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Outdoor pollen is a trigger of child and adolescent asthma ED presentations: a systematic review and meta-analysis

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Running title: Review of pollen on asthma ED visits in children and teens

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41 **ABSTRACT**

42 **Background:** In the context of increased asthma exacerbations associated with climatic
43 changes such as thunderstorm asthma, interest in establishing the link between pollen
44 exposure and asthma hospital admissions has intensified. Here, we systematically reviewed
45 and performed a meta-analysis of studies on pollen and ED attendance.

46

47 **Methods:** A search for studies with appropriate search strategy in Medline, Embase, Web of
48 Science and CINAHL was conducted. Each study was assessed for quality and risk of bias.
49 The available evidence was summarised both qualitatively and meta-analysed using random
50 effects models when moderate heterogeneity was observed.

51

52 **Results:** Fourteen studies were included. The pollen taxa investigated differed between
53 studies, allowing meta-analysis only of the effect of grass pollen. A statistically significant
54 increase in the percentage change in the mean number of asthma ED presentations (MPC)
55 (pooled results from three studies) was observed for an increase in 10 grass pollen grains per
56 cubic meter of exposure 1.88% (95%CI = 0.94%, 2.82%). Time series studies showed
57 positive correlations between pollen concentrations and ED presentations. Age stratified
58 studies found strongest associations in children aged 5 to 17 years old.

59

60 **Conclusion:** Exposure to ambient grass pollen is an important trigger for childhood asthma
61 exacerbations requiring ED attendance. As pollen exposure is increasingly a problem
62 especially in relation to thunderstorm asthma, studies with uniform measures of pollen and
63 similar analytical methods are necessary to fully understand its impact on human health.

64

65 **Key words:** Asthma, Pollen, Aeroallergens, Acute Exacerbations, Emergency medical
66 services

67 **Abbreviations:** ED: emergency department; WAO: World Allergy Organization;

68

69 **Author Contributions:** BE, MA, SD developed the research question and review protocol. MJ,
70 KL, RT conducted search and initial review for article inclusion. MJ, BE, KL qualitatively
71 synthesized the included studies. KL, LP was responsible for meta-analysis and KL, LP and BE
72 interpreted analysis. KL, MJP conducted the quality assessment. JD, EN, CK contributed to
73 interpreting the qualitative synthesis and meta-analysis. BE, MJ, KL, SD drafted the manuscript. BE,

74 MJ, KL, RT, JD, EN, MA, SD were involved in the revisions of the manuscript. All authors read and
75 approved the final manuscript before submission. BE and SD accept full responsibility for this work
76 and act as guarantors for the study.

77

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95 Wymedical, and Meda Pharmaceuticals.

96

97 **INTRODUCTION**

98 Asthma is one of the most prevalent diseases in industrialised societies, particularly among
99 children and adolescents (1). Reports from the World Allergy Organization (2) indicate a
100 steady increase of asthma prevalence globally especially in “Westernised” countries such as
101 Australia, UK and the US, where a high proportion of this increase occurs in children and
102 young adults. The global burden of asthma is estimated to affect 300 million people (1) and
103 prevalence is higher in 0 to 14 year old males (11.4%), but is higher among females aged 15
104 years or older (3).

105

106 Medications usually control persistent asthma; however up to 30% of children who
107 experience severe exacerbations require emergency department (ED) care (3). Exacerbations
108 can be triggered by respiratory viral infections, air pollutants, exercise, tobacco smoke, non-
109 compliance with preventive medications, exposure to irritant chemicals and/or aeroallergens
110 such as fungal spores and pollen (4-6). Understanding the major triggers of asthma
111 exacerbations among children and adolescents that result in ED presentations could
112 potentially lead to improved prevention strategies.

113

114 There is a gap in our understanding of changing outdoor environment and respiratory disease,
115 especially in cities with dangerous environmental conditions such as the “Thunderstorm
116 Asthma” outbreak that occurred in Melbourne, Australia, that was fatal (7). In some cities,
117 pollen seasons are severe with temperamental weather patterns and large volumes of pollen
118 being dispersed in the air. For example, in Melbourne Australia grass pollen levels peaked at
119 207 grains/m³ and were well above 50 grains/m³ (defined as high pollen days) for a
120 significant proportion of the grass pollen season during October 2009 and December 2011
121 (5). Recent climate changes, characterised by frequent changes in weather patterns and
122 extended periods of extreme rainfall and heat, are predicted to be impacting on intensity and
123 duration of the pollen season.

124

125 High pollen days during peak pollen seasons combined with changing climatic conditions can
126 cause serious attacks requiring emergency department presentations or subsequent hospital
127 admission. Increasingly studies are examining associations between ambient pollen
128 concentrations and risk of asthma exacerbations (5, 8-12). Therefore, synthesizing the current
129 literature to better understand the role of different types of pollen exposure on asthma

130 exacerbations is important for health and promoting interventions to reduce the burden
131 directly associated with ambient pollen. No systematic synthesis of such evidence has been
132 conducted to date. The aim of this systematic review was to synthesize the current evidence
133 of pollen as a trigger for child and adolescent asthma ED attendances and perform meta-
134 analysis where possible.

135

136 **METHODS**

137 This systematic review was undertaken following both the PRISMA (13) and MOOSE (14)
138 guidelines for reporting systematic review and meta-analysis.

139

140 Search strategy

141 The focus of the search was to identify articles that examined the effects of outdoor pollen
142 exposure on asthma exacerbations in children and adolescents requiring ED attendance. The
143 peer-reviewed literature was searched using the Medline, Embase, Web of Science and
144 CINAHL (EBSCO) databases, 1966 to 2017. Medical Subject Headings (MeSH) search
145 terms used were related to exposure (pollen); outcome (emergency*, asthma*) and population
146 (child*, pediatric* or paediatric*) combined. Further hand searches were conducted using
147 citations from the identified and related review papers. After reviewing the abstract of the
148 identified journal articles, if all inclusion criteria were met, the full text were read for
149 inclusion or exclusion.

