

Common Mistakes in Meta-Analysis And How to Avoid Them

**Common Mistakes in Meta-Analysis
And How to Avoid Them**

**Michael Borenstein
Biostat, Inc., New Jersey, USA**

Biostat, Inc.

This edition first published 2019
© 2019 Biostat, Inc.

Registered office

Biostat, Inc., 14 North Dean Street, Englewood, NJ 07631 USA

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the publisher.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are service marks, trademarks, or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book with the exception of the software Comprehensive Meta-Analysis (CMA).

This publication is intended to provide accurate and authoritative information regarding the subject matter covered. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The examples in this book are intended to provide insight only into statistical issues in meta-analysis. They should not be used to provide information about the safety or efficacy of any of the interventions discussed.

ISBN: 978-1-7334367-0-0 (Hardcover)
ISBN: 978-1-7334367-1-7 (Softcover)

Printed and bound in the Unites States of America

CONTENTS

CONTENTS	V
1. PREFACE	XI
2. ACKNOWLEDGEMENTS	XIII
3. WORKSHOPS ON META-ANALYSIS	XV
4. WEB SITES	XVII
4.1. WEB SITE FOR THIS BOOK	XVII
4.2. WEB SITE FOR THE SOFTWARE	XVII
4.3. WEB SITE FOR OUR WORKSHOPS	XVII
5. HOW TO READ THE PLOT	XIX
6. STATISTICAL MODELS FOR META-ANALYSIS	3
6.1. OVERVIEW	3
6.2. EACH MODEL IS APPROPRIATE FOR A SPECIFIC INFERENCE	8
7. MISTAKES IN CHOOSING A STATISTICAL MODEL	13
7.1. OVERVIEW	13
7.2. CHOOSING BETWEEN FIXED EFFECT (SINGULAR) AND RANDOM EFFECTS	14
7.3. CHOOSING BETWEEN FIXED EFFECTS (PLURAL) AND RANDOM EFFECTS	23
7.4. LIMITATIONS OF THE RANDOM-EFFECTS MODEL	26
7.5. KNAPP-HARTUNG ADJUSTMENT	36
7.6. META-ANALYSIS IN LEGAL APPLICATIONS	39
7.7. PUTTING IT ALL TOGETHER	41
8. ISSUES AND MYTHS ABOUT STATISTICAL MODELS	43

8.1.	OVERVIEW	43
8.2.	RANDOM-EFFECTS MODEL ASSIGNS EQUAL WEIGHT TO ALL STUDIES	44
8.3.	RANDOM-EFFECTS MODEL GIVES TOO MUCH WEIGHT TO SMALL STUDIES	48
8.4.	COMPARING RESULTS FROM THE TWO MODELS	55
8.5.	RANDOM-EFFECTS MODEL IS MORE CONSERVATIVE	59
8.6.	FIXED-EFFECT MODEL HAS BETTER STATISTICAL POWER	64
8.7.	WHEN τ^2 IS ESTIMATED AS ZERO	65
8.8.	SWITCHING MODELS WILL HAVE MAJOR IMPACT ON RESULTS	70
8.9.	META-ANALYSES WITH LARGE N WILL HAVE GOOD POWER	72
8.10.	PUTTING IT ALL TOGETHER	74
9.	HETEROGENEITY	75
9.1.	OVERVIEW	75
9.2.	HETEROGENEITY IS <i>BAD</i>	81
9.3.	THE PREDICTION INTERVAL	85
9.4.	PREDICTION INTERVAL VS. CONFIDENCE INTERVAL	94
9.5.	MISTAKES IN USING THE I^2 STATISTIC	103
9.6.	CLASSIFYING HETEROGENEITY AS LOW, MODERATE OR HIGH	116
9.7.	USING THE P -VALUE AS INDEX OF HETEROGENEITY	121
9.8.	USING THE Q -VALUE AS INDEX OF HETEROGENEITY	126
9.9.	ESTIMATES OF VARIANCE MAY NOT BE RELIABLE	131
9.10.	STATISTICS FOR HETEROGENEITY REFER TO FIXED-EFFECT MODEL	133
9.11.	PUTTING IT ALL TOGETHER	135
10.	MISTAKES RELATED TO SIGNIFICANCE TESTING	139
10.1.	OVERVIEW	139
10.2.	WHEN THE EFFECT SIZE IS CONSISTENT ACROSS STUDIES	142
10.3.	WHEN THE EFFECT SIZE VARIES ACROSS STUDIES	145
10.4.	SIGNIFICANT EFFECT MAY BE HARMFUL IN SOME POPULATIONS	152
10.5.	PUTTING IT ALL TOGETHER	154
11.	PUBLICATION BIAS	155
11.1.	OVERVIEW	155

