CHAPTER 23

Integrative Data Analysis for Research in Developmental Psychopathology

EUN-YOUNG MUN, YANG JIAO, and MINGE XIE

CHAPTER OVERVIEW

The importance of research synthesis from a body of evidence using more rigorous, systematic, and quantitative approaches has been echoed in the field over years; yet most of the literature reviews are narrative or qualitative in nature. It is possible to conduct two different narrative literature reviews and to have contrasting sets of hypotheses if the reviews were not sufficiently extensive or done selectively. Even in extensive and systematic reviews, determining which studies are more important and relevant than others to report or discuss in detail may very well be within the realm of subjective judgments. Iain Chalmers

The project described was supported by Award Number R01 AA 019511 from the National Institute on Alcohol Abuse and Alcoholism (NIAAA). The third author's work was also supported in part by the National Science Foundation (NSF)-DMS1107012. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIAAA, the National Institutes of Health, or the NSF.

We thank Helene R. White and Anne E. Ray of the Center of Alcohol Studies, Rutgers, The State University of New Jersey; Jimmy de la Torre and Yan Huo of the Graduate School of Education, Rutgers, The State University of New Jersey; and David C. Atkins, David Huh, and Mary Larimer of the Department of Psychiatry and Behavioral Sciences, University of Washington, for their contributions to Project INTEGRATE.

We also thank the following researchers who contributed their data to Project INTEGRATE (in alphabetical order): John S. Baer, Department of Psychology, The University of Washington, and Veterans' Affairs Puget Sound Health Care System; Nancy P. Barnett, Center for Alcohol and Addiction Studies, Brown University; M. Dolores Cimini, University Counseling Center, The University at Albany, State University of New York; William R. Corbin, Department of Psychology, Arizona State University; Kim Fromme, Department of Psychology, The University of Texas, Austin; Joseph W. LaBrie, Department of Psychology, Loyola Marymount University; Mary E. Larimer, Department of Psychiatry and Behavioral Sciences, The University of Washington; Matthew P. Martens, Department of Educational, School, and Counseling Psychology, The University of Missouri; James G. Murphy, Department of Psychology, The University of Memphis; Scott T. Walters, Department of Behavioral and Community Health, The University of North Texas Health Science Center; Helene R. White, Center of Alcohol Studies, The State University of New Jersey; and Mark D. Wood, Department of Psychology, The University of Rhode Island.

[1] Color versions of Figures 23.1, 23.3, 23.8 and 23.10 are available at http://onlinelibrary.wiley.com/book/10.1002/9781119125556

(2003) poignantly pointed out missed opportunities of the past citing that, for example, cases of sudden infant death syndrome (SIDS), for babies sleeping on their fronts (tummy), could have been prevented much earlier, had there been a rigorous, systematic and quantitative review of available evidence. He also cited exemplary cases of the past that saved numerous lives (e.g., low doses of aspirin reducing the risk of cardiovascular morbidity and mortality; see O'Rourke, 2007, for a historical account of this report that appeared in the *Lancet* editorial in 1980). Furthermore, as the number of relevant studies increases, it becomes much more difficult to summarize findings from multiple studies in a narrative review.

Quantitative research synthesis can help us to draw inferences that are not afflicted with chance findings and optimism bias, when conducted routinely and vigorously with the most up-to-date compiled evidence. Quantitative research synthesis is aimed at quantifying the overall effect of interest across studies and providing the uncertainty surrounding the point estimate. The resulting summary estimate can be helpful for deciding the benefits of the effect in question if, for example, a new treatment were brought to market. In the field of preventions and interventions, one can examine the average effect size of existing interventions, and subsequently channel efforts into more effective interventions, thus saving limited resources available in the current, tight funding environment. The Cochrane Collaborative Network (Higgins & Green, 2011) and the Human Genome Epidemiology Network (Ioannidis et al., 2006) represent such efforts to promote systematic reviews and to obtain efficient and reliable findings, respectively, by utilizing large-scale evidence in the medical and epidemiological genetic research fields.

In addition, recent high profile reports and discussions have fueled the need for quantitative research synthesis. These reports pointed out that findings from single studies are often not replicable, and are subject to publication bias and afflicted by low power and high false discovery rates (e.g., Begley & Ellis, 2012; Ioannidis, 2005). Thus, findings from single studies that are conducted independently, regardless of how important they may sound, may be best interpreted with some caution and scrutiny. At the same time, data from individual studies may be utilized more often for a large-scale research synthesis to obtain more robust evidence in the future.

Synthesizing data across studies in a meta-analysis allows one to obtain more credible estimates of effects than are possible from individual studies and to achieve better generalization of how causal relationships may change over variations in study features (Shadish, Cook, & Campbell, 2002). From a more discovery-oriented or exploratory perspective, individual single studies are not well equipped for novel discoveries due to lack of power. By combining data from multiple sources, we can overcome several important, inherent limitations of single studies. In the future, single studies may serve two distinct goals: a preliminary investigation for novel discoveries, and a component data set as part of a bigger, pooled data set, for more robust and generalized inference.

The momentum toward more robust research synthesis via quantitative approaches has been building in recent psychological research. Quantitative research synthesis from available data—either published aggregated data (AD) in terms of effect size estimates or raw individual participant-level data (IPD)—has prominently been discussed as one of the central strategies for building a cumulative knowledge base. The journal *Prevention Science* recently published a special issue focusing on subgroup analysis by pooling data from multiple trials or by utilizing more advanced analytic approaches in prevention and intervention research (Supplee, Kelly, MacKinnon, & Barofsky, 2013). In addition, *Psychological Methods* published a special issue focusing on integrative data analysis (IDA) in 2009 (Curran, 2009), discussing advantages and disadvantages of pooling and combining raw data from multiple studies, compared with either single studies (Curran & Hussong, 2009) or meta-analysis using AD (Cooper & Patell, 2009). Similarly, *Perspectives on Psychological Science* recently published a special section on replicability (Pashler & Wagenmakers, 2012). In this special section, the Open Science Collaboration (2012) and other contributors have called for sharing of data and/or publishing raw data for IPD meta-analysis to achieve better transparency and higher standards for research (e.g., Ioannidis, 2012).

