Review Article

Prevalence of Tuberculosis Infection among Various Risk Groups in India: A Systematic Review and Meta-Analysis

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Abstract

Treatment of tuberculosis (TB) infection (TBI) to prevent active TB disease is a key component of the National Strategic Plan to end TB in India, without which the strategies to end TB would be futile. There is a need to rapidly scale up access to effective shorter regimens for tuberculosis preventive treatment (TPT) to a wider set of risk groups. This applies for identifying high-risk groups for TPT expansion. Thus, our aim with this review is to determine the TBI prevalence in different risk groups in India. We searched databases like Embase, Medline, Scopus, and CINAHL for studies published between 2012 and 2023 to estimate TBI in different risk groups in India. The PRISMA guidelines were followed when reviewing the publications, and a predetermined search strategy was used to find relevant sources across various databases. Using MetaXL (MS excel) software, we pooled data based on a random-effects model, along with heterogeneity testing using Cochrane's Q and I^2 statistic. A total of 68 studies were included from 10,521 records. TBI pooled prevalence was estimated using the IGRA data, while in the absence of IGRA data, TST data were utilized. The key findings revealed a total of 36% pooled TBI prevalence for all risk factors, 59% among smokers, 53% among diabetics and alcoholics, 48% among malnourished, 47% among contacts of TB patients, 44% among HIV, 36% among pregnant women, 35% among COVID-19 patients, 31% among healthcare workers, 18% among sarcoidosis patients, and 15% among rheumatoid arthritis patients in India. Our review depicted a high TBI burden among groups such as diabetes mellitus, smokers, malnourished, and alcoholics. WHO has yet to recommend for systematic screening and treatment for TBI among these groups for want of evidence which this study provides, highlighting the need to reprioritize the risk groups for tailored TPT strategies.

Keywords: Burden, meta-analysis, risk groups, systematic review, tuberculosis infection

Background

Infection with Mycobacterium tuberculosis (M.Tb), the causative agent for tuberculosis (TB), can lead to development of an active form of TB, including the subclinical form or TB infection (TBI) (earlier known as latent TB infection), an asymptomatic stage of infection.[1] There are an estimated 2 billion TBI cases worldwide, which makes up a significant reservoir for the development of new TB cases and a recurring source of M.Tb transmission.[2] In TBI, due to the host immunological response, the bacilli prevail in a quiescent state.[2] Further, the risk of developing active TB is 5–15% within the first 2 years following an infection with *M.Tb*, in addition to a 5% risk of developing active TB in the remaining lifetime of the host due to wanning immunity.[2] On the contrary, there is a 30% lifetime risk for diabetics and a 7–10% yearly risk for HIV patients of developing active TB. TBI is therefore a major obstacle to the worldwide TB elimination endeavor, especially in high-burden nations like India.

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India accounts for the highest (28%) TB as well as TBI burden globally.[3] In 2021, the National TB prevalence survey estimated the adult TBI prevalence as 31.3%.[4] A systematic review by Chauhan *et al.* reported a 41% community level prevalence of TBI in India, regardless of the risk of contracting it.[5] The development of TBI into active TB is accelerated by a number of risk factors, including HIV infection, injection drug abusers, malnutrition, contacts of individuals having active TB, silicosis, diabetes mellitus (DM), and immunocompromised conditions.[6] The second highest concentration of diabetics worldwide is found in India.[7] Furthermore, 3 million individuals in India endure exposure to silica dust, putting them at risk for developing silicosis and eventually TB.[8] There are around 2.1 million individuals living with the HIV infection in India.[9] Malnutrition and overcrowding are recognized challenges in India.[10,11] India's National Strategic Plan (NSP), TB envisages TB elimination by 2025, five years before the sustainable development goals for 2030.[12] One of the four main priorities set by the NSP is the prevention of development of active TB, especially among the high-risk groups.[12]

Prevention of TB by treatment of TBI is a vital yet underutilized integrant of the NSP.[12] The World Health Organization (WHO) at present advises tuberculosis preventive treatment (TPT) for those with HIV infection, household contacts of people with bacteriologically confirmed pulmonary TB, people who are starting anti-TNF treatment, individuals on dialysis, preparing for a hematological or organ transplant, prison inmates, silicosis, health care staff, immigrants from nations with high TB prevalence, vagrants, and drug users.[13] However, WHO does not recommend TPT for diabetics, alcoholics, malnourished, and tobacco smokers, highlighting the need for more evidence on other risk groups beyond the WHO guidelines.[13] As per the Lancet report, a comprehensive approach to end TB would be futile without the engagement of TPT in diagnosis and treatment strategy.[14] Thus, pragmatism suggests active treatment of TBI, especially in high-risk groups. This includes identifying the high-risk groups, assessing the TBI and offering the TPT. Thereby, estimating the prevalence of TBI across different risk groups is crucial for the expansion of TPT policy in India. In light of this, the current systematic review and meta-analysis set out to determine the TBI prevalence across different risk categories in India.

Methods

Protocol and inclusion criteria

In accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guideline, a systematic review of different studies investigating TBI among people in India was carried out. The review was registered on the PROSPERO (CRD42023422890).

Study design and data sources

Databases such as Embase, CINAHL, Medline, and Scopus, indexing the peer-reviewed journals, were systematically reviewed for literature published between January 1, 2013 to October 31, 2023 in order to find the various studies investigating the TBI among individuals in India. An exhaustive search was carried out with the help of the Medical Subject Headings (MeSH) terminology and keywords for TB including sub-clinical Tuberculosis, Inactive Tuberculosis, Tuberculosis Infection, Latent Tuberculosis, Pulmonary Tuberculosis, Extra-pulmonary Tuberculosis, Tuberculin Skin test, Interferon gamma release assay, and Enzyme-linked immunospot assay. The detailed search strategy is provided in the supplementary material (Supplementary File S1). All four of the aforementioned datasets were independently searched by two authors (AC and JS). Manual searching of reference lists was conducted in order to find potentially missing articles.

Methodological quality appraisal

Two independent researchers (AC and JS) evaluated the methodological quality and risk of bias among the included studies employing the Joanna Briggs Institute (JBI) Critical Appraisal tools designed for systematic reviews. JBI tool consists of different questionnaires for cohort and cross-sectional studies.[13,14] Based on the grade they obtained, studies were classified as having a "low," "moderate," or "high" risk of bias. The majority of the studies,[15] with a JBI critical assessment score of >70%, were considered to have a low risk of bias. Two studies, however, received a moderate risk of bias rating (50–69%). None of the articles were excluded based on the quality evaluation [Supplementary Tables].

Selection criteria

Based on the objective of the study, we included primary studies conducted among people residing in India and reported TBI in the participants regardless of the test used to assess. We disclosed the conduct of any test among the participants, including tuberculin skin test (TST) and interferon gamma release assay (IGRA). Studies that reported data on TBI risk groups such as HIV, DM, COVID-19, immunocompromised illnesses, sarcoidosis, rheumatoid arthritis, smoking, alcohol, and undernourishment were included, whereas study protocols, conference abstracts, case reports, reviews, editorials, and any unpublished material were excluded. TBI is defined as an immunological response to M.Tb antigen in the absence of clinical indications of active TB disease.

Data extraction and analysis

Duplicate entries were eliminated by importing all the citations acquired from electronic searches into EndNote. Using the Rayyan software, a total of 10,311 papers were screened, and 124 full-text articles were extracted and examined independently by two researchers. Two independent researchers (AC and JS) screened the titles and abstracts of the retrieved studies to determine studies that might qualify for inclusion. The consensus decision (KCS) of a third reviewer was used to resolve any doubt or disagreement. A similar procedure was carried out for the full-text screening. Using the PRISMA guidelines for inclusion and exclusion criteria, 67 articles were included [Figure 1]. All the articles selected were reviewed by all the authors.

Data on study characteristics, including sample size, sociodemographic factors, percentage of TBI, study design, study setting, and tests used, were extracted using a standardized data extraction form. Furthermore, information for determining the risk of the bias risk was taken out. In cases where data were lacking, a piece of information was missing, or the entire text was not available, we emailed the respective authors of the original articles to obtain the relevant information.

The study design was used to categorize the studies, while standard deviations or the median for continuous variables and frequencies and percentages for categorical variables were used to summarize the study parameters. Through the use of STATA, the pooled prevalence of TBI was derived at a 95% confidence interval in order to account for the small difference that exists between studies. Based on the risk groups, the prevalence of TBI was evaluated. Using a random effect model, the studies were weighted. Based on the demographic characteristics, a subgroup meta-analysis was undertaken. The odds ratio and weighted mean difference were used to show the effect sizes for both continuous and dichotomous data, respectively. The 95% CI was used to express each effect estimate. Publication bias was assessed with the help of funnel plot and Beggs test for quantification. Using MetaXL (MS excel) software, we pooled data based on a random-effects model, along with heterogeneity testing using Cochrane's Q and I2 statistic.

Results

Out of the 68 articles, 37 studies were cross-sectional, while 31 were cohort studies (data extracted from cross-sectional of cohort studies at the starting point). The majority of the studies were carried out in the southern part (9057 patients/38.9% of patients), followed by the northern region (5229 patients/22.4% of patients), south-western region (4475 patients/19.2% of

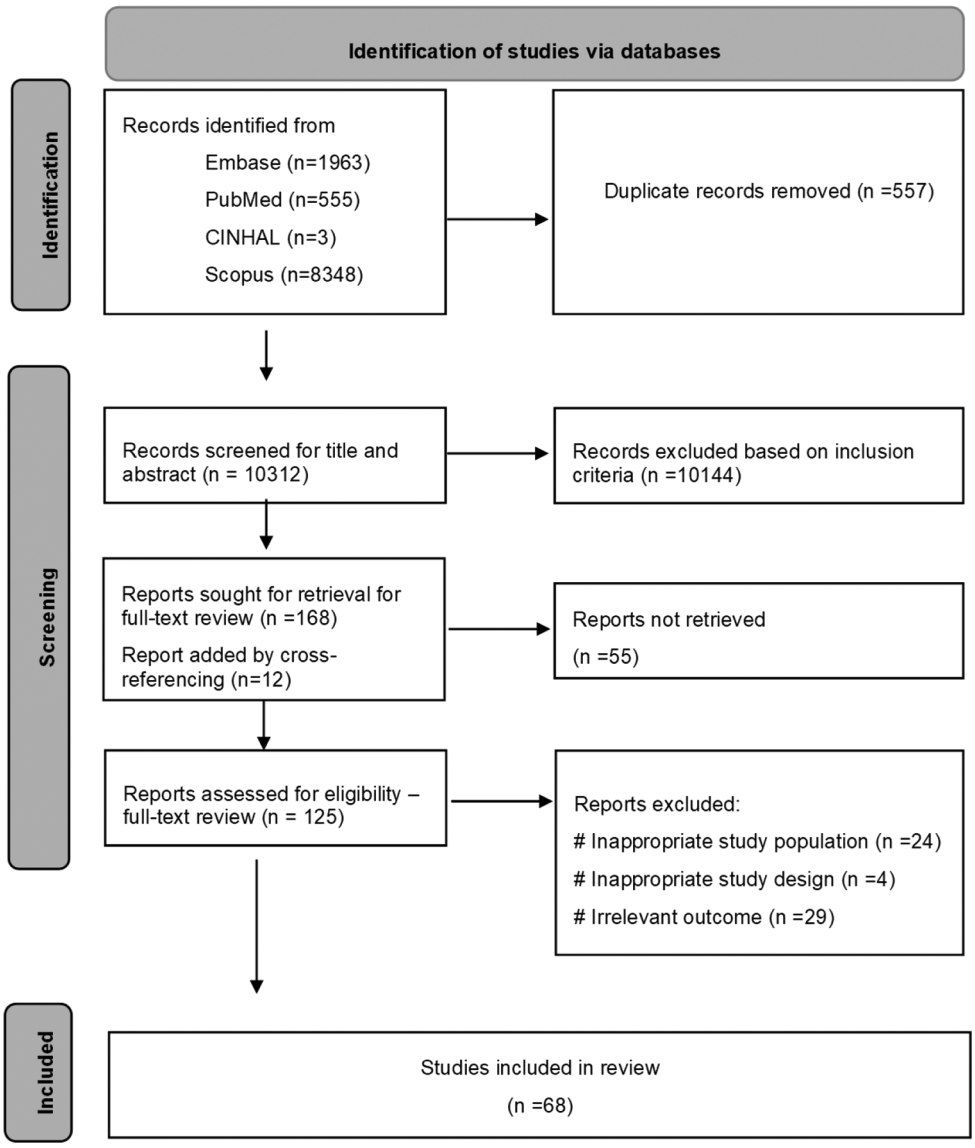

Figure 1: PRISMA flow diagram

patients), western region (2338 patients/10.0% of patients), central region (2146 patients/9.2% of patients) region, and north-eastern region (52 patients/0.22% of patients) of India.[16] The majority of the studies used TST for diagnosing TBI (62/68), 36/68 studies employed the use of both TST and IGRA, 26/68 studies used only TST, and 6/68 studies utilized only IGRA. The majority of the studies recognized TST positivity as more than 10 mm induration (50/62), whereas 12/62 studies considered it as more than 5 mm. The included articles featured a total of 23,283 individuals, ranging from 15 to 1,523 individuals per article [Table 1]. Household contacts, healthcare workers (HCWs), DM, PLHIV, smokers, alcoholics, sarcoidosis, rheumatoid arthritis, hemodialysis, inflammatory bowel disease, retinal detachment, COVID-19, malnutrition, pregnancy, migrants, and psoriasis were the risk factors studied among the included articles. The pooled prevalence of TBI among various risk groups was estimated using the IGRA data owing to its increased specificity compared to TST for diagnosis TBI.[5] When IGRA data were not available, TST data were used for estimation.