150

151 Eligibility criteria

152 Inclusion criteria were human subjects and published in English. Study populations were
153 children and adolescents aged less than 18 years who attended an ED with a diagnosis of
154 asthma. Studies must have reported exposure to outdoor levels of pollen.

155

156 Data extraction and assessment

157 From each study included, data regarding study design, method of analysis, study location,
158 time period of the study, method of pollen collection, age range and number of children,
159 exposure definition (pollen species such as grasses, weeds, trees and conifers), pollen count,
160 outcome definition, effect estimates together with 95% confidence intervals were extracted
161 where available. A quality assessment of each study was conducted independently by two
162 researchers using a quality assessment framework developed by Zaza et al (15). Quality

163 assessment examined selection and description of the study sample, outcome assessment,
164 exposure assessment, appropriateness of statistical methods and adjustment for confounders.

165

166 Assessment for Meta-analysis

167 Of the articles included in the review, we only considered studies with grass pollen as the
168 primary exposure for inclusion in the meta-analysis because of the limited number of
169 estimates for the other pollen types. To enable greater comparison, effect estimates were
170 standardised to an increase per 10 grains/m³ of grass pollen and the transformed variances
171 computed using the delta method (16). Meta-analyses of the chosen studies were carried
172 using linear mixed effects models that assumed the presence of a random effect where the
173 DerSimonian-Laird estimator was used to estimate the variance parameter (17). Stratification
174 analyses were not possible due to the limited number of studies. The analyses were
175 undertaken using the R package metafor (18) and statistical software STATA version 14.1
176 (Stata Corp LP, College Station, TX, USA) was used to create forest plots of these analyses.

177

178 Exposure assessment - Pollen monitoring methods

179 Daily pollen counts are given as grains/m³ over a 24 hour period. Where reported, the two
180 instruments used for pollen counts were Rotorod Samplers (Sampling Technologies, MN,
181 USA) and Burkard Volumetric traps (Burkard, Hertfordshire, UK). There are differences in
182 the efficiency of these instruments for pollen collection (19).

183

184 **RESULTS**

185 Search Results

186

187 Electronic and hand searching yielded 227 articles after duplicates were removed, of which
188 213 were excluded (Figure 1). We identified 14 eligible studies where pollen was considered
189 the primary exposure variable.

190

191 Characteristics of the Studies

192 In Table 1 we describe the study design, location of the study, time period, method of pollen
193 collection/measurement, sample size of the study, and the age group of the participants if
194 reported. Studies were from a number of different regions in the world, predominately in the

195 USA and Canada (8, 9, 10, 11, 20-24), Spain (12, 25) and Australia (5, 26). One earlier study
196 was conducted in Tel Aviv in Israel (27).

197

198 Pollen exposure in these studies was classified into four broad groups; grass, tree, weed, and
199 conifer following the guidelines of Weber (28). Of these 14 studies: two reported grass pollen
200 exposure only (5, 26); one reported tree pollen exposure only (20); one reported tree and
201 weed pollen exposures (10); seven reported grass, tree and weed pollen exposures (9, 11, 21-
202 25); and three studies reported pollen from all these categories (8, 12, 27).

203

204 Quality Assessment

205 The included studies appeared to have an overall moderate risk of bias. The main sources of
206 bias arises from the inclusion of children aged <2 years, with whom diagnosis of asthma is
207 very difficult and prone to misclassification. Only one study (21) did not include children
208 aged <2 years, while three studies (8, 20, 24) reported age stratified results. The method of
209 pollen sampling varied between studies with six using the Burkard volumetric pollen and
210 spore trap (5, 10, 12, 20, 22, 25), four using the Rotorod sampler (8, 9, 11, 27) and three not
211 stating the instrument used (21, 23, 24). One study did not use pollen counts, instead
212 compared emergency department visits in the pollen season to those not in the pollen season
213 (26). The ambient pollen concentration for each day was assumed to be every individuals'
214 exposure due to lack of individual level pollen data. All but two studies (12, 25) used data
215 from a single collection site. Reporting bias is evident in some studies that investigated
216 multiple lag points but reported only on the most significant associations (11, 12). Potential
217 confounding bias from the lack of adjustment for individual level variables such as
218 sensitization to pollen or other allergens also contributed to low levels of the quality of the
219 studies included.

220

221 Synthesis of findings

222 A summary of the findings from each study is presented in Table 2. Two studies (5, 25)
223 utilized non-linear modelling to investigate short-term effects of different types of pollen on
224 child asthma ED visits. Erbas et al (5) found a threshold level of 20 grains/m³ for grass pollen
225 in child asthma ED presentations in Melbourne. To add to the findings from Erbas et al (5),
226 Tobias et al (25) reported the threshold level for weed pollen was 37 grains/m³ and for tree
227 pollen was 13 grains/m³.

228

229 Lierl & Hornung (11) examined exposure to grass, trees and weeds among children and
230 adolescents attending emergency department in Cincinnati, USA using a Poisson regression
231 of incidence on a given day of exposure. Although they reported total pollen effects of log
232 pollen lagged 3 days RR=1.089 (95% CI 1.027-1.155) they did not present results for
233 different pollen types.