The current chapter discusses quantitative methods for research synthesis. We discuss any quantitative methods aimed at synthesizing information from multiple, independent sources under the big IDA tent. The covered methods encompass meta-analysis using AD for different outcomes, such as odds ratio, mean difference, or other effect size estimates; meta-analysis using IPD; and other approaches to analyzing multiple, independent data sets. This chapter is intended to provide a more inclusive coverage of these various quantitative approaches under the umbrella of IDA (Figure 23.1). Curran and Hussong (2009) defined IDA more specifically as "the statistical analysis of a single data set that consists of two or more separate samples that have been pooled into one" (p. 82) to distinguish IDA from either AD meta-analysis or single studies and to highlight the unique advantages and

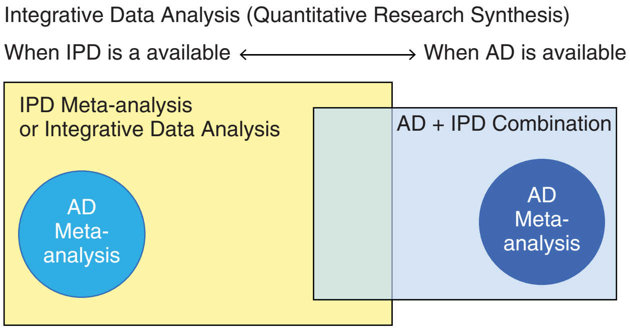

Integrative Data Analysis (Quantitative Research Synthesis)
When IPD is a available
When AD is available
IPD Meta-analysis or Integrative Data Analysis
AD + IPD Combination
AD Meta-analysis
AD Meta-analysis

Figure 23.1 Integrative data analysis (IDA) and meta-analysis using individual participant-level data (IPD) and aggregated data (AD). AD meta-analysis can be conducted either as part of IDA when IPD is available (see the circle inside the rectangle on left) or based on reported AD in publications (the circle inside the right rectangle). See footnote 1.

challenges associated with analyzing raw IPD. In contrast, we include AD meta-analysis under the IDA framework because results from AD meta-analysis can be obtained by using raw IPD (Figures 23.1 and 23.2). For example, the overlap in the middle between the two rectangles in Figure 23.1 indicates situations where IPD is available for some of the studies and consequently AD meta-analysis is possible. The circles for AD meta-analysis within the two rectangles are shaded in different colors to reflect some differences in the procedures and possibly different results involved in AD meta-analysis depending on the source of data. The strict distinction between AD and IPD may not be useful for the purpose of research synthesis. Because IPD is not always available and IPD analysis can be quite challenging, analysis based on combinations of AD and partially available IPD may provide an alternative in some situations (see Yamaguchi et al., 2014, for a proposed method that combines these two data structures) while taking advantage of all available data. Figure 23.1 shows the relationships between IDA, IPD meta-analysis, and AD meta-analysis. Note that in the current chapter, we use the term IDA in two different ways. On one hand, we broadly use IDA as a general evidence-based framework for research synthesis that includes all quantitative methods. At the concrete level of analysis, on the other hand, we use IDA interchangeably with IPD meta-analysis and contrast it against AD meta-analysis. Table 23.1 provides a list of several important approaches and summarizes notable characteristics and challenges of each approach.

Despite some differences across various methods, these quantitative approaches under the broad umbrella of IDA share many benefits identified by Curran and Hussong (2009): built-in replication, increased statistical power, increased sample heterogeneity, increased frequencies of low base-rate behaviors, broader psychometric assessment of constructs, extended period of study, and increased efficiency in time and money. Analysis utilizing IPD may provide an especially good framework for facilitating new discoveries, as well as strengthening research practices, by improving the sample analyzed and by adopting advanced, better analytical approaches that may not have been available before. From the perspective of single studies, this approach may also propel desirable changes in the way individual single studies are conducted in the future. For example, in the field of brief motivational interventions to reduce excessive drinking and related harm among college students, Mun and her colleagues (2015) recommended that single studies be designed and implemented to increase overlap in measures and follow-up assessments across trials, to reduce heterogeneity in intervention groups across trials, and to improve transparency and documentation overall.

Figure 23.2 depicts various analytic approaches to research synthesis in a snapshot. First, at the broadest level, we distinguish methods based on whether IPD is available. In the absence of IPD, one has to rely on AD for quantitative synthesis. For the analysis of AD, one can combine AD across studies using fixed-effects or random-effects meta-analysis models (see the Model-Based Approaches section). One can further analyze between-study variation by using meta-regression, which can reveal study-level moderators of the effect under investigation. Meta-analysis using AD tends to be larger in scale in terms of the number of studies and sample size because collecting and analyzing AD is relatively straightforward and also because there is no need to establish commensurate measures. Effect size estimates provide readily available standardized measures in AD meta-analysis.

Meta-analysis has been on the rise in clinical research. It has had an exponential rise in the number of publications as a publication type in PubMed and also as a method covered in an influential journal, *Statistics in Medicine*, between 1990 and 2006 (Sutton & Higgins, 2008). Similarly, between 1997 and 2012, the papers published in a flagship journal in the field of developmental psychopathology, *Development and Psychopathology*, increasingly either reported findings from a meta-analysis or utilized evidence from a meta-analysis reported elsewhere when generating hypotheses or discussing findings (Figure 23.3).

When IPD is available, meta-analysis using IPD can be conducted. One can closely check and correct data, if necessary, and reanalyze data by using more suitable analytical models for robust inference. IPD meta-analysis has long been championed and discussed as a promising method in the field of medical research synthesis (e.g., Steinberg et al.,

TABLE 23.1 Research Synthesis Methods

Approaches	Notable characteristics	Weaknesses or challenges
Nonempirical research synthesis		
Narrative review of single studies	• Can quickly be conducted • Can draw information from a wide range of studies (e.g., animal models, cross sectional studies, experimental studies) • Vote counting, the process of counting the number of significant and nonsignificant studies, is often used	• May be subject to publication bias and reviewer subjectivity • Variations across studies can become too complex as the number of studies increases • Limitations of single studies cannot be overcome • The results from single studies cannot be quantified using a precise metric • Vote counting is not a valid approach
Empirical research synthesis		
Classical meta-analysis approaches	• Relatively easy to conduct • Essentially fixed-effects model	• Groups or conditions to be compared should be similar across studies • Publication bias remains a threat, which can be countered by conducting an extensive search of the published and unpublished literature
Model-based meta-analysis: Fixed-effects model (using either AD or IPD)	• One common true effect for all studies is assumed • Within-study variability, not between-study variability, is assumed • Between-study heterogeneity may be accommodated by grouping similar studies together and stratifying them or by including covariates • Covariates can be included	• Between-study heterogeneity is not part of the model, which may be an unreasonable assumption • Study-level missing data (i.e., did not assess) can cause difficulty estimating a common model across studies • Inference cannot be generalized beyond the sample of studies analyzed (in terms of sample characteristics and study designs/effects)
Model-based meta-analysis: Random-effects model (using either AD or IPD)	• A distribution of true study-specific effects is assumed • Between-study heterogeneity (i.e., different intervention effects and design/sample characteristics) can be taken into account • Population-based inference can be made • Compared to a fixed-effects model, relatively greater weights are assigned to smaller studies • Compared to a fixed-effects model, this will result in wider confidence intervals around pooled effect estimates • Covariates can be included	• Study-level missing data (i.e., did not assess) can cause difficulty estimating a common model across studies • Relatively a large number of studies are needed. With a few studies, estimates may not be reliable • Can be difficult to characterize the population to which inference is made
Complex research synthesis—multivariate meta-analysis, network meta-analysis, IDA*		
Network meta-analysis (using either AD or IPD but much more promising for IPD)	• When IPD analysis is used, it is widely considered the “gold standard”—efficient, unbiased, and powerful • With IPD, both study-level and participant-level covariates can be included • Particularly useful for research synthesis of randomized controlled trials (RCTs) • Multiple intervention comparisons are possible via direct, indirect, and mixed evidence of intervention effects	• Randomization of groups within studies is needed to derive relative intervention effects • Within-study covariance matrix can be hard to obtain in analysis using AD • Without IPD, ecological inference bias may occur when using study-level covariates • Can be computationally intensive with IPD
Multivariate meta-analysis (using either AD or IPD but much more promising for IPD)	• When IPD analysis is used, it is widely considered the “gold standard”—efficient, unbiased, and powerful • With IPD, both study-level and participant-level covariates can be included • With IPD, analytic models are not limited to those used in single studies; many different statistical models are feasible • Correlated parameters for multiple outcomes, time points, or intervention groups can be estimated	• Randomization of groups within studies is needed to derive relative intervention effects • IPD may not be available for clinical trial data due to privacy concerns • With IPD, data cleaning and checking take considerable time and resources • With IPD, common metrics across studies need to be established to minimize missing data and to interpret individual-level findings • Key study design characteristics may vary, causing study-level missing data • Can be computationally intensive with IPD
Other etiological (longitudinal) IDA**	• Take advantage of existing data sets that are expensive to collect (e.g., fMRI, DNA, or longitudinal data) • Create a pooled data set that has more desirable characteristics than possible from single studies • More advanced and appropriate analysis can be conducted • Used for validation and to quantify an average effect size • Have greater power to detect small effects	• Data dimensions can be exceedingly large • Compiled data can be very sparse due to study-level missing data (e.g., candidate genes not available in some studies) • Common metrics across studies need to be established to minimize missing data and to interpret individual-level findings • Can be computationally intensive • Typically a few studies are analyzed together as a single data set

