Introduction to Systematic Review and Meta-Analysis with Application to Occupational Medicine

H.S. Teitelbaum, DO, PhD, MPH, FAOCOPM(d)

Clinical Professor of Medicine
Michigan State University

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Disclosures

- I have no relevant financial relationships.

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Outline of what we will be doing

- **Describe a SYSTEMATIC REVIEW and META-ANALYSIS**
- **Present Components of such a study using examples from the literature**
- **Explain the Components and how to interpret them**
- **Apply the structure and presentation of a Meta-Analysis to a published paper**

3

In Preparation

- **Identify the keystrokes needed on your computer to FIND a term or phrase in a paper (Ctrl F) for example.**
- **Identify the keystrokes that will alternate between open windows on your computer (Alt Tab) for example.**

4

Please Open the following

- **THE POWERPOINT PRESENTATION**
- **THE FOLLOWING ARTICLE:**

The Effect of Long Working Hours and Overtime on Occupational Health: A Meta-Analysis of Evidence from 1998 to 2018
Kapo Wong *, Alan H. S. Chan and S. C. Ngan
Department of Systems Engineering and Engineering Management, City University of Hong Kong, Hong Kong, China;
Received: 19 May 2019; Accepted: 10 June 2019; Published: 13 June 2019

https://pubmed.ncbi.nlm.nih.gov/31200573/

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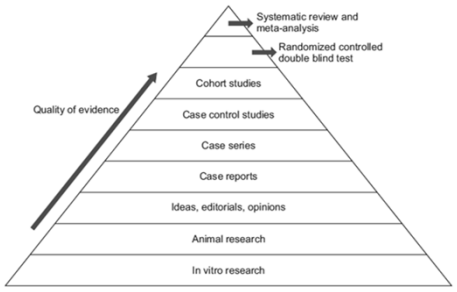

Fig. 1. Levels of evidence.

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Clinical Question	Suggested Research Design(s)
All Clinical Questions	Systematic review, meta-analysis
Therapy	Randomized controlled trial (RCT), meta-analysis *Also:* cohort study, case-control study, case series
Etiology	Randomized controlled trial (RCT), meta-analysis, cohort study *Also:* case-control study, case series
Diagnosis	Randomized controlled trial (RCT) *Also:* cohort study
Prevention	Randomized controlled trial (RCT), meta-analysis *Also:* prospective study, cohort study, case-control study, case series
Prognosis	Cohort study *Also:* case-control study, case series
Meaning	Qualitative study
Quality Improvement	Randomized controlled trial (RCT) *Also:* qualitative study
Cost	Economic evaluation

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What and Why

First a Systematic Review is a summary of research articles all purported to address the same topic. They cover different variables, but the focus is on the same outcome. It essentially is a collection of articles that have a common outcome.

Second, although not always associated with Systematic Reviews, a Meta-Analysis is a statistical mechanism for COMBINING, POOLING, or otherwise AGGREGATING results from the different studies into a single OVERALL Statistical estimate of what is going on. To STATISTICALLY summarize the results.

This is not without criticism as a technique – I will mention later – and it does not exclude or excuse professional judgment.

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Another way of saying it: Systematic Review and Meta-Analysis

a. Systematic Review
  a. Attempts to collect all possible studies
  b. Presents a criteria for selection
    I. Assesses quality of studies
    II. Done by more than one person

b. Meta-Analysis
  a. Tries to show objective analysis of combined results
  b. Tries to demonstrate any "bias" in the selection of articles
  c. Provides a quantitative measure of the outcome after combining studies.

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Warning 1

A key limitation of systematic reviews and meta-analyses is that they produce estimates that are as reliable as the studies summarized. A pooled estimate derived from meta-analysis of randomized trials at low risk of bias will always be more reliable than that derived from a meta-analysis of observational studies or of randomized trials with less protection against bias.

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Warning - 2

There is both a SUBJECTIVE (professional) component and a STATISTICAL Component of doing a Systematic Review and Meta-Analysis

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Think for a moment – if you had a collection of articles addressing the same thing, what do you think you would cause the results to vary?

Structural
- Definitions
  - Outcome
  - Input
  - Intervention
- Study Design
  - Prospective
  - Retrospective
  - RCT
- We will evaluate PROFESSIONALLY

Statistical
- Same measure of Outcome
- Same measure of Input
- Number of subjects
- Help vs. Harm
- HOW BIG A DIFFERENCE
  - Average
  - Variance
  - Sample size
- We will Evaluate STATISTICALLY

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This collection of things that are different is called HETEROGENECITY

- By strict definition this is the DIFFERENCES BETWEEN STUDIES THAT IS NOT DUE TO CHANCE.
- It is all the things we mentioned on the previous slide.
- This is measurable.