234

235 Some studies used mean percentage change (MPC) to report the estimated effects. In
236 examining the effects of daily levels of grass pollen on ED presentations, Tobias et al (12)
237 found significant associations for 3-day lag period exposure to grasses which resulted in a
238 17.1% MPC increase in ED presentations (95%CI: 3.2-32.8) for an increase of ~100
239 grains/m³ of grass pollen (this figure was obtained as the 95-99th percentile increase in the
240 pollen level in Madrid). In Montreal, Canada, Heguy et al (9) also identified a significant
241 increase of 1.73 % MPC in ED presentations (95%CI: 0.24-3.25) at 3-day lag of an increase
242 of 10 grains/m³. They stratified their analysis by first visit to ED or readmission to ED and
243 found the relationship between grass pollen levels and ED visits was stronger during the first
244 visit (lag 3: 2.08 95%CI: 0.28-3.91; lag 5: 1.43 95%CI: 0.09-3.76). Babin et al (24) also
245 found an increase in paediatric (1-17 years old) ED visits at 3-lag with an increase of 10
246 grains/m³ of grass pollen (MPC: 2.6; 95%CI: 0.3-5.0). They further stratified results into
247 three age groups, 1-4, 5-12, 13-17, presenting only the results for those aged 5-12 years old.
248 The effect of pollen on ED visits was consistently stronger in this age group. An increase in
249 100 grains/m³ of tree pollen showed an increase of 1.8% MPC (95%CI 0.9-2.6) in ED visits
250 on the day (lag 0). This association attenuated, though remaining significant, as the lag
251 increased. Conversely, the relationship between grass pollen counts and ED visits
252 strengthened with increasing lag, up to 3 days after which it abruptly drops off (lag 0: 1.6
253 95%CI: -2, 5.4; lag 1: 3.5 95%CI: 0.1, 7.1; lag 2: 4.3 95%CI: 0.9, 7.9; lag 3: 5.5 95%CI: 2.2,
254 9; lag 4: 3.1 95%CI: -0.5, 6.8).

255

256 Amongst the four descriptive time-series studies (10, 22, 26, 27) investigating the
257 associations between airborne pollen levels and ED presentations, Jariwala and colleagues
258 (10) found that when tree pollen was the major airborne pollen type in the area, the highest
259 daily number of ED visits for children was observed. Averaging pollen counts and ED visits
260 over a seven year period, Jariwala et al (22) found tree pollen counts to be significantly
261 correlated with paediatric asthma related ED visits during the peak pollen season ($\rho=0.28$,
262 $p<0.001$). This association persisted throughout the year (excluding the winter months)

263 (rho=0.33, p<0.001). In inland Australia, Hayden and Muscatello (26) reported that peak
264 asthma count days for children (defined as top 0.1 percentile for daily asthma ED
265 presentations over 13 years at nine inland New South Wales hospitals) corresponded with the
266 rye grass season. No formal statistical tests were used to assess the differences overall or by
267 specific age group. A two-year study conducted in Wilmington, Delaware in the USA
268 categorized the rate of paediatric ED presentations into low and high levels defined as the
269 percent of the overall average monthly value (23). They looked at effects of air pollutants,
270 pollen and meteorological factors with multiple comparisons and t-tests. They found tree and
271 weed pollen counts were higher on days with \geq seven asthma-related ED visits (p=0.05), but
272 no significant difference in grass pollen counts between high- and low-visit days.

273
274 In their single taxon models investigating linear effects of pollen on ED presentations in
275 Atlanta, USA, Darrow and colleagues (8) found a positive association between a variety of
276 pollen types and risk of ED presentations. In age specific investigations, they found that
277 children aged 5-17 years showed the strongest association with oak (*Quercus* species) pollen
278 (RR=1.046; 95%CI: 1.033 to 1.059 per standard deviation (SD) increase in pollen
279 concentration). This result is supported by a recent study (20), that also showed a positive
280 association between ED visits and oak pollen that was strongest amongst children aged 5 – 17
281 years. Ito et al. (20) also examined a number of other single taxon models, which showed, in
282 general, highly positive associations in the 5-17 years age group with ash pollen (RR= 2.6
283 95%CI: 2.1 to 3.1 per 0-to-98th percentile increase for ash pollen). Gleason et al (21) showed
284 grass pollen to only be minimally associated with paediatric asthma ED visits, while tree and
285 weed pollen were strongly associated.

286

287 Meta-analysis

288 Although many studies reported estimated effects, conducting meta-analysis was difficult for
289 studies reporting relative risk and odds ratios because no two studies reporting these
290 estimates used the same pollen type or same lag day average. However, we could conduct a
291 meta-analysis for studies reporting mean percentage change in ED presentations (9, 12, 24).
292 All studies reported on a three day lag, two reported the estimated effect per increase in 10
293 grains/m³ of pollen (9, 24) and we were able to transform estimated effect for the other study
294 (12) and perform a meta-analysis (Figure 2). Meta-analysis showed a significant increase in
295 MPC of ED presentations (MPC=1.88 95%CI:0.94-2.82, p = 0.001) associated with an

296 increase of 10 grains/m³ of grass pollen. The measure of heterogeneity was very close to
297 zero.