*AD = Aggregated data; IPD = Individual participant-level data (or individual patient-level data in medical research).

**In principle, IDA investigations of etiological and/or long-term longitudinal studies can use the same analytical methods as those listed under the complex synthesis methods. It is listed separately to highlight the challenges of harmonizing and analyzing extremely high dimensional data.

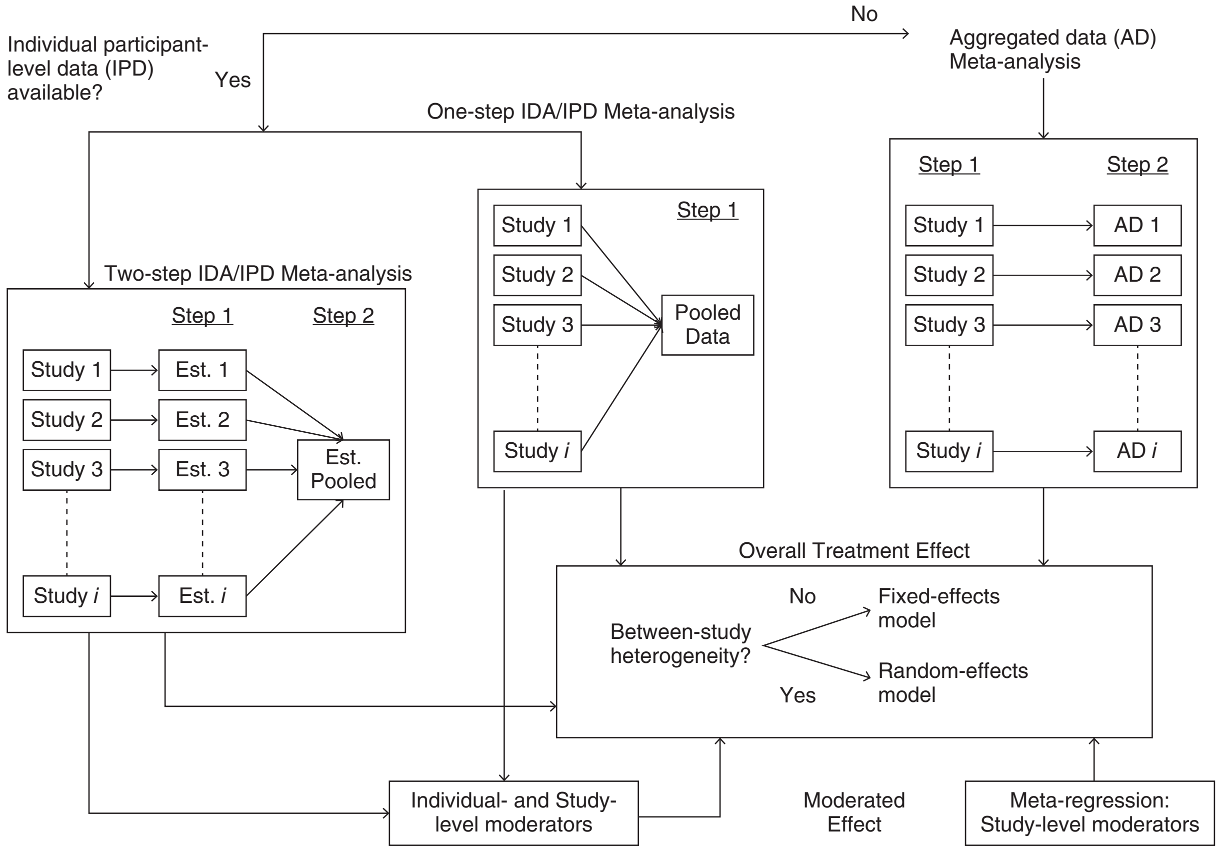


Figure 23.2 Analytical approaches under IDA.

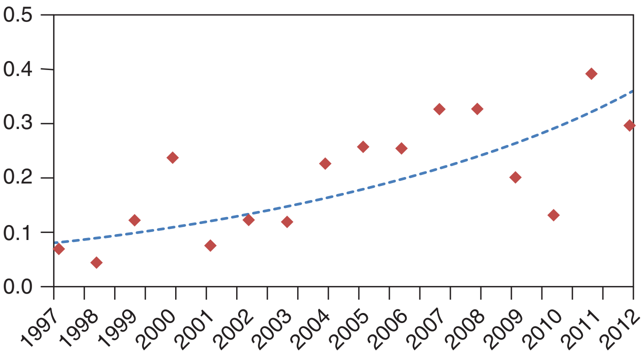


Figure 23.3 Proportion of the articles citing meta-analysis studies published in *Development and Psychopathology* from 1997 to 2012. See footnote 1.

1997; Stewart, 1995) but is a newly emerging approach for psychological research. IPD meta-analysis studies in psychological research have been rare primarily because of the challenge to establish measurement invariance across studies for valid inference. This can be a formidable challenge particularly for psychological measures (Hussong, Curran, & Bauer, 2013). Establishing measurement invariance can be challenging enough even when the same measure is used across key target groups (e.g., different developmental periods or different countries; Steenkamp & Baumgartner, 1998). It can be quite another challenge when different items or measures are used across studies and any overlap in items and measures is tenuous. Once measurement invariance across groups or studies is established, individuals can be placed on common metrics across different groups or studies.

