Hedges' g effect sizes.

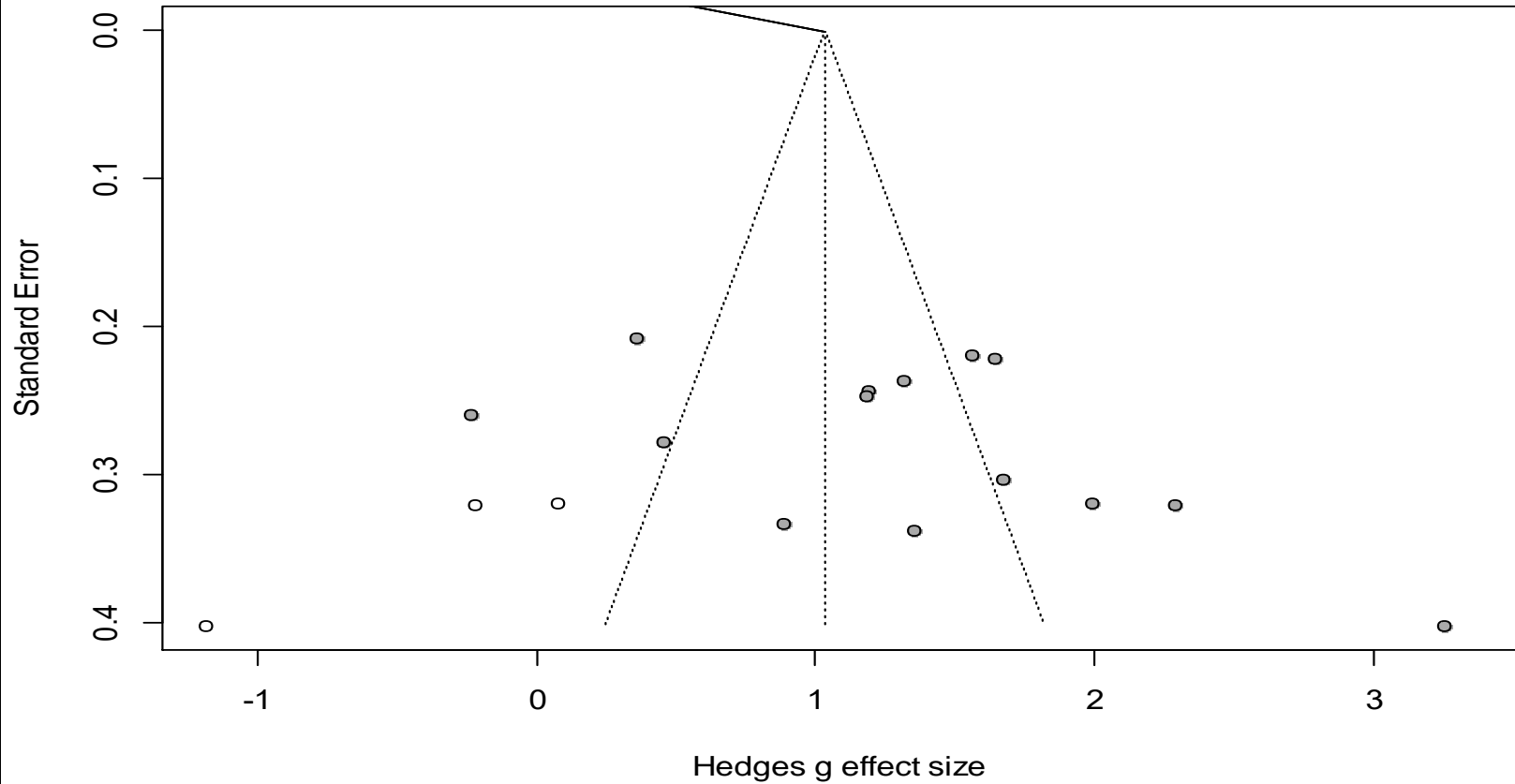


Figure ۴. Funnel plot of Hedges g effect sizes of ۱۱ studies with ۱۴ Hedges' g effect sizes. Three studies specified with blank circles were studies added by the Trim and Fill adjustment method.