298

299 **DISCUSSION**

300 In this systematic review of a variety of pollens and meta-analysis of grass pollen, we have
301 presented evidence of effects of pollen, especially of grass, on child asthma ED presentations
302 from various regions around the world. An increase in risk of childhood asthma ED
303 presentations between 1% and 14% was observed when pollen was the primary exposure.
304 Higher concentrations of grass pollen were associated with daily increases in ED visits for
305 asthma up to 3 days after exposure. In some places, the minimum threshold of grass pollen
306 exposure, at which sensitised individuals may experience symptoms was as low as 10
307 grains/m³ per day. The observed pooled effect of 1.88% per 10 grains/m³ suggested that
308 increased levels of grass pollen 3-days prior was associated with increased ED presentations
309 for childhood asthma (MPC 1.88% [0.94, 2.82] per 10 grains/m³). If pollen levels at lag 3
310 were 20 grains/m³ higher than baseline, then we would expect a 3.76% increase in ED
311 presentations for childhood asthma. If pollen levels three days prior (lag 3) were 50 grains/m³
312 higher than baseline, then we would expect a 9.4% increase in ED presentations for
313 childhood asthma. A wide range of pollen levels during the pollen seasons can occur such as
314 the maximum level of 106.5 grains/m³ as reported by one of the studies included in the meta-
315 analysis. This gives a 18.8% increase in MPC, which would be a clinically important change
316 in the expected ED presentations for hospital planning purposes. However, typically the
317 estimated risk was highly dependent on the methodological approach undertaken to assess
318 these associations. The non-linear effects of pollen reported in two studies (5, 25) indicated a
319 positive association between the grass pollen and asthma ED presentations up to a threshold,
320 after which the effect flattened off. However, the threshold level is somewhere between 20
321 and 50 grains/m³.

322

323 The possibility that local variations in pollen levels, pollen types and pollen combinations
324 across areas affecting child and adolescent asthma ED presentations should also be
325 considered in such studies. In Australia, grass pollen seems to be an important trigger (5),
326 trees and weeds in various regions in the USA (20, 23), grass and weeds in Canada (9) and
327 grass and olive tree pollen in Madrid, Spain (12, 25). The location of pollen count stations
328 will also contribute to variations in the levels and types of pollen measured (29) No study
329 reported on the percentage of children/adolescents who were first diagnosed with asthma

330 following the ED visit after high pollen load exposure; whether the children had a prior
331 diagnosis of allergic rhinitis; or were undergoing allergen specific immunotherapy.

332 While some of study areas now have pollen monitoring and prediction programs either app
333 based or website (such as Melbourne, Australia); these are only recently available to the
334 public and did not exist when many of the studies were conducted. It is only the most recent
335 studies that could have been impacted by these programs.

336
337 There are a number of limitations associated with combining studies investigating the effects
338 of pollen on child and adolescent asthma ED presentations. There was inter-study variation in
339 the types of pollens examined at the taxa level, such as grasses, trees, conifers and weeds;
340 also at the species level, such as different species of grasses, trees, conifers or weeds. To
341 further complicate this, there was likely to have been geographic and seasonal variation in
342 species of vegetation that produced pollens. Analysis of pollen at a high taxa level (e.g.
343 ‘grasses’, ‘weeds’ or ‘trees’) may have included different species in different sites making
344 comparability difficult to ascertain. Different statistical analytical methods made it difficult to
345 compare the results of studies which used nonlinear models with no estimated effects with
346 correlational studies. In addition, there were differences in the cut-off points for age groups
347 between studies. This raised potential diagnosis misclassification bias associated with
348 possible misdiagnosis of asthma in the 0-2 years age group due to the ambiguity of the
349 respiratory symptoms in this age group (30). Some studies combined the age groups; which
350 made it difficult to untangle any age specific effects that may modify the associations.

351
352 Variations in ecological and climatic conditions may also contribute to the differences
353 observed. All studies reporting significant effect sizes were from highly urbanized regions. In
354 some regions with high levels of urbanisation, greater traffic flow and increased levels of
355 traffic related air pollutants may provide greater risk even during low pollen periods.
356 Conversely, during peak pollen periods these environmental factors may interact thereby
357 further increasing the likelihood of an ED presentation for asthma. Pollen is also dependent
358 on changing climatic conditions and its effect will vary by climatic region (31).

359
360 There are different methods for measuring pollen such as the Rotorod sampler and Burkard
361 pollen and spore trap. These two methods of pollen sampling have different efficiency for
362 different particle sizes (19). According to Frenz (19), both Rotorod and Burkard volumetric

363 samplers are affected by wind speed. The maximum change in collection efficiency could be
364 up to 40%. These two instruments are affected by wind speed in fundamentally different
365 ways and this can lead to potential measurement and ascertainment bias. All these variations
366 make it difficult to compare the studies with each other directly.

367
368 Our upper airways carry air into our lungs and consecutive days of high pollen trigger
369 swelling of these airways constricting our breathing. Among asthmatics, this can be fatal as
370 there is further restriction of air getting into the lungs. High pollen days during peak pollen
371 seasons combined with changing climatic conditions can cause serious and widespread
372 asthma attacks requiring emergency department presentations or subsequent hospital
373 admission. In the situation of Thunderstorm Asthma” many individuals experience severe
374 symptoms due to grass pollen exposure, up to 60% of whom were previously known to suffer
375 from allergic rhinitis without prior diagnosis of asthma (7).

376
377 Our qualitative synthesis and meta-analysis show increasing evidence that children and
378 adolescents exposed to outdoor pollen may be at an increased risk of asthma exacerbations
379 requiring emergency department presentation. Given this risk, simple yet effective
380 interventions for the management of asthma exacerbations could be developed. This an
381 important and timely review because many simple and cost effective local public health
382 preventative strategies can avoid pollen exposures during pollen seasons such as planting
383 non-allergenic plants, not mowing grass and staying indoors on high pollen days. In some
384 cities, including Melbourne, media alerts of high pollen day forecasts are implemented in
385 mass media campaigns and public health networks during the pollen seasons. At the primary
386 care level, better understanding risk will enable health professionals to direct patients to be
387 diligent with medication use as a precautionary measure. For some, clinical interventions
388 such as immunotherapy may be necessary.