Integrated analysis can then be conducted under various advanced analytical model frameworks (Figure 23.2). IPD meta-analysis can be very attractive in the sense that it can achieve two important goals: (1) strengthening our inference on prespecified (or confirmatory) hypotheses; and (2) giving an opportunity for serendipity, namely exploring new insights from IPD. In relation to the second goal, subgroups or moderated relationships can be examined via analyzing IPD (Borenstein & Higgins, 2013; Brown et al., 2013; Sutton & Higgins, 2008). Moderated effects require large samples to detect when they truly exist. The availability of both individual-level and study-level covariates makes it feasible to formally test these moderated relationships.

Within the IDA framework, one-step analysis is probably more typical, but places a greater burden on IDA researchers to resolve any discrepancies between studies and to deal with missing data as pooled IPD is analyzed in a single analytical model. Alternatively, two-step integrative analysis can proceed as follows: IDA researchers, after harmonizing data across studies (see the Selection of Variables and Harmonization of Groups and Measures section), develop a common analytical model and conduct separate analysis for each study included in the pooled data set. Estimates resulting from separate analyses from the first step can then be pooled across studies in the second integrative step (see the Outcome Analysis section for examples). Relative to the one-step approach, this may more flexibly address design differences across studies when analyzing the combined data. Alternatively, the two-step IDA can be conducted by original investigators under the same analytic strategy instead of sharing original data sets with IDA researchers (Brown et al., 2013). Brown and colleagues called this a *parallel analysis* strategy. Choosing an appropriate method for IPD meta-analysis may depend on several factors, including how easily data can be shared among researchers; how similar and dissimilar studies are in relation to research questions; the number of studies and, more generally, the dimension of the combined data; and how resources and research credits can be shared between research teams. IDA or IPD meta-analysis is a relatively new approach, but its applications are expected to increase in the coming years.

The current chapter will present methods of research synthesis for the field of developmental psychopathology, present classical and emerging meta-analysis approaches, provide data examples, and discuss future directions.

UTILITIES FOR RESEARCH IN DEVELOPMENTAL PSYCHOPATHOLOGY

In a review of the past achievements of developmental psychopathology and its future directions, Cicchetti and Toth (2009) stated that developmental psychopathology as a discipline has long sought to transcend many existing dualisms to better understand the developmental processes involved in maladaptive, as well as competent, trajectories across the life course. In addition to breaking down the schism between normative and nonnormative development, developmental psychopathology as a field has advocated a systems perspective (Ford & Lerner, 1992) and a holistic approach to development (Magnusson, 2000) to better understand complex developmental processes. The dynamic systems perspective and its nonlinear analytic tools, when combined with better known concepts and tools for linear statistical modeling approaches, may help to break the existing knowledge barriers in the literature.

Researchers in the field of developmental psychopathology have been early adopters of advanced analytical methods and led debates about their utilities (e.g., Bergman & Magnusson, 1997; Sterba & Bauer, 2010). Furthermore, researchers have championed the importance of maintaining feedforward and feedback loops between etiological discovery-oriented research and prevention and intervention research, while emphasizing that cultural vistas may affect the developmental processes of those living in them (Cicchetti & Toth, 2009). In essence, developmental psychopathology is a discipline that synthesizes data either directly or indirectly in single studies or multiple studies across multiple systems, across scales, and across time. By doing so, developmental psychopathology transcends the typical boundaries of disciplines in search of new insights and ideas.

We discuss ways in which methods for research synthesis can help shed new light for the field of developmental psychopathology. Some of the application examples in the literature are discussed to highlight the benefits of IDA, as well as the areas for improvement in the future.

Etiology

One of the critical challenges for research in developmental psychopathology is to understand developmental continuity and discontinuity of an underlying problem despite changing or different norms across age, gender, race and ethnicity, and other contexts. Focusing on age-related patterns, specific behaviors can repeatedly be assessed using the same set of questions across age. However, the same behavior observed at different ages may signal different levels or forms of risk. Likewise, different behaviors observed at different ages may indicate the same underlying trait. There are many excellent examples across different research fields. In the field of alcohol research, for example, there is a clear age-related trend in the prevalence of alcohol use prior to, during, and after college years (Substance Abuse and Mental Health Services Administration, 2012), and its associated risks and consequences vary across these distinctive developmental phases (e.g., White, Lee, Mun, & Loeber, 2012). Similarly, the legal drinking age differs across countries (Kuntsche et al., 2013), which affects the meaning of early onset drinking and its associations with other risky behaviors across nations.

The basic understanding of the underlying continuity and discontinuity across developmental phases is needed for screening individuals for intervention and for a better understanding of the etiology of alcohol problems. This issue of the continuity and discontinuity across time has been widely noted as an important research goal in developmental psychopathology (Sroufe & Rutter, 1984). In reality, however, this goal is difficult to achieve in individual studies. The complexity related to age is exacerbated when we consider race and ethnicity, as well as other situational and contextual influences. Single studies are typically limited in terms of demographic, contextual, and other situational influences. When data from multiple studies are combined, however, one can examine age-related continuity and discontinuity across different contexts and evaluate its generalizability.

In one of the early research studies that utilized meta-analysis in developmental psychopathology, Weiss and Garber (2003) examined developmental differences in the manifestation of depressive symptoms by meta-analyzing core, as well as associated, symptoms from 20 studies that varied in age, gender, and source of samples (clinical, diagnosed, normative). A total of 29 symptoms were examined in relation to age by using Cohen's effect size estimate *d* (Cohen, 1988). They found that for the vast majority of symptoms, significant study-to-study (i.e., between-study) heterogeneity in estimates existed, indicating that age-related patterns in symptoms substantially differed across studies. Of the 10 symptoms that were not significantly heterogeneous, the following five symptoms—anhedonia, hopelessness, hypersomnia, weight gain, and social withdrawal—showed higher levels among older individuals, which supported the notion that the specific manifestations of depressive symptoms may vary with development. Due in part to the high percentage of study-level heterogeneity, however, Weiss and Garber concluded the evidence inconclusive to call depression developmentally isomorphic. However, the implicit assumption involved in the meta-analysis under which this question was examined (i.e., a common true effect across studies under fixed-effects models) may have been unnecessarily too strict.

Recent meta-analytic studies tend to focus on explaining between-study variation in effect sizes (between-study heterogeneity) rather than assuming that effect sizes are the same across all studies. In general, it is more plausible to assume that study-specific effect sizes exist across studies, due to observed and unobserved differences in study contexts, designs, outcome measures, interventions, and subjects (Borenstein, Hedges, Higgins, & Rothstein, 2009). When the results from various studies differ, one can use this as an opportunity to investigate factors that may account for the observed heterogeneity across studies by allowing study-level covariates to be included in meta-regression (see the Model-Based Approaches section). When IPD is available, the search for explanations can be done at both the individual- and study-level.