Pooled prevalence of TBI

Our analysis of 68 studies found the prevalence of TBI in the presence of any risk factors to be 36% (95% CI: 31%–41%) [Figure 2]. For the publication bias, the funnel plot did not reveal any noticeable asymmetry [Figure 3]. On performing Begg's tests, there was no evidence of a publication bias (Kendall's Tau -0.02518, $P = 0.7614$).

Subgroup analysis

Pooled prevalence of TBI among household contacts

A total of 28 studies assessed TBI prevalence among household contacts. The pooled prevalence of TBI among household contacts was observed to be 47% (95% CI: 39%–55%), with the highest 65% (95% CI: 51%–77%) prevalence observed in those aged above 45 years [Table 2] [Supplementary Figures 1 and 2].

The pooled prevalence among household contacts of microbiologically confirmed pulmonary TB cases was 54% (95% CI: 51%–58%, Q = 69.6, I2 = 81%), and that among contacts of clinically confirmed pulmonary TB was also 54% (95% CI: 41%–67%, Q = 21.96, I2 = 91%).

TBI prevalence among HCWs

In 12 studies among HCWs, the pooled TBI prevalence was observed to be 31% (95% CI: 21%–42%, Q = 27.8, I2 = 98%). Among 15–45 years, it was found to be 22% (95% CI: 16%–29%, Q = 7.18, I2 = 72%), and among > 45 years, it was 27% (95% CI: 3%–59%, Q = 4.62, I2 = 8%) as per the availability of the data.

TBI prevalence among DM

Fourteen studies reported TBI data among diabetics. The pooled TBI prevalence among diabetics was observed to be 53% (95% CI: 43%–63%, Q = 248.56, I2 = 95%). Four studies in them also had separate data on prediabetics; the pooled prevalence was 42% (95% CI: 17%–69%, Q = 113.5, I2 = 97%). Two studies specifically mentioned newly diagnosed DM patients; the pooled prevalence was 24% (95% CI: 19%–29%, Q = 0.03, I2 = 0%), and in three studies, it was mentioned among known DM, the pooled prevalence was 49% (95% CI: 24%–75%, Q = 65.2 I2 = 97%). Diabetes was associated with increased risks of TBI with a pooled odds ratio of 1.50 (95% CI: 0.89–2.52), though statistically insignificant [Figure 4].

TBI prevalence among HIV

A total of 7 studies examined TBI among people living with HIV infection; the prevalence was found to be 44% (95% CI: 16%–74%).

TBI prevalence among COVID-19

Based on the 3 studies reporting COVID-19, the pooled TBI prevalence was 35% (95% CI: 22%–49%).

TBI prevalence among other risk groups

The pooled prevalence of TBI among smokers, alcoholics, malnourished individuals, pregnant females, sarcoidosis, rheumatoid arthritis, psoriasis, hemodialysis, retinal detachment, and inflammatory bowel disease is given in Table 3 [Supplementary Figures 3 and 4]. Combined pooled prevalences of various risk factors with household contacts were found to be higher than individual risk factors, for example, household contacts with DM (64% CI: 45%–81%, n = 2), household contacts with smokers (60% CI: 24%–75%, n = 3), household contacts with HIV (58% CI: 43%–73%, n = 3), and household contacts with malnutrition (45% CI: 36%–54%, n = 2), whereas the pooled prevalence of TBI among hypertensives with DM was observed to be 31% (CI: 27%–35%, n = 2), while only one study provided data on HIV patients having DM, which reported all HIV-DM patients positive with TBI.

Discussion

The high prevalence of TBI in India is consistent with the high prevalence of active TB, indicating an ongoing breakdown from TBI to active TB. With this background, we assessed the burden among various groups at risk of TBI in India. Our review found a high pooled prevalence among smokers, diabetics, malnourished individuals, alcoholics, household contacts, HIV, and HCWs. Further, those with presence of two risk factors, such as household contacts and smokers or diabetics and hypertensives, exhibited high TBI prevalence.

We found a high prevalence of TBI among various risk groups in India. Currently, WHO does not recommend systematic TBI testing and treatment in DM, malnutrition, smokers, and alcoholics.[83] In 2018, the Asia Latent Tuberculosis (ALTER) expert panel suggested diabetics and malnourished can be considered for TPT based on the local epidemiology.[84] Countries such as Myanmar and Japan have included DM as an at-risk group for TBI.[85,86] Philippines has "*No test, treat only*" policy for diabetics, malnourished, and smokers.[87,88] A possible explanation for *treat only* policy could be less reliability of QFT and high chances of false negative results

Table 1: Study characteristics of the included articles

Author, Year	State	Study design	Sample size	Risk group	Test	TST size
Agarwal *et al*., 2014[17]	UP	cross-sectional	250	Inflammatory bowel disease	TST	≥10 mm
Agarwal *et al*., 2015[18]	Delhi	cross-sectional	185	Dialysis	IGRA & TST	≥10 mm
Arya *et al*., 2018[19]	UP	Cohort	43	Healthcare workers	TST	≥10 mm
Aravindham *et al*., 2022[20]	Tamil Nadu	cross-sectional	170	Diabetes	IGRA	NA
Bajgai *et al*., 2015[21]	Haryana	cohort	100	Retinal detachment	TST	≥10 mm
Bari *et al*., 2023[22]	Telangana	cross-sectional	24	HCWs	TST	≥10 mm
Bekken *et al*., 2020[23]	Andhra Pradesh	cross-sectional	476	Contacts	IGRA & TST	≥10 mm
Benachinmardi *et al*., 2019[24]	Karnataka	cross-sectional	77	Contacts	IGRA & TST	≥5 mm
Benachinmardi *et al*., 2021[25]	Karnataka	cross-sectional	77	Contacts	IGRA & TST	≥5 mm
Boddu, *et al*. 2019[26]	Tamil Nadu	cohort	80	Contacts	IGRA & TST	≥10 mm
Chandrasekharan *et al*., 2018[27]	Maharashtra and TN	cohort	869	Contacts	IGRA & TST	≥5 mm
Chauhan *et al*., 2013[28]	UP	cross-sectional	200	Contacts	TST	≥10 mm
Christopher *et al*., 2014[29]	Tamil Nadu	cohort	755	Healthcare workers	TST	≥10 mm
Dayal *et al*., 2018[30]	UP	cross-sectional	271	Contacts	TST	≥10 mm
Dabhi *et al*., 2022[31]	Tamil Nadu	cross-sectional	200	Diabetes	IGRA & TST	≥10 mm
Dinkar *et al*., 2022[32]	UP	cross-sectional	561	Healthcare workers	TST	≥10 mm
Dolla *et al*., 2019[33]	Maharashtra and TN	cohort	1020	Contacts	IGRA & TST	≥5 mm
Girish *et al*., 2021[34]	Maharashtra	cohort	200	Healthcare workers	IGRA & TST	≥10 mm
Gupta *et al*., 2020[35]	Maharashtra	cross-sectional	205	Contacts	IGRA & TST	≥5 mm
Gupta *et al*., 2021[36]	Delhi	cohort	60	COVID	TST	≥10 mm
James *et al*., 2014[37]	Karnataka	cross-sectional	100	HIV	IGRA & TST	≥10 mm
Janagond *et al*., 2017[38]	Tamil Nadu	cohort	206	Healthcare workers	TST	≥10 mm
Jenum *et al*., 2014[39]	Andhra Pradesh	cross-sectional	702	Contacts	IGRA & TST	≥10 mm
Kabeer *et al*., 2018[40]	Tamil Nadu	cohort	572	General population	IGRA & TST	≥10 mm
Kashyap *et al*., 2014[91]	Maharashtra	cohort	162	Contacts	IGRA & TST	≥10 mm
Kaul *et al*., 2022[41]	Delhi	cohort	80	Contacts	IGRA	NA
Kubaik *et al*., 2019[42]	Tamil Nadu	cross-sectional	1113	Diabetes	TST	≥10 mm
Kim *et al*., 2023[43]	Maharashtra & TN	cross-sectional	170	Contacts	IGRA & TST	≥5 mm
Kinikar *et al*., 2019[44]	Maharashtra	cohort	200	Healthcare workers	IGRA & TST	≥10 mm
Krishnamoorthy *et al*., 2021[45]	Tamil Nadu	cross-sectional	1523	Contacts	TST	≥5 mm
Kumar *et al*., 2014[46]	Karnataka	cohort	125	Healthcare workers	TST	≥10 mm
Kumar *et al*., 2019[47]	Karnataka	cohort	598	Healthcare workers	TST	≥10 mm
Kumar *et al*., 2022[48]	Delhi	cohort	171	Inflammatory Bowel disease	TST	≥10 mm
Kumar *et al*., 2014[49]	Tamil Nadu	cross-sectional	150	Diabetes Mellitus	IGRA & TST	≥12 mm
Madan *et al*., 2021[50]	Delhi	cohort	60	COVID	TST	≥10 mm
Madan *et al*., 2022[51]	Delhi	cohort	327	Sarcoidosis	TST	≥10 mm
Malviya *et al*., 2018[52]	Delhi	cross-sectional	730	Rheumatoid arthritis	IGRA & TST	≥10 mm
Malviya *et al*., 2019[53]	Delhi	cross-sectional	44	Rheumatoid arthritis	IGRA & TST	≥10 mm
Mantri *et al*., 2021[54]	Delhi	cohort	257	Inflammatory bowel disease	IGRA & TST	≥10 mm
Mathad *et al*., 2014[55]	Maharashtra	cross-sectional	401	Pregnancy	IGRA & TST	≥10 mm
Mathad *et al*., 2016[56]	Maharashtra	cross-sectional	252	Pregnancy	IGRA & TST	≥5 mm
Mave *et al*., 2019[57]	Maharashtra and TN	cross-sectional	780	Contacts	IGRA & TST	≥5 mm
Mishra *et al*., 2017[58]	UP	cross-sectional	200	Contacts	TST	≥10 mm
Narsimhan *et al*., 2017[59]	Tamil Nadu	cross-sectional	663	Contacts	IGRA & TST	≥10 mm
Neema *et al*., 2019[60]	Maharashtra	cohort	105	Psoriasis	TST	≥10 mm
Neema *et al*., 2019[61]	Maharashtra	cross-sectional	75	Psoriasis	IGRA & TST	≥10 mm
Pattnaik *et al*., 2021[62]	Delhi	cohort	15	Sarcoidosis	TST	≥10 mm
Paradkar *et al*., 2020[63]	Maharashtra and TN	cohort	997	Contacts	IGRA & TST	≥5 mm
Prabhavathi *et al*., 2015[64]	Tamil Nadu	cohort	144	General population	IGRA & TST	≥10 mm
Prabhavati *et al*., 2015[109]	Tamil Nadu	cross-sectional	53	HIV	IGRA	NA
Patil *et al*., 2014[65]	Maharashtra	cross-sectional	100	HIV	TST	≥10 mm
Rajamanickam *et al*., 2020[66]	Tamil Nadu	cross-sectional	133	COVID	IGRA	NA
Rajalakshmi *et al*., 2017[67]	Tamil Nadu	cross-sectional	196	Diabetes	IGRA & TST	≥10 mm
Reddy *et al*., 2021[68]	Tamil Nadu	cohort	1189	Contacts	TST	≥10 mm

Contd...