Table 1. Characteristics of included studies for the lead (Pb) in the blood ($\mu\text{g/dl}$) of patients and control

Authors/Year	Study population	Route of administration	Sample size and gender	Tissue	Mean age	Duration of opium addiction (y)	Amount of opium use	Type of used substance	Outcome	The inclusion criterion for the patient group	The inclusion criterion for the control group	County
Rezaei et al. 2019	Opium user: Clinical patients. Non-users: Healthy voluntary without opium consumption	OR IN	Opium user: 60 Non-users : 30	Blood	Opium user: 48.91±13.14 Non-users: 39.2	OR: 19.17 ± 10.4 y IN: 14.8 ± 10.5 y	OR: 2.19 ± 3.51 g IN: 3.04 ± 1.88 g	38% opium, 23.5% methadone, 17.5% heroin, 17.5% methamphetamine, 3% concentrate heroin	Blood lead concentration in both addicted and non-addicted groups showed a significant difference.	Opium addicts who declared that they had ever used opium and continue.	Controls were healthy voluntary without opium consumption.	Tehran
Salehi et al. 2009	Opium user: Clinical patients. Non-users: their family members	OR*	Opium user: 22 Non-users: 22	Blood	Opium user: 38.8 ± 6.7	2 to 5	1 – 5 g daily with a mean of 3.03±1.13.	100% used opium	The Pb mean The difference between both groups was statistically significant. The Pb had a significant correlation with the amount of opium ingestion, but there was no significant correlation between Pb and the duration of opium ingestion in the patient group.		healthy subjects with no history of opium addiction who accompanied the patients and was matched with the patient group in age and sex	Rafsanjan

Table 2. Quality assessment of studies included in the meta-analysis of lead (Pb) in opium user and control: Based on the Newcastle-Ottawa Scale for case-control studies

Authors	Selection				Comparability	Exposure			Total score
	Case definition	Representativeness of the cases	Selection of Controls	Definition of Controls	Comparability of cases and controls on basis of the design or analysis	Ascertainment of exposure	The same method of ascertainment for cases and controls	Non-Response rate	
Ahmadinejad et al., 2019	a	a	b	a	a	c	a	a	6
Amiri and Amini, 2012	a	a	b	a	a	c	a	a	6
Azarion et al., 2016	a	a	b	a	a	c	a	a	6
Fakoor et al. 2019	a	a	b	a	a	c	a	a	6
Ghaemi et al., 2017	a	a	a	a	a	c	a	a	7
Hashemi Domeneh et al., 2014	a	a	a	a	a	c	a	a	7
Khatibi-Moghadam et al., 2015	a	a	a	a	a	c	a	a	7

- ❑ Route of administration, gender, and duration of opium abuse was associated significantly with BLC in opium addictions but not in the mean age.
- ❑ Soltaninejad and Shadnia (۲۰۱۸), they found a higher BLC in patients with oral opium abuse.

- ❑ Tolerable daily intake (TDI) of Pb amounts to **۲۴۰ µg per day** for a person with an average body weight of **۶۸ kg**
- ❑ It is estimated that addicts consume approximately **۳۰ g of opium per day**, which is equivalent to at least **۲۰%** of TDI
- ❑ Pb can **gradually accumulate** in the **bones** over time which in certain conditions such as aging and osteoporosis it becomes an internal source of Pb in the **blood**

- ❑ BLC in opium addicts was **significantly higher** than that in the healthy control group
- ❑ It's known as a routine action that **opium retailers** mix opium **with Pb** and other substances to increase their weight for greater profit and possible lead toxicity in Iran
- ❑ According to studies in this systematic review, the BLC in the opium addicts in **Tehran and southern cities** such as Sistan and Kerman has been reported to be much higher than other regions of Iran