Some studies may combine data from just a few studies. AD meta-analysis starts with an extensive search of all eligible and available evidence. However, three-quarters of meta-analyses indexed in the *Cochrane Database of Systematic Reviews* include five or fewer studies (Davey, Turner, Clarke, & Higgins, 2011). Nonetheless, evidence from two studies is better than evidence from one study, if all else is equal. By pooling original data from multiple sources, even if limited in number, one can extend the period under observation and test hypotheses in a more heterogeneous, diverse sample, which can strengthen our confidence in the derived conclusions. These benefits may be particularly salient for IDA studies that combine data from long-term, longitudinal studies because these studies are virtually impossible to replicate and also because they tend to feature homogeneous samples.

For example, Hussong et al. (2007) obtained original IPD from two longitudinal studies of children of alcoholics (COAs) and combined them to examine externalizing behavior problems in COAs. The two longitudinal studies combined and harmonized were the Michigan Longitudinal Study (MLS; Zucker et al., 2000), a community-based study of alcoholic parents and their young biological children and comparison families within the same neighborhoods, and the Adolescent/Adult Family Development Project (AFDP; Chassin et al., 1991) that followed adolescent COAs and their matched controls as well as their parents. Most cohorts for the MLS were originally between the ages of 3 and 5 and followed up every 3 years thereafter, with yearly assessments between the ages of 11 and 17. The AFDP project interviewed the adolescents when they were between the ages of 11 and 15. They were followed up twice when they were between the ages of 12 and 16 and again between the ages of 13 and 17. The MLS had observations covering mostly from ages 3 to 14, whereas the AFDP had observations spanning from ages 10 to 17. When these two samples were combined, the overlap that existed for ages 10 to 14 provided an important chain in measurement models and the basis to test subsequent, substantive hypotheses. With the two distinctive but similar samples combined, an observational period was stretched from ages 2 to 17 for the entire combined sample. This pooled sample had some of the core characteristics (i.e., COAs and non-COAs) in common, but differed in other aspects (e.g., race/ethnicity, and geographical and socioeconomic backgrounds).

With the combined data described above, Hussong and her colleagues (2007) examined whether (1) the number of alcoholic parents in families; (2) comorbid parental diagnoses (i.e., depression and antisocial personality disorder); and (3) subtypes of parental alcoholism (i.e., controls, depressed alcoholic type, and antisocial alcoholic type) were linked to the development of externalizing behavior problems. They found that children in multialcoholic families were at greater risk for externalizing symptoms that emerged by mid-adolescence. Children in comorbid alcoholic families had a stable early risk for greater externalizing symptoms, compared to those in noncormobid alcoholic families. These observations were internally replicated—meaning that the effect was observed in two samples—within the same analytic model. Thus, in addition to lengthening an observational window and increasing sample heterogeneity, IDA can be used to provide opportunities for built-in, internal replications and for better-powered studies compared with single individual studies (Curran & Hussong, 2009; Hussong et al., 2013).

Infrequently or Rarely Observed Behaviors

Compiling and analyzing data from multiple, similarly designed studies can be particularly beneficial for research in developmental psychopathology when rare behaviors are of particular interest. In typical single studies, a low base rate behavior or atypical behavior is often ignored—neither researched nor reported. However, when isolated or infrequent behaviors of interest are aggregated across multiple studies, this combined information can provide a valuable insight for developmental psychopathology. For clinical trials, it is now required to report adverse effects as one of the basic data for the ClinicalTrials.gov site (Tse, Williams, & Zarin, 2009). Adverse effects can then be compiled across studies and used to assess the overall safety risk of clinical interventions, as well as the efficacy.

In the field of pharmaceutical clinical trials, there has been a high profile case in recent years, demonstrating the importance of infrequently observed behaviors and its treatment in analysis. It involves Avandia (rosiglitazone), marketed by GlaxoSmithKline (GSK), which was intended to improve blood sugar levels in diabetics. Nissen and Wolski (2007) compiled adverse event data from 42 studies and concluded that the drug significantly increased the risk for myocardial infarction (heart attacks). According to Finkelstein and Levin (2012), GSK's stock price dropped 7.8% on the day of the publication of the study by Nissen and Wolski. Thousands of lawsuits were filed against GSK, and in 2010 alone GSK had charges totaling $6.76 billion against earnings to deal with the Avandia cases (Finkelstein & Levin, 2012). Several other subsequent meta-analysis publications ensued that used different approaches (e.g., Liu, Liu, & Xie 2014; Tian et al., 2009) from the one taken by Nissen and Wolski. One of the most contentious issues surrounding this controversy involved the treatment of zero adverse observations in studies. Because the rate of adverse outcomes was low (i.e., approximately 0.5%), it was possible not to see any adverse outcomes in some of the small studies. In typical two-arm (i.e., treatment and control) clinical trials, if adverse outcomes are not observed in both arms, it is difficult to quantify the risk, because the risk is mathematically undefined using well-known risk measures, such as odds ratio. Nissen and Wolski chose to exclude data altogether from any studies with zero adverse observations and used Peto's method of combining odds ratios (Yusuf, Peto, Lewis, Collins, & Sleight, 1985; see the Peto's Odds Ratio section for Peto's method) only from studies with nonzero observations. Subsequent investigations tackled zero adverse observations in original studies by adding a constant, by imputing data, or by using alternative methods by which risk differences could be defined.

We can learn from this Avandia controversy that zero events can be important to report in original studies, and that they can and should be investigated by compiling data from multiple studies. Even if no reasonable statistical approach can be taken, zero events out of 100,000 cases certainly carry a different meaning than zero events out of 1,000 cases. Especially in the field of developmental psychopathology, many behaviors of interest that occur rarely have not been studied extensively. Although rare, these behaviors are nonetheless important to better understand because of their potentially huge impact. For example, using data from a longitudinal project on the development of delinquency and antisocial behavior among boys, Lee and White (2012) reported that those who experienced childhood maltreatment were more likely than those who did not experience it (defined as an officially substantiated record by age 13) to die before the ages 27–32 and ages 34–38, respectively, for two different birth cohorts. More specifically, 7.4% of 202 maltreated men died, whereas 2.5% of 711 nonmaltreated men died. Overall, 35 deaths were observed during the 913 person-year observation period, yielding an average mortality rate of 3,834 deaths per 100,000 person-years (7,426 for maltreated vs. 2,813 for nonmaltreated men). Many individuals followed-up by this project were exposed to violence in childhood and adolescence, and died from, or committed, homicide (see also Loeber et al., 2005). Childhood maltreatment, for this high-risk sample, further increased their risk of early death.

As the example described above shows, rare behavioral data have the potential to provide an important new insight in the field, yet many such behaviors have been understudied. From the analyst's perspective, it also makes sense to combine data from individual studies because low base-rate, binary behaviors (such as death or maltreatment) and their associated binomial confidence intervals can be quite erratic (Brown, Cai, & DasGupta, 2001). When data from multiple studies are combined, the number of cases increases, although average prevalence rate remains the same, which improves the stability of model estimation and reduces the influence of extreme observations, thus achieving better precision.