Table 1: Contd...

Author, Year	State	Study design	Sample size	Risk group	Test	TST size
Sawhney *et al*., 2015[69]	Haryana	cross-sectional	200	Healthcare workers	TST	≥10 mm
Shah *et al*., 2019[70]	Maharashtra	cross-sectional	33	Contacts	IGRA & TST	≥10 mm
Sharma *et al*., 2017[71]	Delhi	cohort	1511	Contacts	IGRA & TST	≥10 mm
Shivakumar *et al*., 2018[72]	Maharashtra and TN	cross-sectional	639	Diabetes	IGRA & TST	≥5 mm
Shobha *et al*., 2018[73]	Karnataka	cross-sectional	178	Rheumatoid arthritis	IGRA & TST	≥10 mm
Shrivastava *et al*., 2020[74]	UP	cross-sectional	152	Contacts	TST	≥10 mm
Singh *et al*., 2013[75]	Delhi	cohort	1389	Contacts	TST	≥10 mm
Singh *et al*., 2021[76]	UP	cross-sectional	469	HIV	IGRA & TST	≥10 mm
Siddiqui *et al*., 2022[77]	Sikkim	cross-sectional	52	Migrant population	IGRA	NA
Surve *et al*., 2021[78]	Maharashtra	cohort	299	Contacts	IGRA & TST	≥10 mm
Thamke *et al*., 2018[79]	Maharashtra	cohort	80	Contacts	IGRA & TST	≥10 mm
Vyas *et al*., 2015[80]	Tamil Nadu	cross-sectional	62	Sarcoidosis	IGRA & TST	≥10 mm
Zwerling *et al*. 2013[81]	Maharashtra	cross-sectional	226	Healthcare workers	IGRA	NA
Zia *et al*., 2021[82]	Delhi	cross-sectional	100	Rheumatoid arthritis	TST	≥5 mm

Table 2: Age-wise pooled TBI prevalence among household contacts

Age group	Studies (*n*)	Random-effects model		Heterogeneity I^2 (%)
		Prevalence	95% CI	
<5 years	9	25%	16% - 34%	90
6-14 years	9	45%	35% - 55%	92
15-44 years	8	42%	25% - 60%	99
>45 years	5	65%	51% - 77%	94

Note: Forest plot and funnel plot provided in supplementary Figure 1 and Figure 2

among DM, malnourished, and smokers due to impaired T-cell function.[89,90,92] India has the second highest diabetic population in the world.[7] Noubiap *et al.* estimated 19.9% pooled prevalence of diabetes among TB patients in India.[93] Diabetics have three times higher risk of TB compared to general population.[94,95] Researchers in Indonesia found a higher TB incidence among diabetes with TBI (1.7 per 100 person-years) compared to those without TBI.[96] Forbes *et al.* in their mathematical model suggested among chronic conditions such as diabetes, TST and IGRA have poor predictive value when the TBI prevalence is above 40%.[97] A study conducted by Koesoemadinata *et al.* found patients with DM were less likely to be IGRA-positive compared to TB contacts.[98] Further, three observational studies conducted in Germany (1950) and Russia (1960) and among Indians in USA (1992) suggested preventive treatment with either isoniazid or an isoniazid analog, respectively, reduced the primary and secondary risk of TB in diabetes patients.[99,100] Another drug, rifapentine, included in TPT is a potent inducer of cytochrome p450, interfering with the metabolism of oral antidiabetic drugs.[101] However, Huang and colleagues reported 3HP to be safer among poorly controlled diabetic patients with only 2.9% patients experiencing mild fluctuations in glucose levels.[101] Zheng *et al.*, based on the pharmacokinetics and drug–drug interactions, reported rifapentine to be suitable even in diabetics with poor renal function and age above 65 years.[102] Considering TBI treatment valid for other pathologies that cause immunosuppression, it is worthwhile to consider the use of TPT among other risk groups.

We found a 59% pooled prevalence of TBI among smokers and 53% among alcoholics. Similar findings were reported by Feng *et al.*, who reported 40.8% prevalence of TBI among smokers in Taiwan.[103] Three comprehensive meta-reviews conducted among homeless, incarcerated, and immigrants have suggested smoking doubles the risk of TBI (RR 1.8–2.2).[104–106] However, the impact of tobacco on TBI has been negated by its universal association with alcohol, poverty, and overcrowding. Similarly, malnutrition also predisposes an individual to TB.[107] We observed a 48% TBI prevalence among malnourished individuals. Malnutrition subverts the immune system and causes either TB disease immediately after TBI or reactivation of TBI into TB disease.[107] Increased metabolism due to disease *per se* causes an increased in metabolism, which along with reduced appetite compounds already presents malnutrition.[107] Rajamanickam *et al.* reported malnourished individuals have low chemokine levels, which could promote *M.tb* proliferation or alter anti-TB immune responses.[66] So, if TPT is offered to risk groups such as DM, HIV, tobacco users, and malnourished, approximately 46% of the total population would be covered. Thus, not only reprioritization of risk groups is vital but also tailored strategies involving scaling-up of TPT is necessitated.

Our review observed a 47% TBI prevalence among household contacts. Similar findings (42%) were reported by Velen *et al.* in their systematic review among contacts of active TB disease.[90] We also observed a higher TBI prevalence among adults and older adults. This is commensurate with the National TB prevalence survey, 2020–21, findings from India.[4] Further, our review observed those with presence of two risk factors demonstrated higher TBI prevalence. Clustering of immunosuppressive triggers such as malnutrition, tobacco, and alcohol use among household contacts increases the susceptibility to TB disease. We also observed contacts of microbiologically confirmed and clinically confirmed

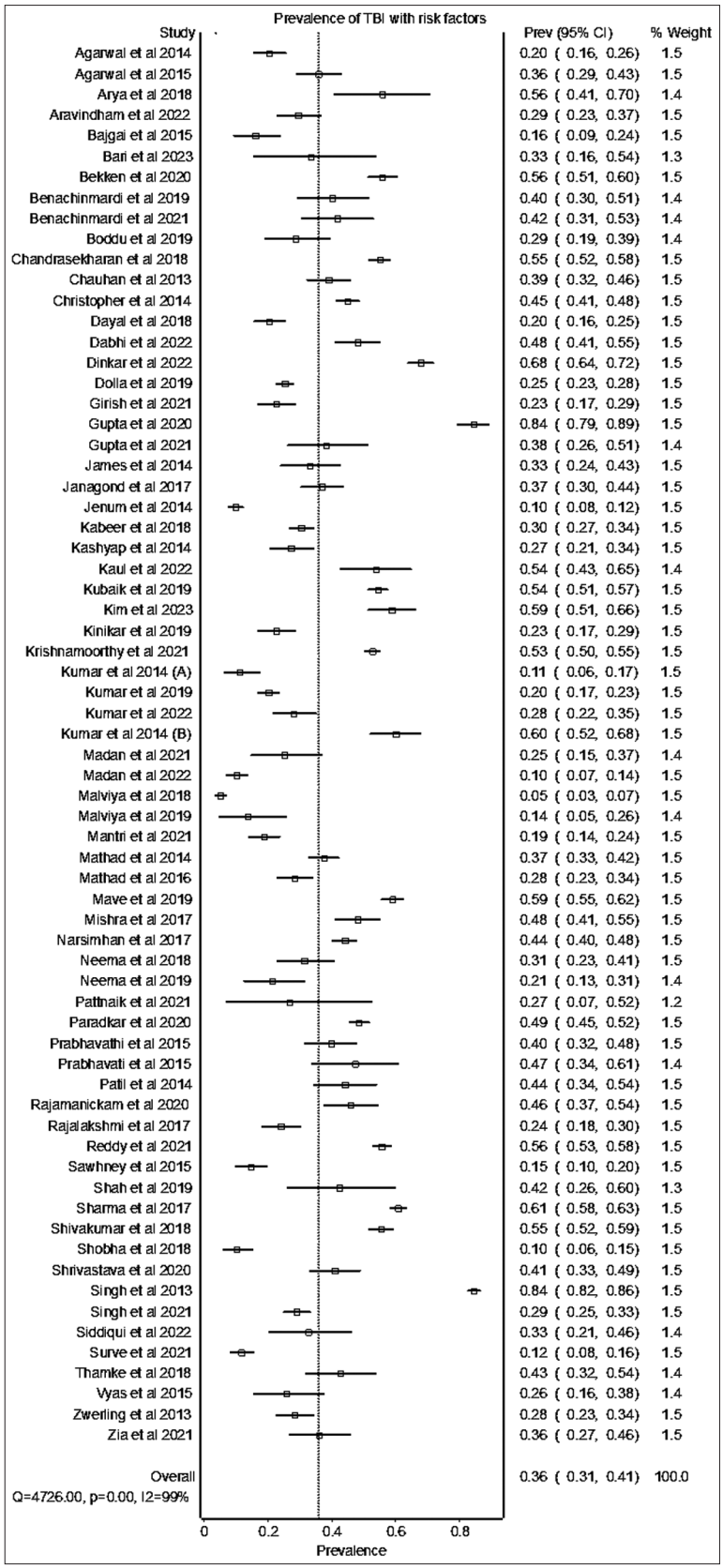

Figure 2: TBI prevalence with risk factors

Table 3: TBI prevalence among various risk groups in India

Risk group	Studies (*n*)	Random-effects model		Heterogeneity
		Prevalence	95% CI	I^2 (%)
Smokers	7	59%	40% - 77%	94
Diabetes mellitus	14	53%	43% - 63%	95
Alcohol	7	53%	38% - 67%	88
Malnutrition	11	48%	43% - 53%	76
Household contacts	28	47%	39% - 55%	99
HIV	7	44%	16% - 74%	98
Pregnancy	3	36%	28% - 44%	80
COVID- 19	3	35%	22% -49%	76
HCWs	12	31%	21% - 42%	98
Rheumatoid arthritis	5	15%	7% - 27%	93
Sarcoidosis	3	18%	6% - 34%	83
Psoriasis	2	27%	17% - 37%	55
Inflammatory bowel disease	2	20%	16% -23%	0

Note: Forest plot and funnel plot provided in supplementary Figure 3 and Figure 4