389
390 In summary, pollen of different taxa is an important risk factor for asthma exacerbations and
391 one of the few modifiable environmental exposures. Guided by clinicians and inter-agency
392 pollen monitoring alert systems, early warnings of high-danger periods could be developed
393 and avoidance measures incorporated by families for “at risk” children.

394

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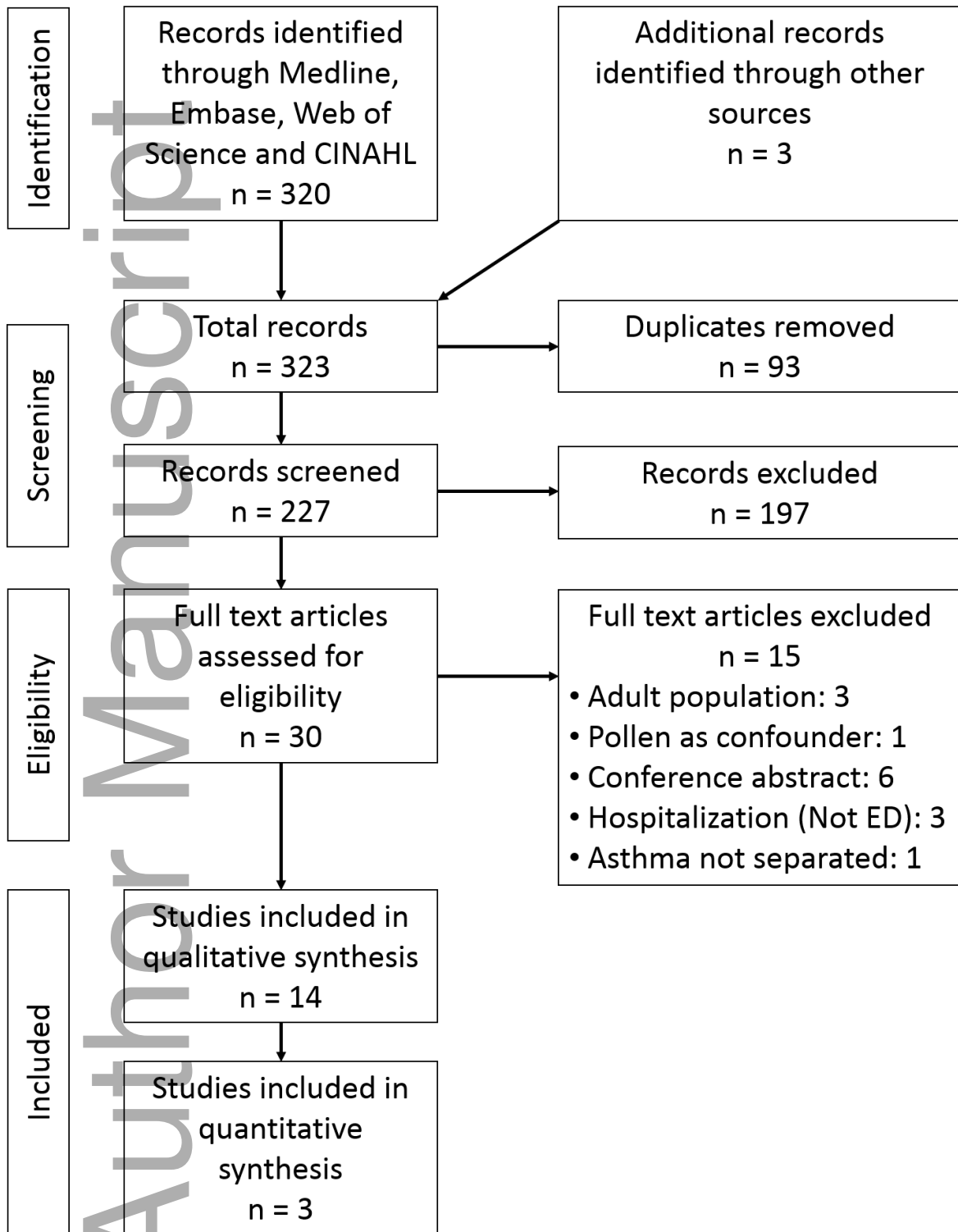
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479 Figure 1. PRISMA flow diagram showing the progress of studies through the review



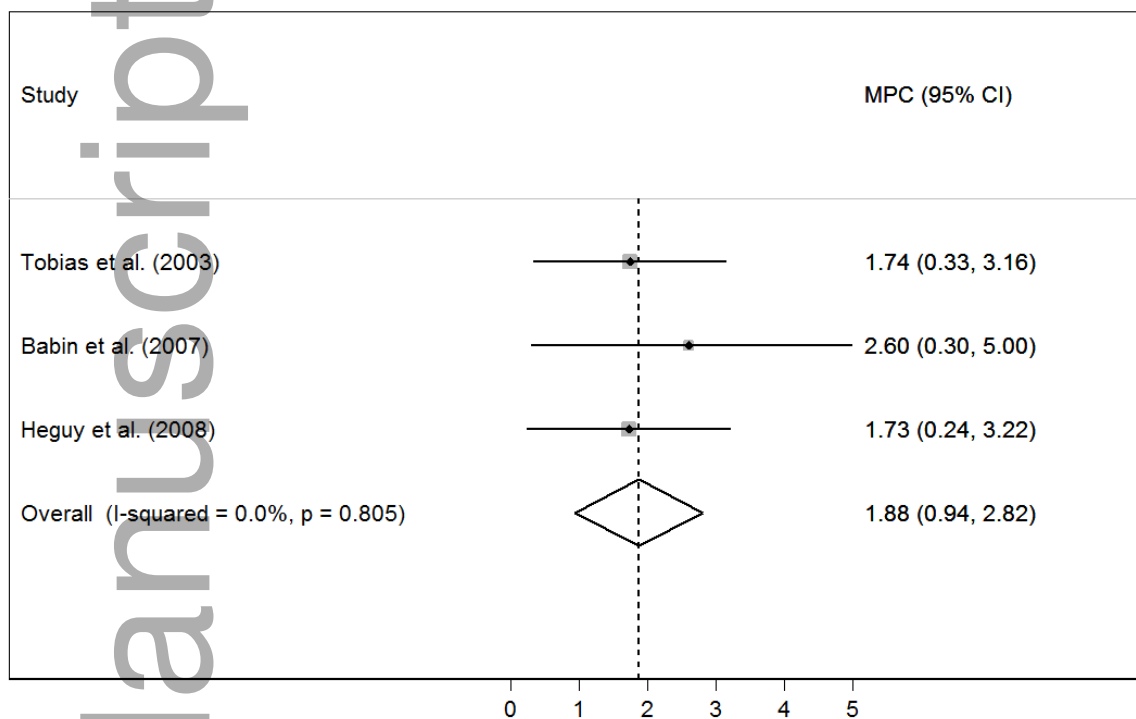
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483 Figure 2. Associations between an increase of 10 grains/m³ of grass pollen and Mean Percent
484 Change (MPC) of ED presentations in children and adolescents pooled using a random-
485 effects meta-analysis.