Even when behaviors of interest may not be as rare as what was previously discussed, many clinical outcomes of interest have generally low base rates. Behaviors with prevalence rates of 10 to 20% are huge numbers at the population level, but can still be difficult to study in single studies. The median and mean total sample sizes for articles published in four major psychological journals (*Journal of Abnormal Psychology, Journal of Applied Psychology, Journal of Experimental Psychology: Human Perception and Performance,* and *Developmental Psychology*) in 2006 were 40 and 196, respectively (Marszalhk, Barber, Kohlhart, & Holmes, 2011). At this level of sample size, a behavior with the prevalence of 5% or less, despite highly prevalent at the population level, would be practically impossible to examine in single studies. Furthermore, some of the advanced analytic approaches for nonnormally distributed data, including Poisson or zero-inflated hurdle mixed models, tend to be more complex and challenging and require many parameters to be estimated (Atkins, Baldwin, Zheng, Gallop, & Neighbors, 2013). Thus, pooling data from multiple, similar studies and analyzing them together for research synthesis can be particularly attractive for many clinical behaviors of interest.

Screening and Diagnostic Tests

It is important to develop screening and diagnostic tests and to derive cut-off scores that are sensitive for detecting true cases (i.e., sensitivity) yet correctly differentiate those cases that, in truth, do not meet the criteria (i.e., specificity). Only a small proportion of individuals typically meet any clinical criteria by definition. Thus, one can achieve better sensitivity and specificity estimates of a screening tool by combining multiple data sets. Both estimates—sensitivity and specificity—are important to simultaneously consider when making informed decisions under which a particular screening tool should be used. This is because these estimates are typically considered in the context of the cost of administering diagnostic or screening tests, and the consequences of missing potential cases and of falsely diagnosing noncases. In addition, these two estimates are *negatively related within studies* because lowering a threshold may enhance sensitivity but increase the likelihood that noncases are falsely identified as meeting the cutoff. As a result, these estimates are also related across studies. Thus, one estimate (either sensitivity or specificity) needs to be considered in the context of the other in the same analysis when pooling data from multiple sources (Reitsma et al., 2005). Failing to do so can lead to misleading or inaccurate conclusions.

One of the recent advances made in the meta-analysis methodological literature involves analysis of multiple, related outcome variables (see Jackson, White, & Thompson, 2010; see the Complex Research Synthesis section). The capacity to examine multiple related outcomes in a meta-analysis framework is an important advance when examining comparative advantages of various tools for diagnostic accuracy. In the field of medical research, Reitsma et al. (2005) reanalyzed data previously reported in a univariate meta-analysis that examined a single combined measure of sensitivity and specificity—the log of the diagnostic odds ratio (DOR; Scheidler, Hricak, Yu, Subak, & Segal, 1997)—using a bivariate meta-analysis. Their reanalysis provided contextualized, richer conclusions than the previous univariate meta-analysis of DOR (Scheidler et al., 1997). More specifically, Scheidler et al. concluded that three screening tools—lymphangiography (LAG), computed tomography (CT), and magnetic resonance imaging (MRI)—performed similarly when diagnosing lymph node metastases in women with cervical cancer. They further suggested that given the invasive nature of the LAG procedure, CT and MRI may be preferable over LAG. When both sensitivity and specificity were jointly estimated as two related outcomes in a bivariate meta-analysis, however, CT and MRI were found to be comparable in terms of sensitivity but LAG was significantly more sensitive than CT (Reitsma et al., 2005). In addition, LAG was lower in specificity compared to either CT or MRI. Thus, even though the three screening tools could not be distinguished in terms of their overall accuracy based on a single combined measure of sensitivity and specificity in the previous univariate meta-analysis (Scheidler et al., 1997), this new bivariate meta-analysis approach provided useful information about the relative accuracy of three different screening tools. Based on the new results, one may suggest that for high-risk individuals, the invasive nature of the LAG procedure be weighed less, in favor of its better sensitivity, when making a decision about which screening tool to use. In contrast, for non-high-risk individuals, the lower specificity of the LAG procedure, which could lead to unnecessary anxiety, combined with its invasive nature, suggest that other screening procedures may be more preferable.

As illustrated in the example of cervical cancer screening tools, there is a value in knowing the unique estimates of both sensitivity and specificity from a clinical perspective when deciding which tools to use for whom. Given the purpose of screening measures, pooling data from independent studies can provide a *needed scale and diversity* in terms of both sample and clinical tool when examining relative advantages and disadvantages. In a way, it can emulate a multisite planned study without the enormous resource required. Similarly for etiological research, pooled data from multiple sources can provide a better sense of how strict or lenient one should be when deriving cutoff scores for positively meeting the diagnostic criteria, as the recommendation based on the finding from a single homogeneous sample may not be ideal for general populations. Screening individuals and reaching accurate diagnoses are the critical initial steps for formulating strategies for prevention and intervention. Therefore, research synthesis through innovative methods holds important promise for the field of developmental psychopathology.

Prevention and Intervention

In the era of evidence-based, health decision-making, central questions become those of *what works* (on the whole), *what works for whom* (subgroups or treatment modifiers), and *how it works* (mechanisms of behavior change). Although individual studies have long attempted to address these questions, there are good reasons to believe that findings from single studies alone may not be sufficient in guiding these evidence-based treatment decisions. First, there is a growing concern about the dismal reproducibility (replicability) in the biomedical and psychological research fields (Begley & Ellis, 2012; see also Ioannidis, 2005; Nosek, Spies, & Motyl, 2012), prompting further high-profile publications illustrating ironies about the *p*-values (Nuzzo, 2014) and calling for better standards for clinical trials (Begley & Ellis, 2012). Second, the effect sizes reported in single, typically small studies may be overestimated (Cumming & Maillardet, 2006; Kraemer, Mintz, Noda, Tinklenberg, & Yesavage, 2006). The magnitude of any intervention effect is important to correctly estimate to determine its cost effectiveness and to develop strategies for dissemination. However, effect size estimates vary widely across studies that differ in designs, measures, and participants; thus, research on the true magnitude of the intervention effect may be necessary via large, controlled multisite studies or meta-analysis studies.

The danger of overly relying on evidence from individual studies can be seen in the case of the efficacy of antidepressants in recent literature. Turner, Matthews, Linardatos, Tell, and Rosenthal (2008) meta-analyzed the data submitted to the Food and Drug Administration (FDA) between 1987 and 2004 (i.e., 74 individual trials for a total of 12 drugs and 12,564 patients), and compared their own findings with the published findings from the same trials. Their reanalyses indicated that effect sizes had been substantially overestimated in published studies (i.e., publication bias; see the Publication Bias and Selection Bias section). On average, Turner and colleagues found a 32% difference in effect size estimates between the FDA data and the published data. Thus, supporting evidence for intervention efficacy in single studies may be best viewed cautiously. Subsequent analysis found that this positive outcome bias was associated with deviations from study protocol, such as switching from an intent-to-treat analysis to a per-protocol analysis (Moreno et al., 2009). Similarly, a recent reanalysis of randomized clinical trial data reported that 35% of the reanalyzed studies required a different interpretation from that of the original article, including changed direction, magnitude, and statistical significance of findings (Ebrahim et al., 2014).