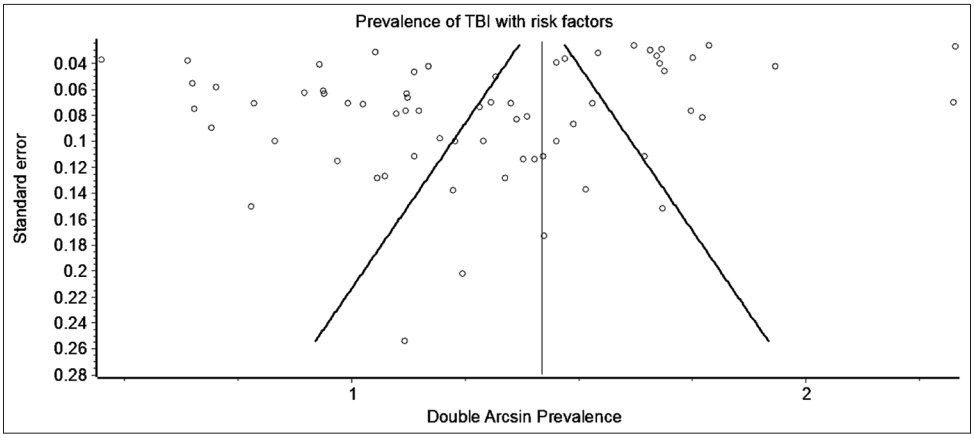

Figure 3: Funnel plot for TBI prevalence

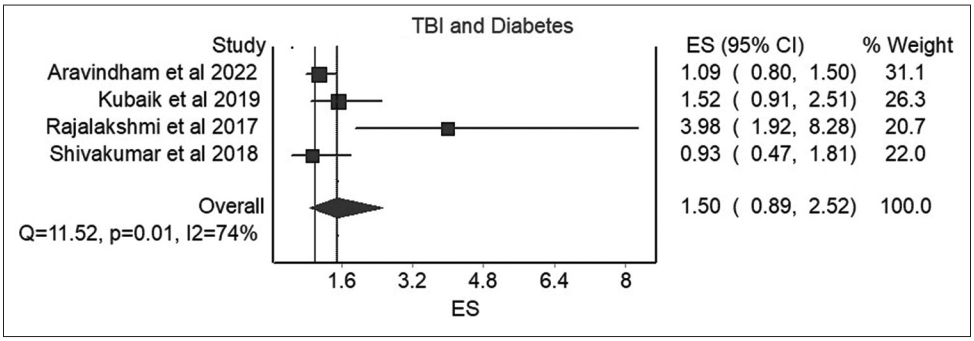

Figure 4: Association between TBI and DM

pulmonary TB disease had a similar TBI prevalence. Current guidelines for Programmatic Management of TPT (PMTPT) in India recommend administration of TPT without testing only among contacts of microbiologically pulmonary TB cases.[108] Based on the findings, contacts of clinically confirmed pulmonary TB cases for TPT without testing should also be contemplated. Hence, along with early diagnosis and treatment of infectious cases to reduce transmission, prevention of TBI and subsequently TB disease by TPT is essential, especially among the locally prevalent risk factor groups.

Limitations

This is the first comprehensive analysis reporting the prevalence of TBI among various risk groups in India. A multidisciplinary team conducted an intensive systematic search of literature and manually searched references. This not only enhanced the

validity but also provided a deeper understanding of the impact of TBI on various risk categories. There were some limitations though. Ideally, for TST, we avoided categorizing the research based on the strength of PPD used in the studies. Furthermore, there was inconsistency in the diagnosis of TBI particularly when employing the TST method as some studies observed TBI positivity as more than 5 mm as TBI regardless of the immunocompromised status. Some subgroups had few studies, which meant there was not enough statistical power to determine the cause of the heterogeneity. The evidence encompasses all of India with the exception of the eastern region, which limits the ability to fully depict the findings throughout the country. However, the information provided here will enable India to implement a more robust programmatic approach for TBI.

Implications and way forward

Considering the likelihood of missing positive individuals as a result of the diagnostic tests' poor predictive value and high operational cost, it is necessary to prioritize the commencement of TPT for risk groups, particularly those with diabetes, smokers, drinkers, and malnourished individuals. After ruling out active TB for specific high-risk groups (DM, smokers, and malnourished), a more thorough approach is required, taking into account the "No test, treat only" strategy, considering the less reliability of diagnostic test in impaired immune conditions. Additionally, for those groups with prevalence more than 40% as well as presence of more than one risk factor over and above DM, smokers and malnourished may also be considered for *treat only* policy. Also, it is essential to identify the factors catalyzing the pathway of TBI resulting in the conversion to active TB. More research is required to ascertain the prevalence of TBI among multimorbidity (the presence of two or more chronic conditions in same individual). Among high-risk groups, having other risk increases the chances of progression to active TB. There is a need for updating and intensive monitoring of effective implementation of TB-Diabetes collaborative framework it is and other comorbidity framework in India. Further evidence is required for silicosis, condominiums, mental homes, and prisoners. The national guidelines need to be reconsidered with contextually and epidemiologically relevant inclusion of more comorbidities.

Conclusion

This review exhibited a high prevalence of TBI among smokers, DM, malnourished, household contacts, alcoholics, HIV, COVID-19, and HCWs. We also observed a high burden among those with an increase in number of risk factors, suggesting a need for revising and revisiting the TBI country-specific strategies targeting patient level interventions. Risk groups and the strategy of 'no test, treat only' need to be reprioritized based on the local epidemiology.

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Conflicts of interest

Malik Parmar, Hardik Solanki, Sandeep Chauhan are affiliated to the World Health Organization (WHO). The views expressed in the submitted article are their own and not an official position of their respective institutions.

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Supple File S1: Search Strategy

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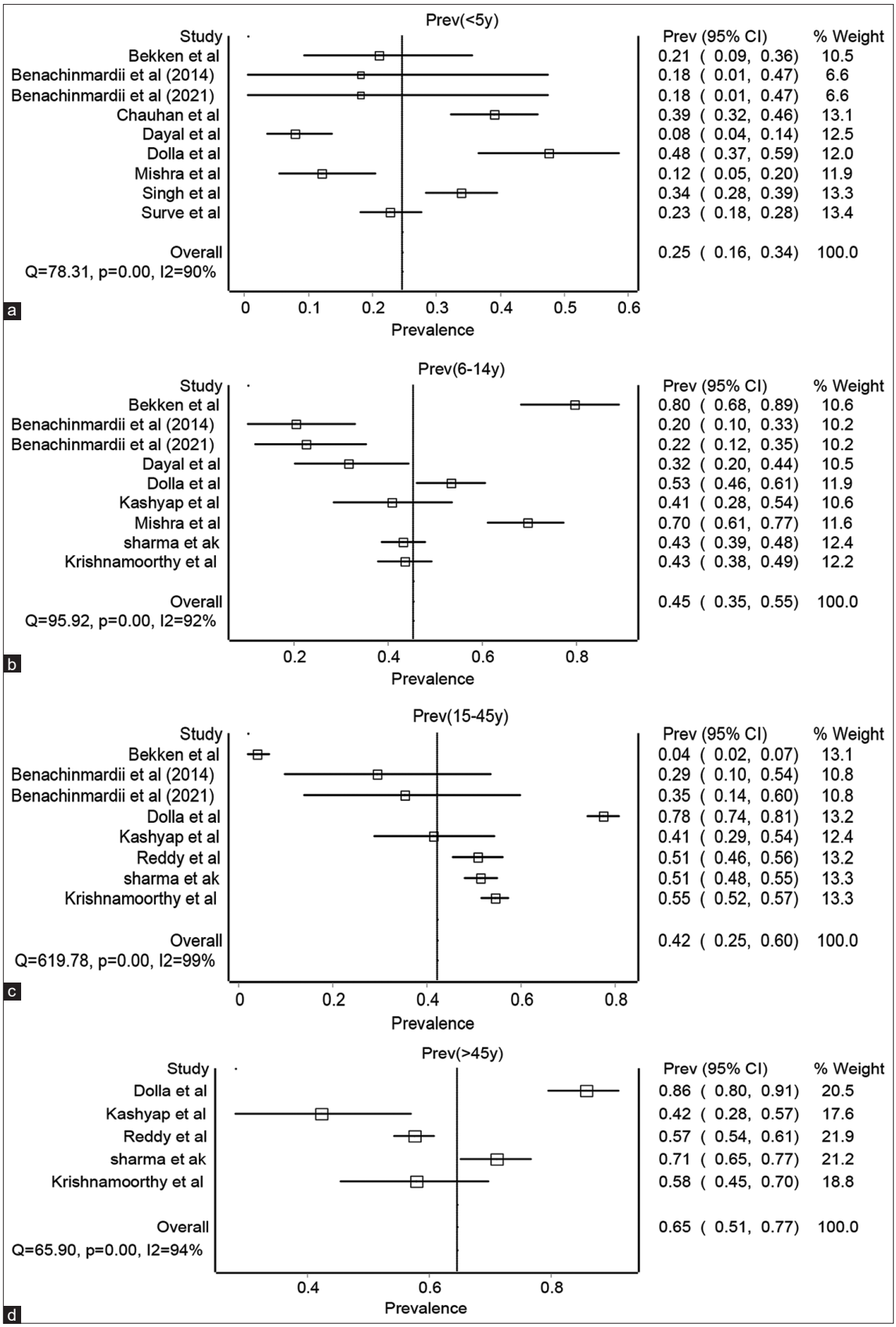
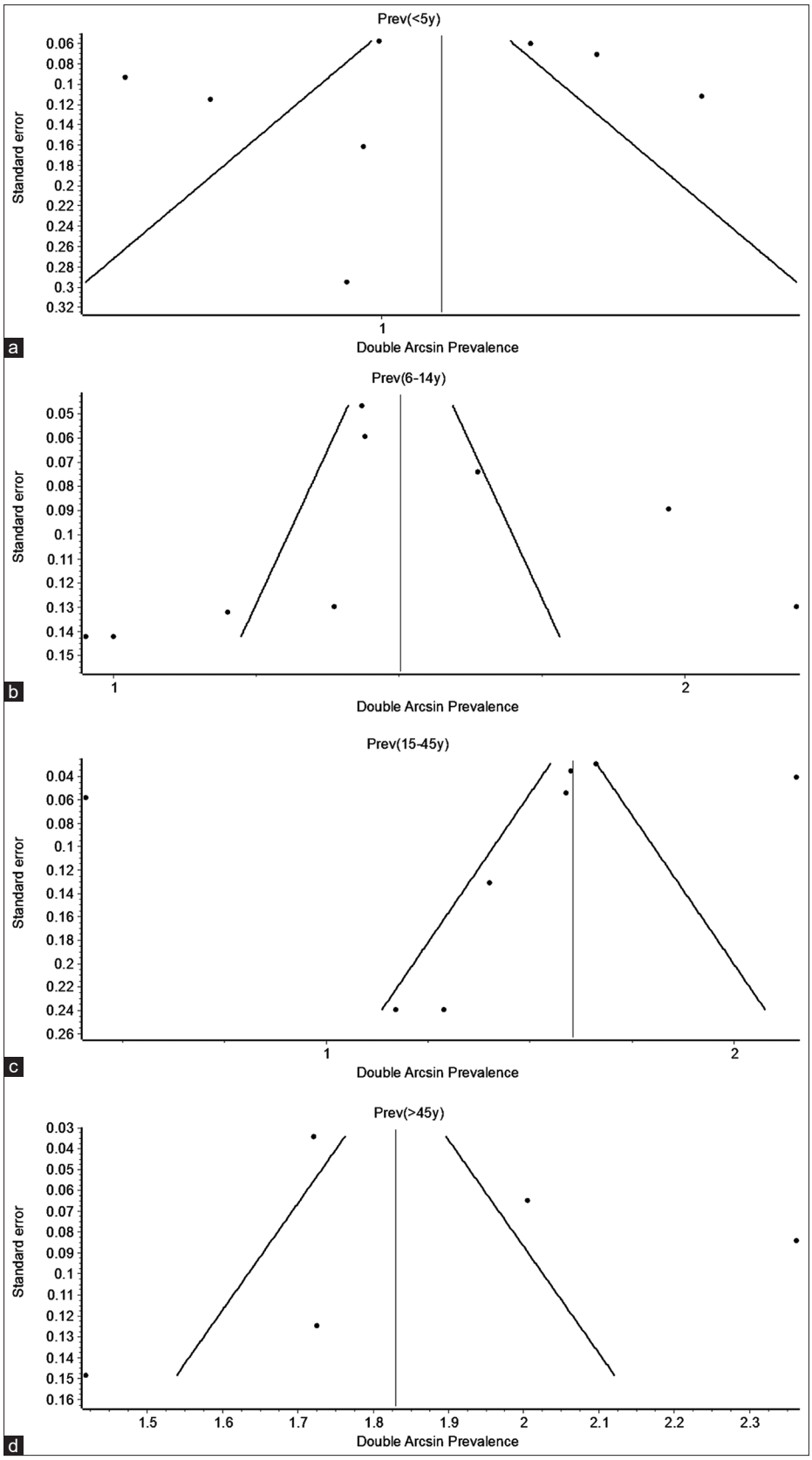
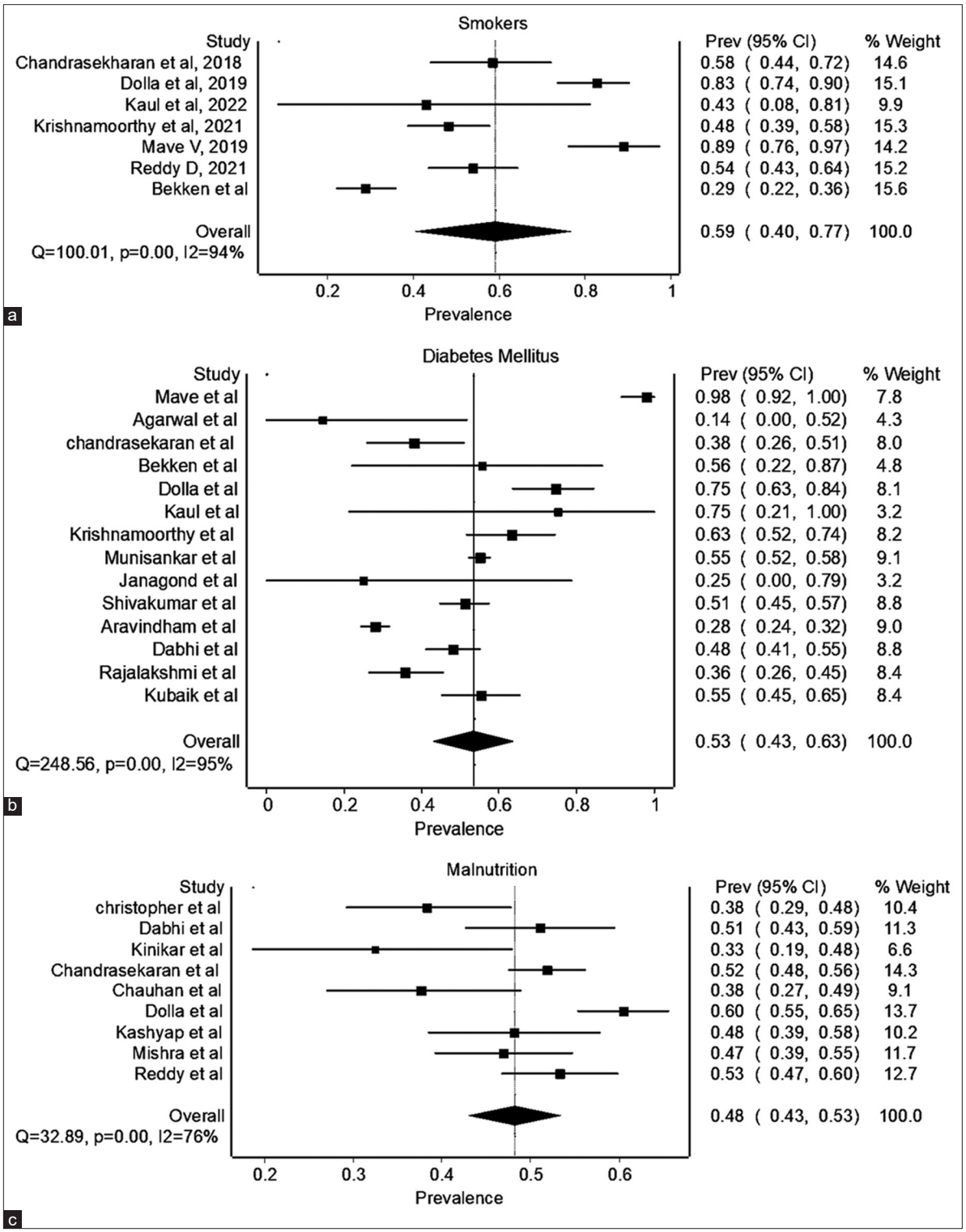