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488 Table 1: Characteristics of included studies

Author (date)	Study Design and Method of analysis	Location	Time period	Method of pollen collection	Age group	Sample size
Ito (2015)	Time series	USA NYC	March-June 2002-2012	Burkard	0-4 5-17	~48,450* ~65,484*
Gleason (2014)	Time-series Case-Crossover	USA New Jersey	April-September 2004-2007	Not stated	3-17	21,854
Jariwala (2014)	Correlational study	USA NYC	2001-2008	Burkard	Not stated	22,717
Erbas (2012)	Time series – GAM ¹	Australia Melbourne	Sept-Dec 2003	Burkard	0-15	2,559
Darrow (2012)	Time-series Case-Crossover	USA Atlanta	1993-2004	Rotorod	0-18	199,533
Hayden (2011)	Descriptive epidemiological	Australia NSW	Jul1996-Dec 2009	None	0-15	9,495
Jariwala (2011)	Correlational study	USA NYC	Complete year 1999	Burkard	0-18	Not stated
Heguy (2008)	Time series	Canada Montreal	1994-2004	Rotorod	0-9	22,756
Babin (2007)	Time series	USA Washington, DC	Oct 2001-Sep 2004	Not stated	1-17 (5-12)	Not stated
Wang (2007)	Observational Retrospective	USA Pennsylvania	Jan 2000-Dec 2003	Not stated	not stated	1,460
Tobias (2004)	Time series – GAM ¹	Spain Madrid	1995-1998	Burkard	0-14	2,400
Lierl (2003)	Time-series- GEE ²	USA Ohio	1996-1997	Rotorod	Not stated	~30,000*
Tobias (2003)	Time series – GAM ¹	Spain Madrid	1995-1998	Burkard	0-14	~2,400*
Garty(1998)	Correlational study	Israel Tel Aviv	Complete year 1993	Rotorod	1-18	1,076

489 *sample sizes are reported as an estimate of daily ED attendance.

490 ¹ Generalized Additive Models, ² Generalized Estimating Equations,

491 Table 2: Definitions of outcome, exposure and summary of findings from each study included in the review

Author(date)	Exposure – pollen species	Outcome	Findings - including common names for pollen species	Confounders/ adjustments
Ito (2015)	Maple, birch, oak, elm, ash, sycamore, beech, hickory and poplar	“asthma”, “wheezing”, “COPD”, common misspelled analogues and ICD-9 codes associated with asthma	Age dependent associations with asthma syndrome ED visits were found with the 5-17 age group showing the strongest association for maple, birch, oak, ash, sycamore, beech and hickory. Elm and poplar were not associated with asthma syndrome ED visits at any age group.	None
Gleason (2014)	Tree, grass, weed and ragweed	Asthma (ICD-9: 493.xx)	Tree and weed pollen were significantly associated with ED presentation at all lags examined with the highest relative risk seen across a five-day average (OR=1.23, 95%CI 1.21–1.25) and (OR=1.13, 95%CI 1.12–1.14), respectively. This relationship held true when a binary cut-off was used (OR=1.61, 95%CI 1.52–1.71 and OR=1.94, 95%CI 1.79–2.12, respectively). For ragweed, a negative association with paediatric visits was observed for all lag periods (OR=0.94 95%CI 0.94-0.95 for five day average). Grass pollen showed a significant increase in the risk of ED presentations for the five day average only (OR=1.02, 95%CI = 1.01-1.03).	3-day moving average temperature, 3-day moving average humidity, holiday indicator and school-in-session indicator
Jariwala (2014)	Grasses, trees and weed	Asthma (ICD-9: 493)	Tree pollen counts significantly correlated with paediatric asthma related ED visits ($\rho=0.33$, $p<0.001$). No correlation between grass or weed pollen counts and paediatric asthma related ED visits.	None
Erbas (2012)	Grasses	Asthma (ICD10-AM)*, J45 J46	Strong dose-response association between grasses below 20 and childhood asthma ED presentations.	Day of week, time trend, temp, relative humidity, API, NO ₂ and O ₃
Darrow (2012)	Grasses, trees, weed and conifer	Asthma (ICD-9** :493.0-493.9)	Overall positive associations were observed with: grasses RR= 1.022, 95%CI: 1.012, 1.033 and Trees (birch RR = 1.022, 95%CI:1.013, 1.032 and oak RR= 1.028, 95%CI: 1.021,1.035)) Overall significant associations were observed for 5 to 17 year olds with trees RR=1.046, 95%CI: 1.033, 1.059 and Conifers RR=1.007, 95%CI: 1.001,1.013	3-day moving average of O ₃ , CO, NO ₂ , SO ₂ , PM ₁₀ and PM _{2.5}
Hayden (2011)	Grasses: Rye grass	Asthma (ICD-9 493 and ICD-10***) J45 and J46	Although actual pollen values were not modelled with ED presentations, the authors reported approximately 16% of children aged 5 to 14 years presenting to emergency with asthma during the peak pollen count days during the pollen season.	None
Jariwala (2011)	Trees and weeds: Tree pollen	Asthma (ICD-9: 493)	Peak asthma ED visits (peak asthma ED visits were identified as the number of visits that exceeded the 99.9% confidence intervals for the identified time interval $n \sim 35$ for children) occurred during spring with high tree pollen counts correlation coefficient 0.9 $p = 0.03$	None
Heguy (2008)	Grasses, trees and weeds	Asthma (ICD-9: 493)	Mean Percentage Change (MPC): For grasses at lag 3 days:1.73, 95%CI:0.24,3.25; lag 5 days:1.43, 95% CI: - 0.06, 2.95 For weed at lag 2 days:-0.54, 95% CI:-0.93,-0.15 and lag 3 days -0.66, 95% CI:-1.07 to -0.25.	Daily maximal concentrations of NO ₂ and O ₃ . Daily minimum and maximum temperature, maximum air pressure and change in air pressure from previous day.