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The Process of Conducting a Systematic Review and Meta-analysis

1. **Formulate the question**
2. **Define the eligibility criteria for studies to be included in terms of Patient, Intervention, Comparison, Outcome (PICO), and study design**
3. **Develop a priori hypotheses to explain heterogeneity**
4. **Conduct search**
5. **Screen titles and abstracts for inclusion**
6. **Review full text of possibly eligible studies**
7. **Assess the risk of bias**
8. **Abstract data**
9. **When meta-analysis is performed:**
   1. **Generate summary estimates and confidence intervals**
   2. **Look for explanations of heterogeneity**
   3. **Rate confidence in estimates of effect**

JAMA How to Read a Systematic Review and Meta-analysis and Apply the results to Patient care. July 9, 2014

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PRISMA

- Preferred
- Reporting
- Items for
- Systematic Review and
- Meta-Analyses

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Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organizations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	

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Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

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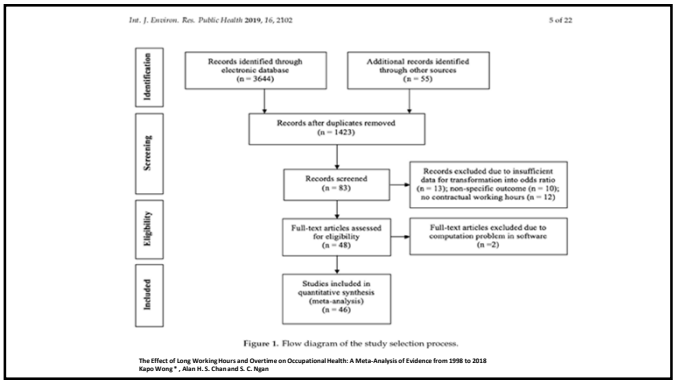

Figure 1. Flow diagram of the study selection process.

The Effect of Long Working Hours and Overtime on Occupational Health: A Meta-Analysis of Evidence from 1998 to 2018
Kapo Wong *, Alan H. S. Chan and S. C. Ngan

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Once we have the studies

- The next step is to combine the results of the studies to accomplish the following:
  - **Generate AN AVERAGE OVERALL ESTIMATE OF THE EFFECT. Pool all the outcomes and get an average**
  - **Assess any BIAS in the collection of articles. If BIAS IS FOUND – we have QUANTIFY it and EXPLAIN IT.**

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SAMPLE SIZE

- Sample size is one of the major problems is assembling the studies.
- Sample size determines:
  - Variance
  - Confidence intervals (precision)
  - Average effect size – like means or Odds Ratios or Risk Ratios etc.
- Studies with LARGE samples as compared to small samples generally
  - Reduce Variance
  - Yield better estimates of success
  - Are more representative of the population from which it is drawn.

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Heterogeneity

- Inspect Results table – **MUST BE PROVIDED**
- Review a PLOT of the Spread of the values
  - **Forest Plot – almost always provided**
  - **Funnel Plot – sometimes provided**
- Review a STATISTIC of the Heterogeneity (Higgins, I^2)
  - The statistic tells us the percentage of the variability that is not due to chance or sampling error. In other words, if it is large something is going on and it must be investigated.

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What is a Funnel Plot?

- A Funnel Plot is a plot of the variability of the individual studies(standard error) against the mean effect size.
- It is called a funnel plot because as study size increases the standard error approaches zero.
- It is assumes that the plot should be symmetrical and there should be as many studies above the mean as there are below the mean.
- It also assumes that there should be a wide distribution of study variabilities.

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Funnel Plot

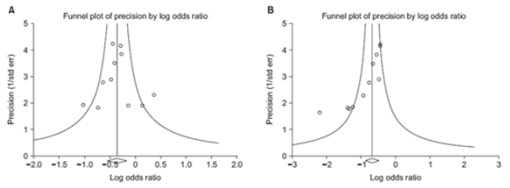

Fig. 5. Funnel plot showing the effect size on the x-axis and sample size on the y-axis as a scatter plot. (A) Funnel plot without publication bias. The individual plots are broader at the bottom and narrower at the top. (B) Funnel plot with publication bias. The individual plots are located asymmetrically.

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So, what happens when you have an asymmetric Funnel Plot?