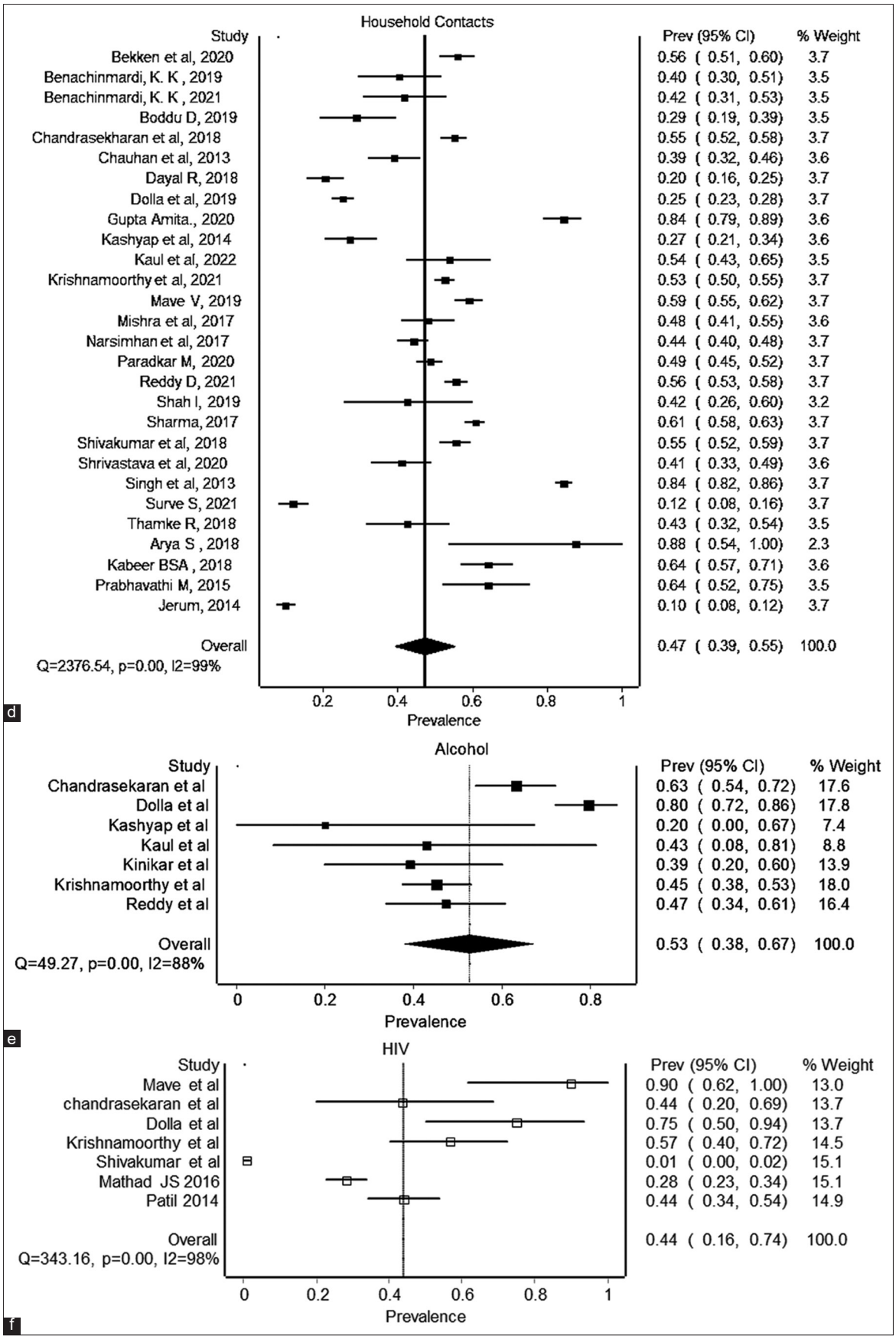
Supplementary Figure 1: (a) Forest plot showing age-wise pooled TBI prevalence among household contacts (<5 Years) (b) Forest plot showing age-wise pooled TBI prevalence among household contacts (6-14 Years) (c) Forest plot showing age-wise pooled TBI prevalence among household contacts (15-45 Years) (d) Forest plot showing age-wise pooled TBI prevalence among household contacts (>45 Years)

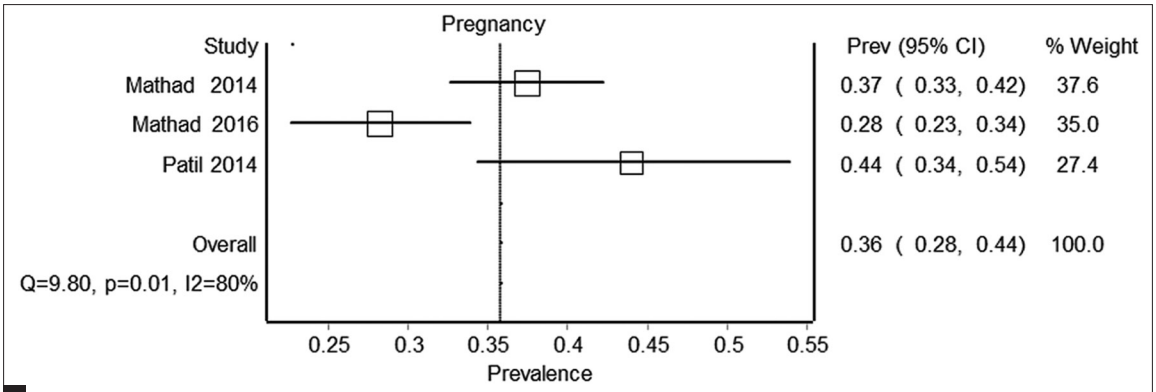


Supplementary Figure 2: (a) Funnel plot Age-wise pooled TBI prevalence among household contacts (<5 Years) (b) Funnel plot Age-wise pooled TBI prevalence among household contacts (6-14 Years) (c) Funnel plot Age-wise pooled TBI prevalence among household contacts (15-45 Years) (d) Funnel plot Age-wise pooled TBI prevalence among household contacts (>45 Years)

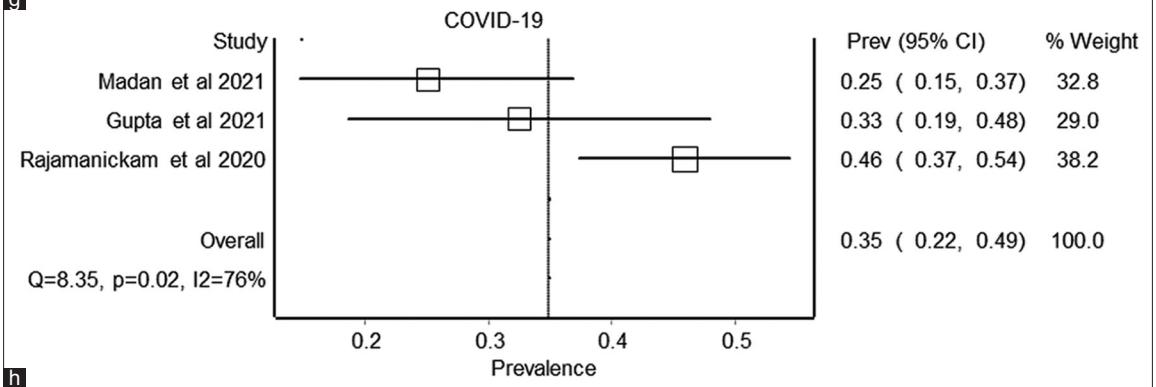
Supplementary Figure 3: (a) Forest plot showing pooled TBI prevalence among smokers. (b) Forest plot showing pooled TBI prevalence among patients with diabetes mellitus. (c) Forest plot showing pooled TBI prevalence among patients with malnutrition. (d) Forest plot showing pooled TBI prevalence among households contacts. (e) Forest plot showing pooled TBI prevalence among alcohol users. (f) Forest plot showing pooled TBI prevalence among HIV patients, (g) Forest plot showing pooled TBI prevalence among pregnant women (h) Forest plot showing pooled TBI prevalence among patients suffered from COVID-19, (i) Forest plot showing pooled TBI prevalence among health care workers (HCWs). (j) Forest plot showing pooled TBI prevalence among patients with rheumatoid arthritis. (k) Forest plot showing pooled TBI prevalence among patients with sarcoidosis. (l) Forest plot showing pooled TBI prevalence among patients with Psoriasis, (m) Forest plot showing pooled TBI prevalence among patients with inflammatory bowel disease