Babin (2007)	Grasses, trees and weeds	Asthma (ICD-9: 493)	MPC: 1-17years Grasses (10 grains/m ³): lag 0: 0.7 (-1.8, 3.1); lag 1: 1.9 (-0.4, 4.3); lag 2: 2.3 (-0.1, 4.7); lag 3: 2.6 (0.3, 5); lag 4: -0.4 (-2.9, 2.3) Tree (100 grains/m ³): lag 0: 0.5 (0, 1.1); lag 1: 0.4 (-0.2, 1); lag 2: 0.5 (-0.1, 1.1); lag 3: 0.2 (-0.4, 0.8) MPC: 5-12years Grasses (10 grains/m ³): lag 0: 1.6 (-2, 5.4); lag 1: 3.5 (0.1, 7.1); lag 2: 4.3 (0.9, 7.9); lag 3: 5.5 (2.2, 9); lag 4: 3.1 (-0.5, 6.8) Tree (100 grains/m ³): lag 0: 1.8 (0.9, 2.6); lag 1: 1.2 (0.4, 2.1); lag 2: 1.5 (0.7, 2.4); lag 3: 1.1 (0.3, 2); lag 4: 1.1 (0.2, 2) Weed (10 grains/m ³): lag 0: -2.9 (-6.8, 1.1)	Ozone, PM2.5, mold spore counts.
Wang (2007)	Grasses, trees and weeds	Asthma (ICD-9: 493)	Tree and weed pollen trended higher on days with \geq seven asthma-related ED visits (p=0.05), but there was no significant difference in grass pollen between high- and low-visit days.	None
Tobias (2004)	Grasses, trees and weeds	Asthma (ICD-9: 493)	Increase in risk for ED presentations was 31.3% to 78.9% for grasses 49.8% for trees	Daily averages of NO ₂ , SO ₂ , PM ₁₀ , temp and humidity. 8 hour maximum O ₃ .
Lierl and Hornung (2003)	Grasses, trees and weeds	Asthma (ICD-9: 493)	log of pollen counts lagged 3 days was the most significant predictor: rate ratio (RR):1.089, (95% CI: 1.027-1.155) in a model with month of the year Pollen counts and season interaction: ln (pollen) spring &summer: RR: 1.145, 95% CI:1.076,1.217	None
Tobias (2003)	Grasses, trees and weeds, conifers	Asthma (ICD-9: 493)	MPC of ED presentations associated with a 95-99 th percentiles increase in different types of pollen levels: Olive lag 1: (1.8 ,95% CI: -7.9,12.5) Grass lag 2: (15.9,95% CI: 6.5,26.2) Grasses lag3: (17.1 , 95% CI: 3.2,32.8) Nettles lag1: (8.4 ,95% CI: 2.8,14.4), Mugwort lag1: (4.4,95% CI :-6.6,16.7) Cypress lag3: (6.0, 95%CI :-3.4,16.5)	Daily averages of NO ₂ , SO ₂ and PM ₁₀ . 8 hour maximum O ₃ . Mean daily temperature, mean relative humidity.
Garty (1998)	Grasses, trees and weeds, conifers.	doctor diagnosed asthma	No significant correlation was observed between the airborne pollen concentration peaks and asthma ED visits peaks.	None

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ICD-10AM: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (1999-present) – codes J45, J46