11.2.	CONFLATING BIAS WITH THE SMALL-STUDY EFFECT	162
11.3.	PUBLICATION BIAS DOES NOT INVALIDATE THE ANALYSIS	165
11.4.	TESTS TO DETECT BIAS MAY BE OVER-INTERPRETED	166
11.5.	TRIM AND FILL	167
11.6.	THE TESTS ONLY WORK UNDER CERTAIN CONDITIONS	171
11.7.	PROCEDURES DO NOT APPLY TO STUDIES OF PREVALENCE	173
11.8.	THE MODEL FOR PUBLICATION BIAS IS SIMPLISTIC	175
11.9.	PUBLICATION BIAS AND THE GREY LITERATURE	177
11.10.	LINES ON FUNNEL PLOT	178
11.11.	FAIL-SAFE <i>N</i>	180
11.12.	USING CUMULATIVE ANALYSIS	182
11.13.	THE FOCUS ON PUBLICATION BIAS IGNORES OTHER TYPES OF BIAS	185
11.14.	PUTTING IT ALL TOGETHER	186
12.	<u>MISTAKES IN SUBGROUP ANALYSES</u>	<u>187</u>
<hr/>		
12.1.	OVERVIEW	187
12.2.	ASSUMING A CAUSAL RELATIONSHIP	190
12.3.	CHOOSING A STATISTICAL MODEL	194
12.4.	MISTAKES IN ESTIMATING T^2	199
12.5.	COMPARING THE EFFECT SIZE IN DIFFERENT SUBGROUPS	203
12.6.	REPORTING AN OVERALL EFFECT SIZE IN THE PRESENCE OF SUBGROUPS	209
12.7.	PUTTING IT ALL TOGETHER	211
13.	<u>COMPREHENSIVE META-ANALYSIS SOFTWARE</u>	<u>215</u>
<hr/>		
13.1.	INTRODUCTION	215
13.2.	FEATURES IN CMA	215
13.3.	TEACHING ELEMENTS	216
13.4.	DOCUMENTATION	217
13.5.	AVAILABILITY	217
13.6.	ACKNOWLEDGEMENTS	217
13.7.	MOTIVATING EXAMPLE	218
13.8.	DATA ENTRY	218
13.9.	BASIC ANALYSIS	221
13.10.	HIGH-RESOLUTION PLOT	224

13.11.	SUBGROUP ANALYSIS	224
13.12.	META-REGRESSION	229
13.13.	PUBLICATION BIAS	232
14.	HOW TO REPORT THE RESULTS OF AN ANALYSIS	237
14.1.	INTRODUCTION	237
14.2.	METHYLPHENIDATE FOR ADULTS WITH ADHD	241
14.3.	HIGH DOSE VS. STANDARD DOSE OF STATINS	247
14.4.	INTERVENTION TO PREVENT ALCOHOL ABUSE	253
14.5.	PREVALENCE OF PTSD	259
14.6.	TRAINING CHILDREN TO AVOID SEXUAL ABUSE	265
14.7.	IMPACT OF INTERVENTIONS ON TRUANCY	271
14.8.	CORRELATION BETWEEN COMMITMENT AND PERFORMANCE	277
14.9.	VIAGRA FOR ERECTILE DYSFUNCTION	283
14.10.	SECOND-HAND SMOKING AND LUNG CANCER	289
14.11.	WEIGHT LOSS BY DRUG	299
15.	GLOSSARY	307
16.	APPENDIX	311
16.1.	APPENDIX I – HOW STATISTICAL MODEL AFFECTS CONFIDENCE INTERVAL	312
16.2.	APPENDIX II – STANDARD ERROR OF THE SUMMARY EFFECT	319
16.3.	APPENDIX III – HOW STATISTICAL MODEL AFFECTS ESTIMATE OF MEAN	321
16.4.	APPENDIX IV – RISK OF BIAS	326
16.5.	APPENDIX V – KNAPP-HARTUNG ADJUSTMENT	328
16.6.	APPENDIX VI – STATISTICS FOR HETEROGENEITY	334
16.7.	APPENDIX VII – COMPUTING A PREDICTION INTERVAL	337
16.8.	APPENDIX VIII – COMPUTING I^2	346
16.9.	APPENDIX IX – PAIRWISE COMPARISONS	350
16.10.	APPENDIX X – POOLING ESTIMATES OF T^2	360
17.	REFERENCES	363
18.	SUBJECT INDEX	375

<u>19.</u>	<u>AUTHOR INDEX</u>	<u>383</u>
-------------------	----------------------------	-------------------