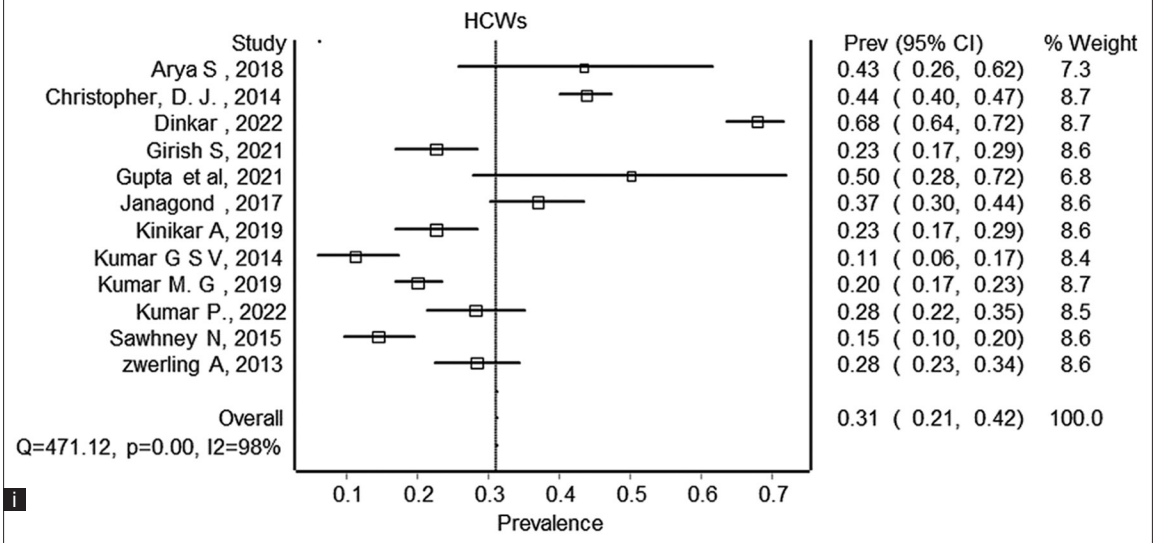

Household Contacts
Study
Prev (95% CI)
% Weight
Bekken et al, 2020 0.56 (0.51, 0.60) 3.7
Benachinmardi, K. K , 2019 0.40 (0.30, 0.51) 3.5
Benachinmardi, K. K , 2021 0.42 (0.31, 0.53) 3.5
Boddu D, 2019 0.29 (0.19, 0.39) 3.5
Chandrasekharan et al, 2018 0.55 (0.52, 0.58) 3.7
Chauhan et al, 2013 0.39 (0.32, 0.46) 3.6
Dayal R, 2018 0.20 (0.16, 0.25) 3.7
Dolla et al, 2019 0.25 (0.23, 0.28) 3.7
Gupta Amita., 2020 0.84 (0.79, 0.89) 3.6
Kashyap et al, 2014 0.27 (0.21, 0.34) 3.6
Kaul et al, 2022 0.54 (0.43, 0.65) 3.5
Krishnamoorthy et al, 2021 0.53 (0.50, 0.55) 3.7
Mave V, 2019 0.59 (0.55, 0.62) 3.7
Mishra et al, 2017 0.48 (0.41, 0.55) 3.6
Narsimhan et al, 2017 0.44 (0.40, 0.48) 3.7
Paradkar M, 2020 0.49 (0.45, 0.52) 3.7
Reddy D, 2021 0.56 (0.53, 0.58) 3.7
Shah I, 2019 0.42 (0.26, 0.60) 3.2
Sharma, 2017 0.61 (0.58, 0.63) 3.7
Shivakumar et al, 2018 0.55 (0.52, 0.59) 3.7
Shrivastava et al, 2020 0.41 (0.33, 0.49) 3.6
Singh et al, 2013 0.84 (0.82, 0.86) 3.7
Surve S, 2021 0.12 (0.08, 0.16) 3.7
Thamke R, 2018 0.43 (0.32, 0.54) 3.5
Arya S , 2018 0.88 (0.54, 1.00) 2.3
Kabeer BSA , 2018 0.64 (0.57, 0.71) 3.6
Prabhavathi M, 2015 0.64 (0.52, 0.75) 3.5
Jerum, 2014 0.10 (0.08, 0.12) 3.7
Overall 0.47 (0.39, 0.55) 100.0
Q=2376.54, p=0.00, I2=99%
0.2 0.4 0.6 0.8 1
Prevalence
d
Alcohol
Study
Prev (95% CI)
% Weight
Chandrasekaran et al 0.63 (0.54, 0.72) 17.6
Dolla et al 0.80 (0.72, 0.86) 17.8
Kashyap et al 0.20 (0.00, 0.67) 7.4
Kaul et al 0.43 (0.08, 0.81) 8.8
Kinikar et al 0.39 (0.20, 0.60) 13.9
Krishnamoorthy et al 0.45 (0.38, 0.53) 18.0
Reddy et al 0.47 (0.34, 0.61) 16.4
Overall 0.53 (0.38, 0.67) 100.0
Q=49.27, p=0.00, I2=88%
0 0.2 0.4 0.6 0.8
Prevalence
e
HIV
Study
Prev (95% CI)
% Weight
Mave et al 0.90 (0.62, 1.00) 13.0
chandrasekaran et al 0.44 (0.20, 0.69) 13.7
Dolla et al 0.75 (0.50, 0.94) 13.7
Krishnamoorthy et al 0.57 (0.40, 0.72) 14.5
Shivakumar et al 0.01 (0.00, 0.02) 15.1
Mathad JS 2016 0.28 (0.23, 0.34) 15.1
Patil 2014 0.44 (0.34, 0.54) 14.9
Overall 0.44 (0.16, 0.74) 100.0
Q=343.16, p=0.00, I2=98%
0 0.2 0.4 0.6 0.8 1
Prevalence
f


Pregnancy
Study
Prev (95% CI)
% Weight
Mathad 2014
0.37 (0.33, 0.42)
37.6
Mathad 2016
0.28 (0.23, 0.34)
35.0
Patil 2014
0.44 (0.34, 0.54)
27.4
Overall
0.36 (0.28, 0.44)
100.0
Q=9.80, p=0.01, I2=80%
0.25 0.3 0.35 0.4 0.45 0.5 0.55
Prevalence

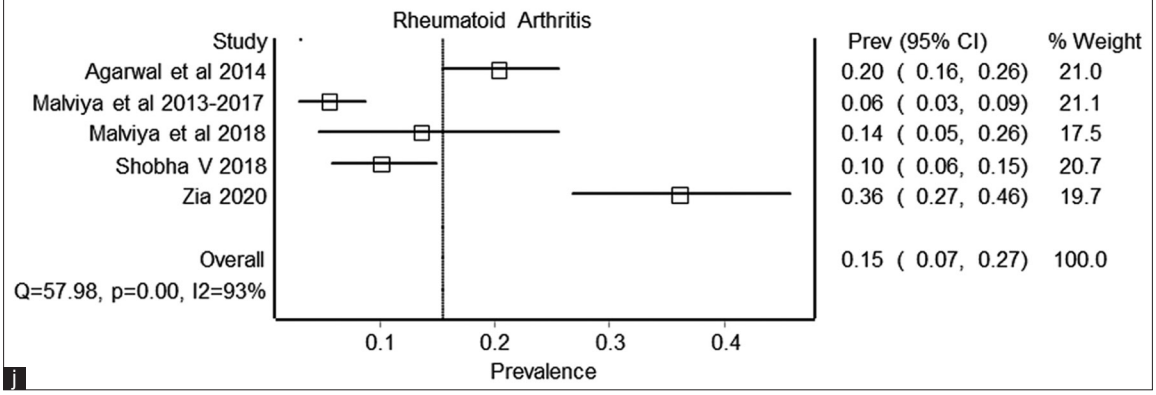
g


COVID-19
Study
Prev (95% CI)
% Weight
Madan et al 2021
0.25 (0.15, 0.37)
32.8
Gupta et al 2021
0.33 (0.19, 0.48)
29.0
Rajamanickam et al 2020
0.46 (0.37, 0.54)
38.2
Overall
0.35 (0.22, 0.49)
100.0
Q=8.35, p=0.02, I2=76%
0.2 0.3 0.4 0.5
Prevalence

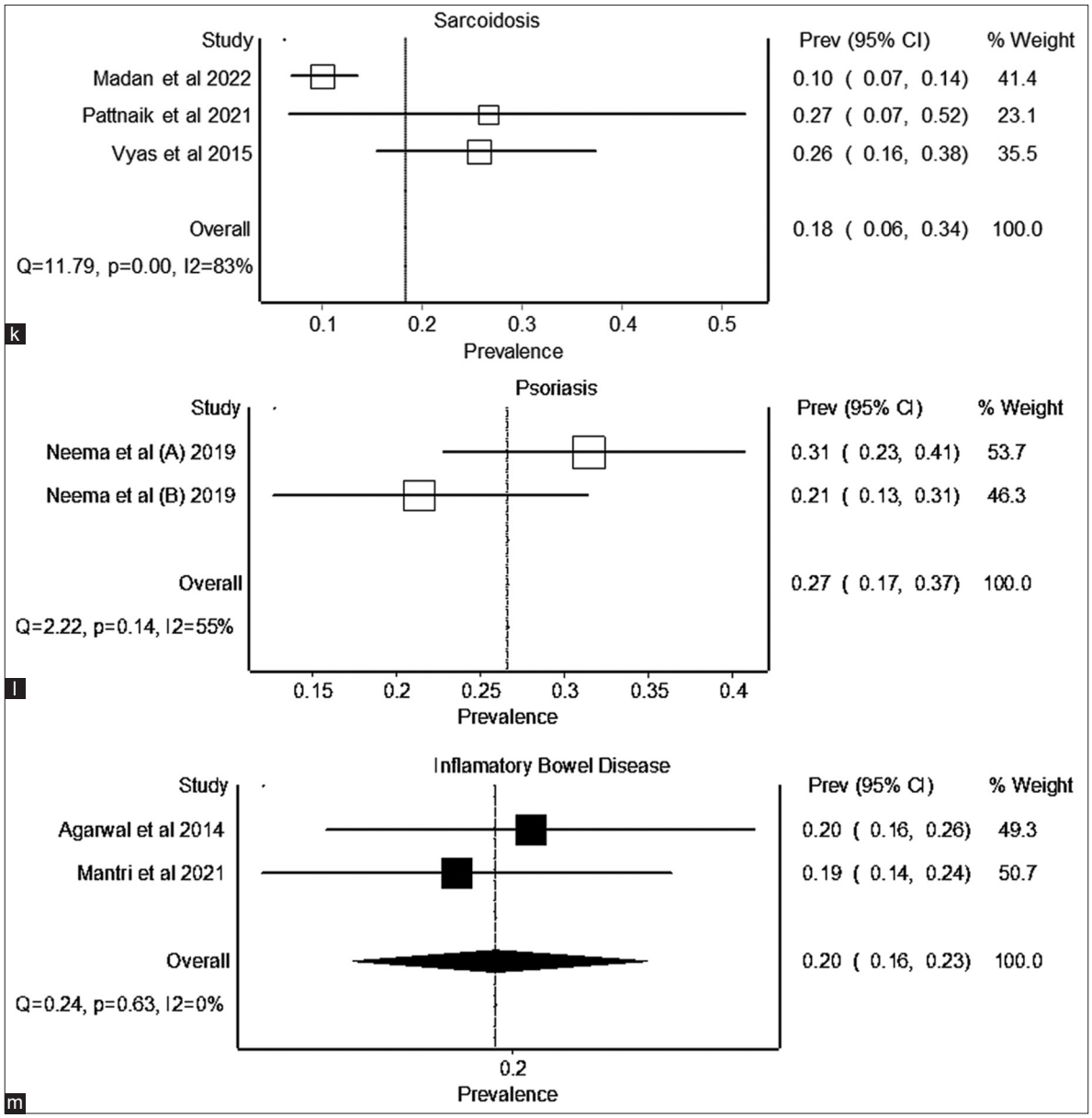
h


HCWs
Study
Prev (95% CI)
% Weight
Arya S , 2018
0.43 (0.26, 0.62)
7.3
Christopher, D. J. , 2014
0.44 (0.40, 0.47)
8.7
Dinkar , 2022
0.68 (0.64, 0.72)
8.7
Girish S, 2021
0.23 (0.17, 0.29)
8.6
Gupta et al, 2021
0.50 (0.28, 0.72)
6.8
Janagond , 2017
0.37 (0.30, 0.44)
8.6
Kinikar A, 2019
0.23 (0.17, 0.29)
8.6
Kumar G S V, 2014
0.11 (0.06, 0.17)
8.4
Kumar M. G , 2019
0.20 (0.17, 0.23)
8.7
Kumar P., 2022
0.28 (0.22, 0.35)
8.5
Sawhney N, 2015
0.15 (0.10, 0.20)
8.6
zwerling A, 2013
0.28 (0.23, 0.34)
8.6
Overall
0.31 (0.21, 0.42)
100.0
Q=471.12, p=0.00, I2=98%
0.1 0.2 0.3 0.4 0.5 0.6 0.7
Prevalence