** ICD-9: International Classification of Diseases, Ninth Revision (1979-1998) – codes 493

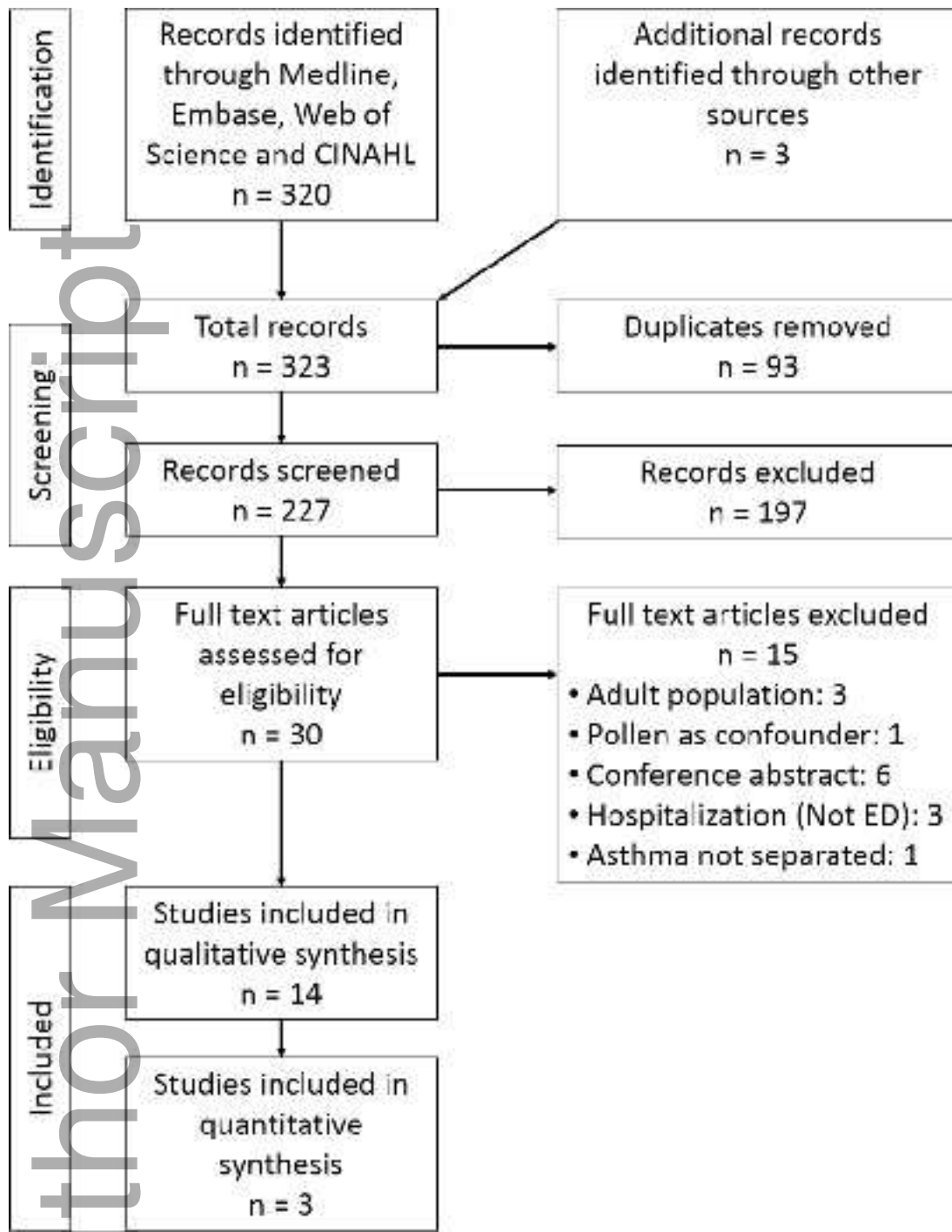
***ICD-10: International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (1999-present) – codes J45, J46

ICD-International Classification of Diseases, a global health information standard for mortality and morbidity statistics.

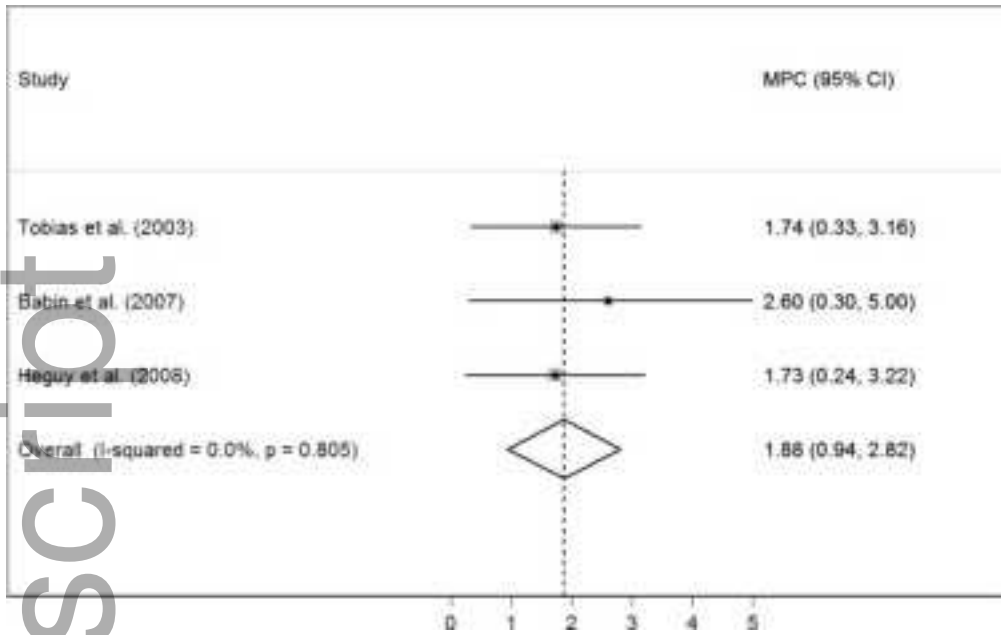
ICD-9-CM-The International Classification of Diseases, 9th Revision, Clinical Modification

-ICD-10-AM refers to the Australian modification of the WHO ICD-10 base classification system. Its proper name is the International Statistical Classification of Diseases and Related Health Problems, Tenth

Revision, Australian Modification. This version of ICD has been modified to serve particular Australian needs and to support the national collection of data relevant to our population's health.



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