There is another source of bias in our perception of evidence for intervention efficacy. Researchers investigating interventions are more likely to cite previous studies with positive outcomes than equally valid studies with disappointing outcomes; this is referred to as the *optimisim bias* (also referred to as the *citation bias*; Chalmers & Matthews, 2006). This bias, along with the publication bias, can have harmful consequences, such as spending limited resources on less promising trials instead of spending time and resources to develop better interventions.

In the next section, we provide a review of quantitative methodologies that are aimed at synthesizing information from multiple studies. We focus on methods for AD meta-analysis, IPD meta-analysis, and IDA.

RESEARCH SYNTHESIS

The first known use of a meta-analytic method was by Karl Pearson in 1904. Pearson examined the association between inoculation and mortality from typhoid among soldiers who had volunteered for inoculation against typhoid for their deployment in various places across the British Empire (O'Rourke, 2007). It was not until 1976 that the term *meta-analysis* was introduced by Gene Glass as "the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings" and the method took off (O'Rourke, 2007; p. 580). Meta-analysis has caught on in many substantive fields, especially in medicine. For the past two decades, the Cochrane Collaboration (2013, http://www.cochrane.org/about-us) has been a major influence in the field of medical research, conducting over 5,000 systematic reviews that can affect evidence-based health decisions. Recent methodological advances in the field of meta-analysis include methods utilizing IPD and complex meta-analysis methods, such as multivariate meta-analysis and meta-regression. Below we review some of the considerations needed for conducting meta-analysis. We then review classical and model-based approaches to meta-analysis as well as complex research synthesis methods involving IPD or multivariate meta-analysis.

Inclusion Criteria for Studies

One of the first decisions in research synthesis involves which studies should be screened and combined. In meta-analysis, inclusion and exclusion criteria for selecting studies need to be carefully specified to protect against selection bias. There are two stages of screening in a typical meta-analysis. The first stage determines eligibility criteria that are based on the goal of the meta-analysis to ensure that only relevant studies are included. The second stage involves more careful screening and coding of relevant information (Berman & Parker, 2002).

As in any empirical research, research synthesis starts with certain goals that it is intended to meet. Is the study intended to derive average effect sizes of the relationships between emotion regulation strategies and symptoms of psychopathology in observational studies? Or is it to validate findings from a new intervention to general populations? Depending on the answers to these questions, studies to be included or excluded can be decided. For the former objective, it may be reasonable to include both cross sectional and longitudinal studies that are observational or etiological in nature, as well as experimental studies. For the latter question of the efficacy of a new intervention, however, it would be reasonable to eliminate any single studies that are not randomized controlled trials.

As an illustration, there are several meta-analysis or systematic review studies in the field of brief alcohol interventions for college students (Carey, Scott-Sheldon, Carey, & DeMartini, 2007; Carey, Scott-Sheldon, Elliott, Garey, & Carey, 2012; Cronce & Larimer, 2011; Larimer & Cronce, 2007). The review by Cronce and Larimer (2011), which was not quantitative but systematic, was intended to provide a quick overview of recent findings in the field of alcohol interventions for college students. Cronce and Larimer used the following inclusion criteria: studies should (1) report alcohol-focused behavioral outcomes from individual-focused preventive interventions for college students; (2) be published or conducted between 2007 and 2010; and (3) utilize a randomized controlled trial (RCT) or quasi-experimental design (i.e., one active condition and one control or wait-listed, and randomization). Similarly, Carey et al. (2007) included any published studies in their meta-analysis if studies (1) examined any educational, behavioral, or psychological alcohol intervention; (2) sampled college or university students; (3) used an RCT design; (4) assessed drinking behaviors as outcome measures; and (5) provided sufficient information to calculate between-group effect size estimates. These inclusion criteria set the boundaries of the generalizability of subsequent inference. Based on these inclusion criteria, a list of search terms may be developed to cast a wide net during the search phase. A flowchart (e.g., the *P*referred *R*eporting *I*tems for *S*ystematic reviews and *M*eta-*A*nalysis [PRISMA]; Moher, Liberati, Tetzlaff, Altman, & The PRISMA group, 2009) is often provided to show the systematic search and selection process of eligible studies, which looks like a CONSORT flowchart (Schulz, Altman, & Moher, 2010) for an RCT.

The American Psychological Association (APA) Publications and Communications Board Working Group (2008) developed the meta-analysis reporting standards (MARS), which are different from the journal article reporting standards (JARS) for typical empirical articles. The MARS includes specific recommendations for all sections of a meta-analysis. Specifically, for describing search strategies, the MARS recommends that the following information be provided:

- Reference and citation databases searched
- Registries searched and keywords used
- Time period in which studies needed to be conducted
- Other efforts to retrieve all available studies, including listserv queries and personal contacts made
- Method of addressing reports in languages other than English
- Process for determining study eligibility, including aspects of studies examined, number and qualification of judges, and their agreement
- Treatment of unpublished studies

And for coding procedures:

- The number and qualification of coders
- Interrater agreement and how disagreements were resolved
- Assessment of study quality
- How missing data were handled

In the case of IDA investigations of etiological and longitudinal studies, the number of similar studies may be fairly limited. Some of the studies considered for IDA investigations may be ongoing and complex, and data may not be available publicly. In such situations, the availability of the original investigators throughout all phases of IDA may become one of the important considerations. Etiological longitudinal studies focusing on developmental pathways of children of alcoholic parents (e.g., Hussong, Huang, Curran, Chassin, & Zucker, 2010) or twin or genome-wide association studies (GWAS; Schumann et al., 2011) that are geared toward understanding genetic susceptibility in the regulation of alcohol consumption may be such examples.

When original studies are under way at the same time as IDA investigations, an additional set of considerations at the outset of IDA investigations may be especially helpful. Hussong et al. (2013) recommended the following steps when building the supportive team science environment needed for IDA research: (1) decide how the responsibility and resources for data preparation will be divided up between the original study teams and the IDA research team; (2) make clear what the IDA study aims to answer that is different from the aims of original research projects; (3) coordinate research teams across manuscripts within the IDA study and the original study teams; (4) reflect the contributions of researchers in a balanced way when deciding publication credit; and (5) communicate about study differences and reconcile any discrepancies between IDA study findings and original study publications.

An alternative model of collaborations between the original and IDA investigators may be a prospective one. In the field of genetic epidemiology, there is a movement toward establishing collaborative networks of consortia prospectively from the onset of studies with the possibility in mind that their data may be utilized as an input data set for a larger investigation down the road (Ioannidis et al., 2006). In prospective collaborations, some of the critical design elements, such as phenotypes, exposures, end points, and analyses, can be coordinated in advance to be sufficiently similar or the same across studies within consortia (i.e., *networks of single studies*; see also Figure 23.4). This type of prospective collaborations among researchers can lessen the burden of labor-intensive data unpacking (Hussong et al., 2013) needed for typical IDA investigations in the future.