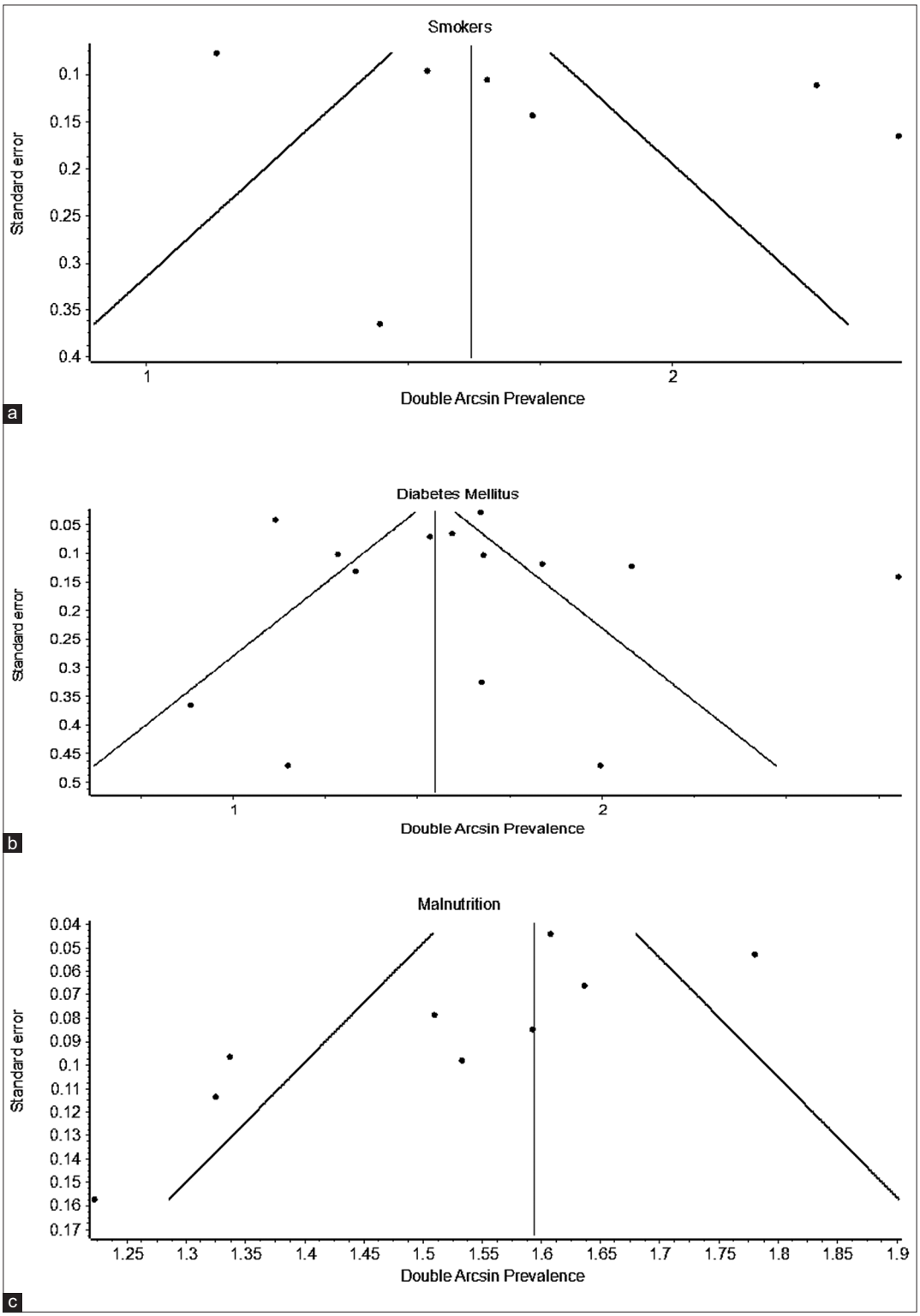
i

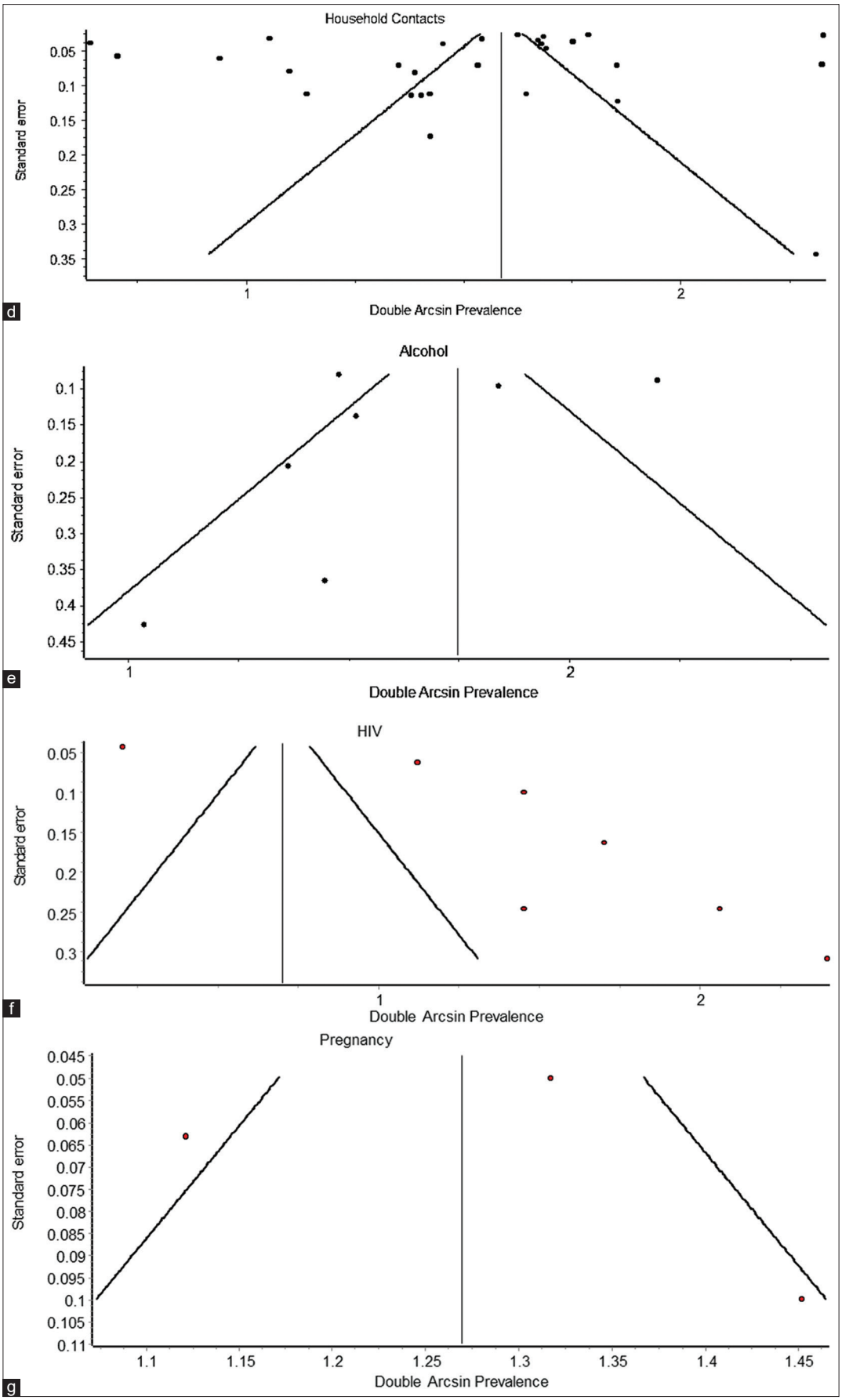

Rheumatoid Arthritis
Study
Prev (95% CI)
% Weight
Agarwal et al 2014
0.20 (0.16, 0.26)
21.0
Malviya et al 2013-2017
0.06 (0.03, 0.09)
21.1
Malviya et al 2018
0.14 (0.05, 0.26)
17.5
Shobha V 2018
0.10 (0.06, 0.15)
20.7
Zia 2020
0.36 (0.27, 0.46)
19.7
Overall
0.15 (0.07, 0.27)
100.0
Q=57.98, p=0.00, I2=93%
0.1 0.2 0.3 0.4
Prevalence