- This suggests, among other things, something called **PUBLICATION BIAS.**
- This happens when there is a tendency to publish only + outcomes.
- The SYSTEMATIC REVIEWERS uses a lot of search engines to locate articles. But this assumes that they are published. Sort of circular argument. How can we get around this?
- Instruct people to look at PROCEEDINGS of meetings, Registries, Information presented at research meetings (like this one!!), etc.
- **BOTTOM LINE: WE HAVE TO EXPLAIN IT!!**

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Two common ways of "fixing" an Asymmetric Plot

- **Trim and Fill**
  - The trim-and-fill method aims at estimating potentially missing studies due to publication bias in the funnel plot and adjusting the overall effect estimate. The fundamental assumption of the trim-and-fill method is that the studies with the most extreme effect sizes, either on the left or on the right side, are suppressed.
- **Sensitivity Analysis**
  - Systematically remove studies and reanalyze. Does the result change significantly?

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Trim and Fill

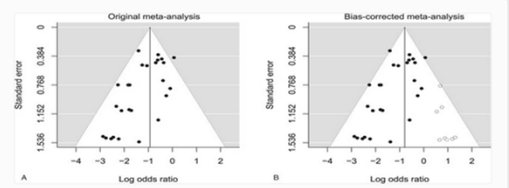

Figure 2

Funnel plots of the meta-analysis by Andersen et al[26] before (panel A) and after (panel B) applying the trim-and-fill method. The closed dots indicate the observed studies, and the open dots indicate the missing studies imputed by the trim-and-fill method (based on the estimator L_0). The dashed lines that create a triangular area indicate the 95% confidence limits (under the fixed-effect setting), and the vertical solid line represents the overall effect size.

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For the next few slides, I will explain what is going on but will not provide any formulae for calculations – the computer will do this.

- Heterogenicity
  - Statistical heterogeneity refers to differences between study results beyond those attributable to chance.
  - IT IS ALWAYS PRESENT
  - Will it SIGNIFICANTLY effect the results?
  - Does it need to be explained?

  This will be done by tables, graphs and statistics

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One statistic that is commonly used to detect Heterogeneity Higgins I^2

- **I^2**
  - **Percentage of variation across studies that is due to heterogeneity and not due to chance**
  - **A suggestion for interpretation**
    - **.2 low heterogeneity**
    - **.5 moderate**
    - **.7 high**

- Julian P T Higgins, Simon G Thompson, Jonathan J Deeks, Douglas G Altman, **Measuring inconsistency in meta-analyses,** BMJ. 2003 Sep 6; 327(7414): 557–560. doi: 10.1136/bmj.327.7414.557PMCID: PMC192859

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How do you adjust?

- What you do is to WEIGHT the studies used according to their sample size, which usually takes the form of messing with the VARIANCE of the study. This is because the formula for the variance involves the average performance and the sample size. Those with larger sample sizes get larger weights. One method uses the "Inverse Variance" YOU DON'T NEED TO REMEMBER THIS. Just know that it is an attempt to give a better representation of the results.

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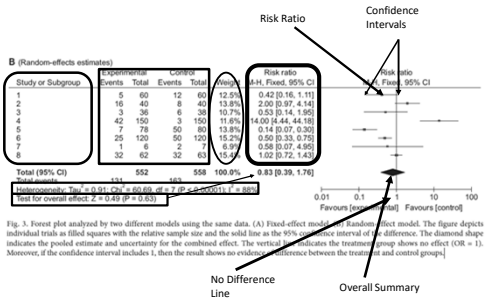

Fig. 3. Forest plot analyzed by two different models using the same data. (A) Fixed-effect model and (B) random-effect model. The figure depicts individual trials as filled squares with the relative sample size and the solid line as the 95% confidence interval of the difference. The diamond shape indicates the pooled estimate and uncertainty for the combined effect. The vertical line indicates the treatment group shows no effect (OR = 1). Moreover, if the confidence interval includes 1, then the result shows no evidence of difference between the treatment and control groups.

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HOW DO WE CONTINUE AFTER DETECTING A BIAS?