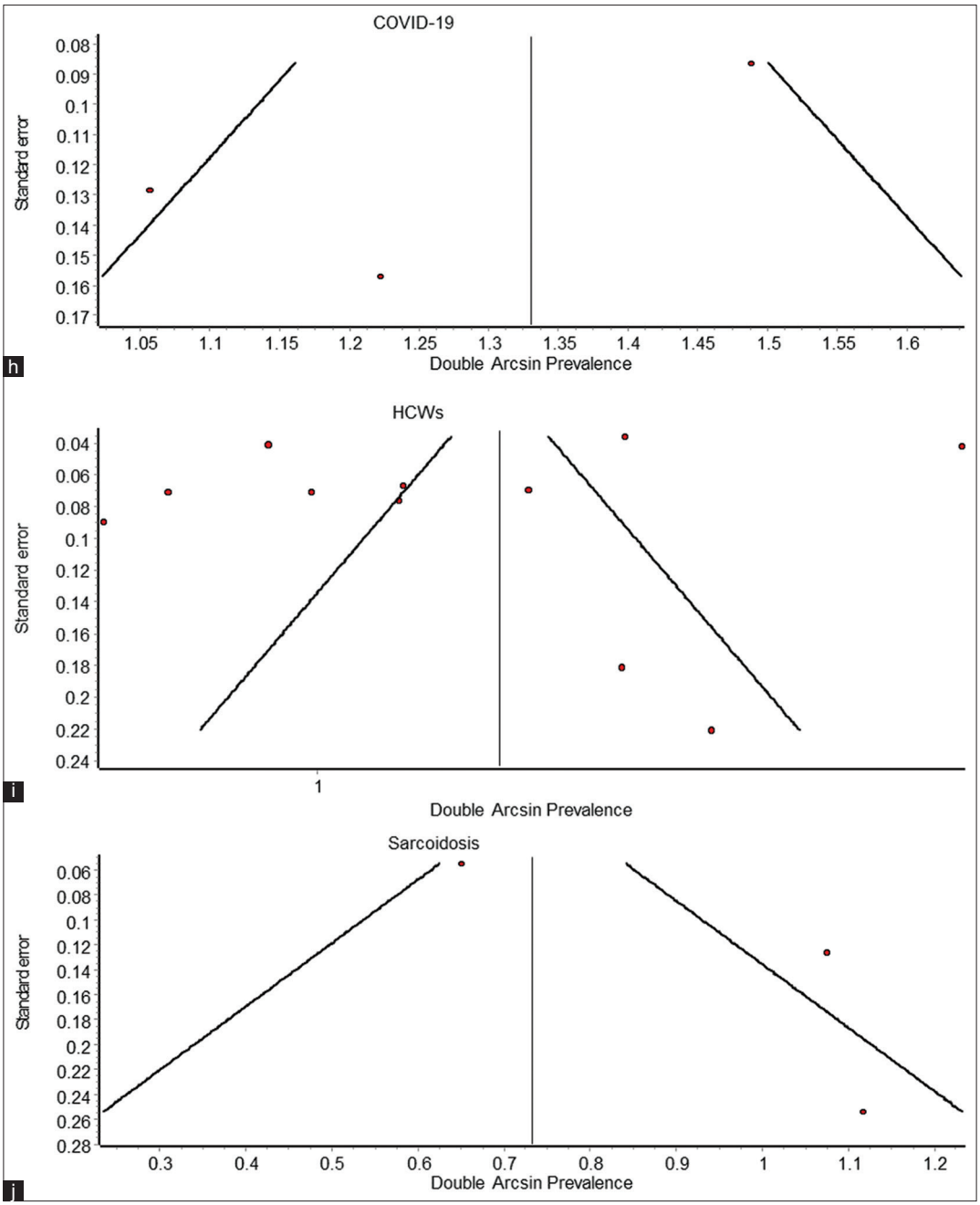
j


Sarcoidosis
Study
Prev (95% CI)
% Weight
Madan et al 2022
0.10 (0.07, 0.14) 41.4
Pattnaik et al 2021
0.27 (0.07, 0.52) 23.1
Vyas et al 2015
0.26 (0.16, 0.38) 35.5
Overall
0.18 (0.06, 0.34) 100.0
Q=11.79, p=0.00, I2=83%
0.1
0.2
0.3
0.4
0.5
Prevalence
k
Psoriasis
Study
Prev (95% CI)
% Weight
Neema et al (A) 2019
0.31 (0.23, 0.41) 53.7
Neema et al (B) 2019
0.21 (0.13, 0.31) 46.3
Overall
0.27 (0.17, 0.37) 100.0
Q=2.22, p=0.14, I2=55%
0.15
0.2
0.25
0.3
0.35
0.4
Prevalence
l
Inflamatory Bowel Disease
Study
Prev (95% CI)
% Weight
Agarwal et al 2014
0.20 (0.16, 0.26) 49.3
Mantri et al 2021
0.19 (0.14, 0.24) 50.7
Overall
0.20 (0.16, 0.23) 100.0
Q=0.24, p=0.63, I2=0%
0.2
Prevalence
m

Supplementary Figure 4: (a) Funnel plot of pooled TBI prevalence among smokers. (b) Funnel plot of pooled TBI prevalence among patients with diabetes. (c) Funnel plot of pooled TBI prevalence among patients with malnutrition. (d) Funnel plot of pooled TBI prevalence among household contacts. (e) Funnel plot of pooled TBI prevalence among alcohol users. (f) Funnel plot of pooled TBI prevalence among HIV patients. (g) Funnel plot of pooled TBI prevalence among pregnant women. (h) Funnel plot of pooled TBI prevalence among patients suffered from COVID-19. (i) Funnel plot of pooled TBI prevalence among health care workers (HCWs). (j) Funnel plot of pooled TBI prevalence among patients with sarcoidosis




Household Contacts
Standard error
0.05
0.1
0.15
0.2
0.25
0.3
0.35
1
2
Double Arcsin Prevalence
d
Alcohol
Standard error
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
1
2
Double Arcsin Prevalence
e
HIV
Standard error
0.05
0.1
0.15
0.2
0.25
0.3
1
2
Double Arcsin Prevalence
f
Pregnancy
Standard error
0.045
0.05
0.055
0.06
0.065
0.07
0.075
0.08
0.085
0.09
0.095
0.1
0.105
0.11
1.1
1.15
1.2
1.25
1.3
1.35
1.4
1.45
Double Arcsin Prevalence
g


COVID-19
Standard error
0.08
0.09
0.1
0.11
0.12
0.13
0.14
0.15
0.16
0.17
1.05
1.1
1.15
1.2
1.25
1.3
1.35
1.4
1.45
1.5
1.55
1.6
Double Arcsin Prevalence
h
HCWs
Standard error
0.04
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
1
Double Arcsin Prevalence
i
Sarcoidosis
Standard error
0.06
0.08
0.1
0.12
0.14
0.16
0.18
0.2
0.22
0.24
0.26
0.28
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
1.1
1.2
Double Arcsin Prevalence
j

Supplementary Table 1: Quality Assessment of Cross-sectional studies

Q1. Were the criteria for inclusion in the sample clearly defined?

Q2. Were the study subjects and the setting described in detail?

Q3. Was the exposure measured in a valid and reliable way?

Q4. Were objective, standard criteria used for measurement of the condition?

Q5. Were the confounding factors identified?

Q6. Were strategies to deal with confounding factors stated?

Q7. Were the outcomes measured in a valid and reliable way?

Q8. Was appropriate statistical analysis used?

Supplementary Table 1: Quality Assessment of Cross-sectional studies

Author name and Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8
Agarwal *et al*., 2014 (42)	Y	Y	Y	Y	Y	Y	Y	Y
Agarwal *et al*., 2015 (43)	Y	Y	Y	Y	Y	U	Y	Y
Aravindham *et al*., 2022 (45)	Y	Y	Y	Y	Y	Y	Y	Y
Bari *et al*., 2023 (47)	Y	Y	Y	Y	Y	Y	Y	Y
Bekken *et al*., 2020 (48)	Y	Y	Y	Y	Y	U	Y	Y
Benachinmardi *et al*., 2019 (49)	Y	Y	Y	Y	Y	Y	Y	Y
Benachinmardi *et al*., 2021 (50)	Y	Y	Y	Y	Y	U	Y	Y
Chauhan *et al*., 2013 (53)	Y	Y	Y	Y	Y	Y	Y	Y
Dayal *et al*. , 2018 (55)	Y	Y	Y	Y	Y	Y	Y	Y
Dabhi *et al*., 2022 (56)	Y	Y	Y	Y	Y	Y	Y	Y
Dinkar *et al*. , 2022 (57)	Y	Y	Y	Y	Y	Y	Y	Y
Gupta *et al*., 2020 (60)	Y	Y	Y	Y	Y	U	Y	Y
James *et al*., 2014 (62)	Y	Y	Y	Y	Y	Y	Y	Y
Jenum *et al*., 2014 (64)	Y	Y	Y	Y	Y	U	Y	Y
Kubaik *et al*., 2019 (68)	Y	Y	Y	Y	Y	Y	Y	Y
Kim *et al*., 2023 (69)	Y	Y	Y	Y	Y	Y	Y	Y
Krishnamoorthy *et al*., 2021 (71)	Y	Y	Y	Y	Y	Y	Y	Y
Kumar *et al*., 2014	Y	Y	y	Y	Y	Y	Y	Y
Malviya *et al*., 2018 (77)	Y	Y	Y	Y	Y	Y	Y	Y
Malviya *et al*., 2019 (78)	Y	Y	Y	Y	Y	Y	Y	Y
Mathad *et al*., 2014 (80)	Y	Y	Y	Y	Y	Y	Y	Y
Mathad *et al*., 2016 (81)	Y	Y	Y	Y	Y	Y	Y	Y
Mave *et al*., 2019 (82)	Y	Y	Y	Y	N	N	Y	Y
Mishra *et al*., 2017 (83)	Y	Y	Y	Y	Y	N	Y	Y
Narsimhan *et al*., 2017 (84)	Y	Y	Y	Y	Y	Y	Y	Y
Neema *et al*., 2019 (86)	Y	Y	Y	Y	Y	Y	Y	Y
Prabhavati *et al*., 2015 (90)	Y	Y	Y	Y	Y	N	Y	Y
Patil *et al*., 2014 (91)	Y	Y	Y	Y	Y	Y	Y	Y
Rajamanickam *et al*., 2020 (40)	Y	Y	Y	Y	Y	Y	Y	Y
Rajalakshmi *et al*., 2017 (92)	Y	Y	Y	Y	Y	Y	Y	Y
Sawhney *et al*., 2015 (94)	Y	Y	Y	Y	Y	Y	Y	Y
Shah *et al*., 2019 (95)	Y	Y	Y	Y	Y	Y	Y	Y
Shivakumar *et al*., 2018 (97)	Y	Y	Y	Y	Y	Y	Y	Y
Shobha *et al*., 2018 (98)	Y	Y	Y	Y	N	N	Y	Y
Shrivastava *et al*., 2020 (99)	Y	Y	Y	Y	Y	Y	Y	Y
Singh *et al*., 2021 (101)	Y	Y	Y	Y	Y	N	Y	Y
Siddiqui *et al*., 2022 (102)	Y	Y	Y	Y	Y	Y	Y	Y
Vyas *et al*., 2015 (105)	Y	Y	Y	Y	N	N	Y	Y
Zwerling *et al*. 2013 (106)	Y	Y	Y	Y	Y	Y	Y	Y
Zia *et al*., 2021 (107)	Y	Y	Y	Y	Y	N	Y	Y

Supplementary Table 2: Quality Assessment of Cohort studies

Q1. Were the two groups similar and recruited from the same population?

Q2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?

Q3. Was the exposure measured in a valid and reliable way?

Q4. Were the confounding factors identified?

Q5. Were strategies to deal with confounding factors stated?

Q6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?

Q7. Were the outcomes measured in a valid and reliable way?

Q8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?

Q9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?

Q10. Were strategies to address incomplete follow up utilized?

Q11. Was appropriate statistical analysis used?

Supplementary Table 2: Quality Assessment of Cohort studies

Author name and Year	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Arya *et al*, 2018 (44)	Y	Y	Y	Y	Y	Y	N	Y	N	U	Y
Bajgai *et al*., 2015 (46)	Y	Y	Y	Y	Y	Y	Y	Y	N	U	Y
Boddu, *et al*. 2019 (51)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Chandrasekharan *et al*., 2018 (52)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Christopher *et al*., 2014 (54)	Y	Y	Y	Y	N	Y	Y	Y	Y	U	Y
Dolla *et al*., 2019 (58)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Girish *et al*., 2021 (59)	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y
Gupta *et al*., 2021 (61)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Janagond *et al*., , 2017 (63)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kabeer *et al*., 2018 (65)	Y	Y	Y	Y	Y	N	Y	Y	N	N	Y
Kashyap *et al*., 2014 (66)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kaul *et al*., 2022 (67)	Y	Y	Y	Y	Y	Y	Y	Y	U	U	Y
Kinikar *et al*., 2019 (70)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kumar *et al*., 2014 (72)	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y
Kumar *et al*., 2019 (73)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kumar *et al*., 2022 (74)	Y	Y	Y	Y	Y	Y	y	Y	y	Y	Y
Madan *et al*., 2021 (75)	Y	Y	Y	Y	Y	Y	y	Y	y	Y	Y
Madan *et al*. , 2022 (76)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Mantri *et al*. , 2021 (79)	Y	Y	Y	Y	Y	Y	Y	Y	Y	U	Y
Neema *et al*., 2019 (85)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Pattnaik *et al*., 2021 (87)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Paradkar *et al*., 2020 (88)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Prabhavathi *et al*., 2015 (89)	Y	Y	Y	Y	N	Y	Y	Y	Y	U	Y
Reddy *et al*., 2021 (93)	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
Sharma *et al*., 2017 (96)	Y	Y	Y	Y	Y	Y	U	U	Y	Y	Y
Singh *et al*., 2013 (100)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y
Surve *et al*., 2021 (103)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Thamke *et al*., 2018 (104)	Y	Y	Y	Y	Y	Y	Y	Y	N	N	Y