- **We need to explain it!!**
- **For our purposes, the SUBGROUP analysis is preferred**.
  - **Sometime a META REGRESSION ANALYSIS is used- this tries to increase or decrease the elements in subgroups.**
- **This is a way of saying there is something that is messing up our overall results.**
- **Start stratifying the studies into groups that make sense to your purpose.**

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MAJOR THING MOST PEOPLE WANT TO KNOW

- After all this "STUFF" what is the overall effect of our efforts?
- That is to say, is there a summary of the EFFECT SIZE after all of this?
- The answer is yes. IT IS AN ADJUSTED EFFECT SIZE. There is a statistical test for this. The authors have a choice and will report it with a statistical test and a p-value. There are several that they might choose. **One is a Cohen's d^2**
- **This has guidelines**
  - **.2 Weak**
  - **.5 Moderate**
  - **.8 Strong**

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Other tests of overall effect size

- **The authors will cite them. Regardless of what the authors use, there will be a p-value associated with it and you will see if it is above or below your criterion (usually .05).**

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Quick and Dirty Checklist

1. Definitions Clear? – Yes, proceed, No – discard
2. Are there at least 2 reviewers? Yes- Proceed No- Discard
3. Is there an INCLUSION/EXCLUSION criteria? –Yes, proceed, No – reconsider
4. Is there a SELECTION CRITERA mentioned? (PRISMA, etc.) Yes, proceed, No – READ THE SELECTION CRITERIA CAREFULLY!!
5. Is there a flow chart to show how many studies were found and used? Yes –proceed, No – CAUTION.
6. Is there a SUMMARY TABLE showing results of : Each Articles Effect size, *sample size,* Confidence Interval, *weight,* Adjusted effect size, Adjusted Confidence Interval and Forest Plots? Yes, proceed, No- CAUTION (it might be included in the text. But should be in the table.

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Checklist Continued

7. Is there a test for Heterogeneity? Yes – Proceed, No – Discard
8. Did the authors ASSESS HETEROGENEITY Usually I^2? Yes, Proceed, No – CAUTION – May be in text. Should be in table.
9. Is there a summary effect size with p-value? Yes, proceed, No – discard
10. Is there an investigation of HETEROCENEITY (Subgroup, Sensitivity, Trim and Fill? Yes, Proceed, No – Discard.
11. Are there limitations cited? Yes – Proceed No-Discard
12. Did the authors summarize the findings? Yes – Proceed No-Discard

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If the above are satisfied

- State the statistical finding
- State your application decision

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Please access

- **The Effect of Long Working Hours and Overtime on Occupational Health: A Meta-Analysis of Evidence from 1998 to 2018**
- **Kapo Wong * , Alan H. S. Chan and S. C. Ngan**

Page

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Page 3 Note 1

- The purpose here was to examine the relationship between the length of work hours and the occupational health of workers.

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Page 4 Note 2

- Google Scholar and Medline (PubMed) by searching the following keywords: (long work hours OR overtime) AND (occupational health OR heart diseases OR cardiovascular disease OR stroke OR diabetes OR blood pressure OR injuries OR pain OR stress OR depression OR anxiety OR exhaustion OR sleep OR smoke OR alcohol OR physical activity). All published papers extracted for the meta-analysis were in **English.** The abstracts of the published papers selected were screened, and the references were all manually checked to identify if the studies cited and described in the papers were appropriate for conducting this meta-analysis. A total of 1423 papers were collected for inclusion in this stage.

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Page 4 Note 3 Exclusion Example

- studies involving **night shift-work schedule and overtime without providing contract hours or regular working hours, for instance, Akerstedt et al. [58] and Sato et al. [38], were excluded from further analysis.**

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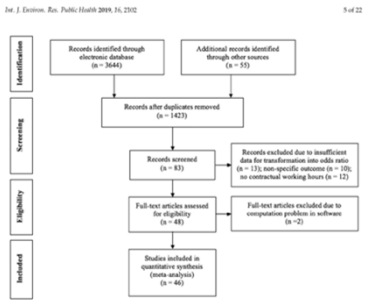
Page 4
Note 4



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Page 5 Note 5 INCLUSION EXAMPLE

- **In the meta-analysis, only the working hours longer than the reference working hours and their corresponding odds ratios were included in the analysis**

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Page 5 Note 6 and 7

- The random effects model was adopted in the meta-analysis here due to the variety of effects in the studies caused by different variables, such as study designs, method of data collection and adjustment for the results involved in the studies [67]. The consistency of the results was tested by the heterogeneity indicator, I-squared (I^2) statistic. The value of **I^2** shows the variations of the studies in term of percentage [68,69]. The greater the value of I^2, the more considerable the heterogeneity, and a value of zero means homogeneity. Furthermore, the **publication bias of the five effect sizes was tested by the trim and fill analysis in which an asymmetry shape in the funnel plots implied the existence of publication bias [70].**

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PAGE 7 NOTE 9

Table 2. Results of meta-analysis between long working hours and occupational health conditions and the adjustment for publication bias.

Occupational Health Condition	Number of Records	Effect Size and 95% Interval			Heterogeneity		Adjustment for Publication Bias			
		Overall OR	Lower Limit	Upper Limit	*p*-Value	I-Squared	Data Points Imputed	Overall OR	Lower Limit	Upper Limit
PH	85	1.177	1.102	1.257	0.000	67.131	6	1.118	1.043	1.200
MH	55	1.366	1.238	1.507	0.000	55.733	12	1.197	1.072	1.336
HB	35	1.100	1.004	1.204	0.000	59.660	0	1.100	1.004	1.204
RH	54	1.465	1.332	1.611	0.000	68.678	7	1.323	1.181	1.473
NH	14	1.065	0.942	1.204	0.001	63.539	0	1.065	0.942	1.204
Overall	243	1.245	1.195	1.298	0.000	67.574				

PH = physiological health, MH = mental health, HB = health behaviours, RH = related health, NH = not specified health, OR = odds ratio.

Int. J. Environ. Res. Public Health **2019**, *16*, 2102 8

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Please observe the tie in between I^2 in the Table Page 7 (Note 9) and Notes 10 and 11 and 12.

- **I-Squared**
- **publication bias was assessed by the trim-and-fill analysis**
- **Twelve new data points were imputed to the condition of mental health, and the odds ratio decreased to 1.197 (95% CI: 1.072–1.336)**
- **Considering that 50% represented a substantial heterogeneity [68,69], the heterogeneity was a problem for these five conditions. Therefore, moderator analysis was conducted to identify the potential sources of the heterogeneity.**

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Funnel Plots on Pages 8 Note 13

- Read at your leisure.

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Page 9 Note 16

- A moderator analysis was conducted to investigate the possible sources of heterogeneity Table 3. **Please turn to those pages**.
- Look at the p-value in the RIGHT-HAND COLUMN
- If less than .05 it is statistically significant. PERMISSION TO SNOOP!!

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Summary Statement

- This meta-analysis synthesizing 243 records from 46 papers with 814,084 participants from 13 countries demonstrated that long working hours had a positive relationship with occupational health problems. The **aggregated odds ratio for the effect of long working hours on occupational health was 1.245 (95% CI: 1.195–1.298).**
- Amongst the five occupational health conditions, the condition 'related health' showed the strongest association with long working hours; the health measures in this category were short sleep duration, sleep disturbance, sleep problem, exhaustion and injuries.

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Page 10

Table 3. The association of long working hours with occupational health in relation to gender, diagnosis, study design, cut-off point for long working hours, working class, country of origin and health measure for the conditions of physiological health, mental health, health behaviours, related health and nonspecified health (effect sizes adjusted, when appropriate, for age, gender, educational level and occupation).

Moderator	Effect Size and 95% Interval			Test of Null		Test to Model		
	Odds Ratio	95% Lower	95% Upper	Z-Value	2-Sided p-Value	Q-Value	df (Q)	Meta-Regression p-Value
Gender								
Males	1.280	1.176	1.394	5.711	0.000			
Females	1.135	1.053	1.222	3.332	0.001			
						5.797	2.000	0.055
Diagnosis method								
Self-report	1.263	1.205	1.324	9.735	0.000			
Health or medical examination	1.188	1.094	1.291	4.086	0.000			
						1.579	1.000	0.209
Study design								
Case-control study **	1.811	1.466	2.239	5.499	0.000			
Cross-sectional study **	1.338	1.267	1.414	10.465	0.000			
Prospective cohort study	1.049	0.997	1.104	1.826	0.068			
						56.377	2.000	0.000 **
Cut-off point for long working hours								
>50 h/week or >10 h/day **	1.420	1.337	1.508	11.446	0.000			
≤50 h/week or ≤10 h/day **	1.097	1.035	1.162	3.130	0.002			
						57.331	2.000	0.000 **
Working class								
White collar occupations	1.095	1.043	1.149	3.668	0.000			
Pink collar occupations	1.168	1.002	1.360	1.992	0.046			
Blue collar occupations	1.275	0.907	1.792	1.400	0.161			
						1.318	2.000	0.517
Country of origin								
Asian Countries **	1.321	1.231	1.418	7.741	0.000			
China **	1.745	1.428	2.132	5.441	0.000			
China and Japan	1.569	0.817	3.013	1.352	0.176			
Japan **	1.333	1.191	1.492	5.010	0.000			
Korea **	1.237	1.124	1.361	4.351	0.000			
Western countries **	1.180	1.126	1.237	6.854	0.000			
Australia and New Zealand *	1.230	1.050	1.442	2.801	0.010			
Denmark	1.091	0.840	1.418	0.656	0.512			
Finland	1.063	0.966	1.170	1.250	0.211			
Italy	1.341	0.993	1.811	1.915	0.055			
Spain *	1.248	1.131	1.377	4.404	0.000			
Sweden	1.198	0.937	1.532	1.438	0.150			
The UK *	1.083	1.008	1.163	2.187	0.029			
The US **	1.274	1.108	1.465	3.393	0.001			
						35.043	12.000	0.000 **
Health measure								
Physiological health						35.773	4.000	0.000 **
All-cause mortality	0.975	0.924	1.029	−0.920	0.358			
Cardiovascular heart diseases **	1.539	1.324	1.789	5.607	0.000			
Metabolic syndrome **	1.100	1.025	1.182	2.630	0.009			
Poor physical health	1.408	0.893	2.221	1.471	0.141			
Type 2 diabetes	0.855	0.497	1.472	−0.565	0.572			
Mental health						5.074	5.000	0.407
Anxiety	1.308	1.041	1.644	2.301	0.021			
Depressive symptoms	1.489	1.220	1.817	3.915	0.000			
Poor mental health	1.239	1.018	1.510	2.134	0.033			
Psychiatric morbidity	1.398	1.184	1.651	3.952	0.000			
Psychological distress	1.110	0.878	1.403	0.870	0.384			
Psychological stress	1.512	1.123	2.034	2.727	0.006			
Health behaviours						2.255	3.000	0.521
Heavy drinking	1.083	0.943	1.244	1.134	0.257			
Physical inactivity	1.234	1.002	1.520	1.978	0.048			
Smoking	1.055	0.890	1.251	0.620	0.535			
Unhealthy food habits	0.990	0.796	1.230	−0.094	0.925			
Related health						9.604	4.000	0.048 *
Fatigue **	1.439	1.149	1.803	3.169	0.002			
Injury **	1.276	1.091	1.492	3.047	0.002			
Poor sleep quality **	1.276	1.128	1.444	3.880	0.000			
Short sleep duration **	1.909	1.502	2.427	5.281	0.000			
Sleep disturbance *	1.395	1.052	1.850	2.312	0.021			
Nonspecified health						-	-	-
Poor health status	1.065	0.942	1.204	1.000	0.317			

** p-value < 0.01. * p-value < 0.05.

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Table 4. Moderating effect of working class on the association of long working hours with physiological health, mental health, health behaviours, related health and nonspecified health (effect sizes adjusted, when appropriate, for age, gender, educational level and occupation).

Working Class	Odds Ratio	95% Lower	95% Upper	Z-Value	2-Sided p-Value	Q-Value	df (Q)	Meta-Regression p-Value
Physiological health						1.449	2.000	0.485
White collar occupations	1.145	1.007	1.303	2.065	0.039			
Pink collar occupations	0.986	0.792	1.226	−0.130	0.896			
Blue collar occupations	1.192	0.747	1.902	0.737	0.461			
Mental health						1.037	2.000	0.595
White collar occupations	1.310	1.166	1.473	4.546	0.000			
Pink collar occupations	1.760	0.961	3.223	1.831	0.067			
Blue collar occupations	1.250	0.962	1.624	1.672	0.095			

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Table 4. *Cont.*

Working Class	Odds Ratio	95% Lower	95% Upper	Z-Value	2-Sided p-Value	Q-Value	df (Q)	Meta-Regression p-Value
Health behaviours						3.069	2.000	0.216
White collar occupations	0.988	0.915	1.066	−0.316	0.752			
Pink collar occupations	1.102	0.745	1.629	0.487	0.626			
Blue collar occupations	1.250	0.962	1.624	1.672	0.095			
Related health						13.143	2.000	0.001 *
White collar occupations	0.887	0.713	1.104	−1.075	0.282			
Pink collar occupations	0.989	0.940	1.040	−0.438	0.662			
Blue collar occupations *	1.366	1.144	1.631	3.445	0.001			
Nonspecified health						3.649	2.000	0.161
White collar occupations	0.970	0.853	1.103	−0.463	0.643			
Pink collar occupations	0.881	0.666	1.165	−0.890	0.374			
Blue collar occupations	1.115	0.987	1.260	1.745	0.081			

* p-value < 0.01.

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