Publication Bias and Selection Bias

When planning a meta-analysis, one needs to consider the potential threat of publication bias. *Publication bias* or *file drawer problem* refers to the selective publication of studies with statistically significant outcomes (e.g., beneficial

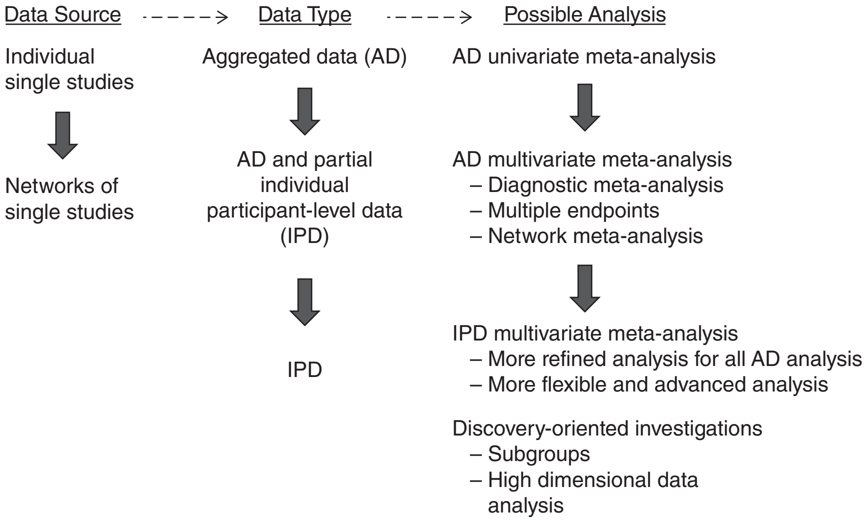

Data Source
Data Type
Possible Analysis
Individual single studies
Networks of single studies
Aggregated data (AD)
AD and partial individual participant-level data (IPD)
IPD
AD univariate meta-analysis
AD multivariate meta-analysis
– Diagnostic meta-analysis
– Multiple endpoints
– Network meta-analysis
IPD multivariate meta-analysis
– More refined analysis for all AD analysis
– More flexible and advanced analysis
Discovery-oriented investigations
– Subgroups
– High dimensional data analysis

Figure 23.4 Current and future directions of research synthesis. Black arrows indicate the emerging directions and dotted arrows indicate the flow of research synthesis from data to analysis. Note that IPD approaches are computationally intensive and may not always be feasible.

intervention effects). The inclusion of unpublished data in meta-analysis may be helpful for avoiding or lessening publication bias. However, some authors have used the inclusion of only published studies to ensure some minimal research standards. As an alternative, individual studies can be scored on a number of items that indicate quality. Summed *quality scores* can then be used when deciding a minimum threshold score for studies to meet to be included or as study weights in a meta-analysis. However, it should be cautioned that quality scores can be calculated in many different ways, which can result in different conclusions (Herbison, Hay-Smith, & Gillespie, 2006), despite sharing common frameworks (Chalmers et al., 1981; Shadish et al., 2002) for assessing the validity of studies.

Publication bias can happen if oversampling of studies with significant findings occurs because they are more easily identifiable or accessible or because they are from colleagues in the same discipline (i.e., citation bias, availability/cost bias, familiarity bias; Borenstein et al., 2009). *Selection bias* can occur when studies are included or omitted for systematic reasons. For example, authors may include certain types of studies in meta-analysis while excluding or missing others selectively, which can result in a biased sample of studies. A recent review of meta-analysis studies published in the American Psychological Association and the Association for Psychological Science journals from 2004 to 2009 indicates that meta-analysis studies that include unpublished studies are just as likely to show evidence of publication bias as those that do not, due to selection bias (Ferguson & Brannick, 2012).

There are several ways to examine publication bias. A *funnel plot* is a graphical approach to examining publication bias. It displays the estimated effect sizes on the x axis and sample size or related measure (e.g., standard error) on the y axis for a sample of studies. It is based on the assumption that smaller studies will exhibit more variable effect sizes due to their lack of precision, and thus the scatter plot should look like a funnel. Figure 23.5 shows examples of a funnel plot. An asymmetrical funnel plot (bottom figure) suggests the presence of publication bias. Several other procedures also exist, such as the trim-and-fill method (Duval & Tweedie, 2000), Begg and Mazumdar's rank correlation test (Begg & Mazumdar, 1994), and Egger's regression asymmetry test (Egger, Smith, Schneider, & Minder, 1997). Nonetheless, the presence of this publication bias is not always examined or adjusted in a meta-analysis. Ferguson and Brannick (2012) found that 30% of the recent meta-analysis studies did not report checking publication bias in their sample of studies.

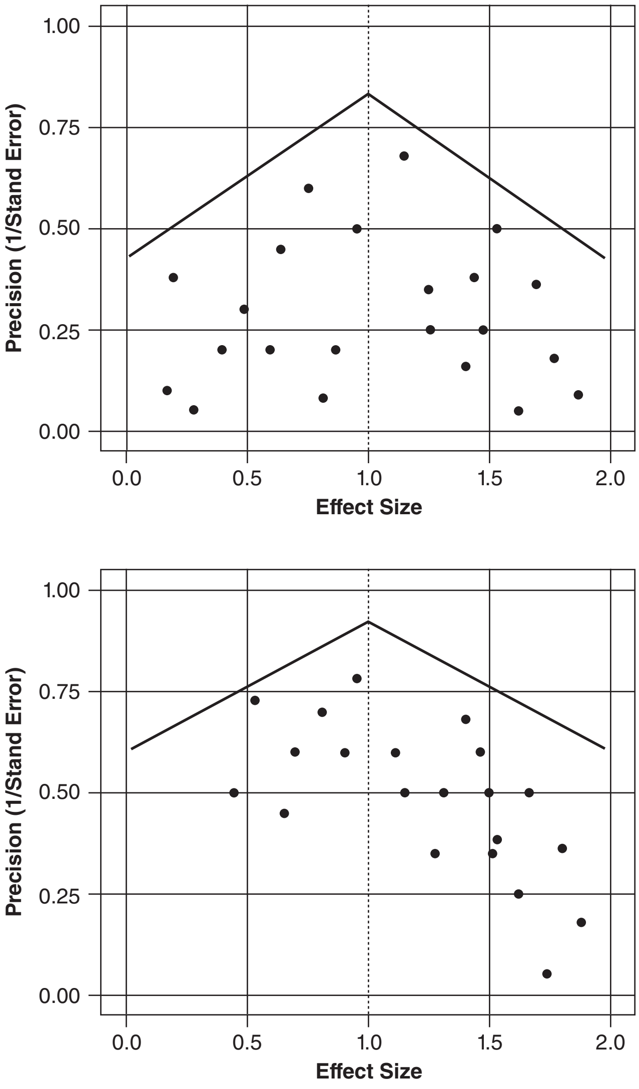


Figure 23.5 Symmetrical (top) and asymmetrical (bottom) funnel plots. The bottom figure shows evidence of publication bias.

Selection of Variables and Harmonization of Groups and Measures

Next, what are the outcomes of interest? For this question, outcome variables need to be operationally defined. In medical research, often an outcome is the occurrence of a certain binary event, such as morbidity (yes–no) and mortality (yes–no) as end points of a disease, and therefore can clearly be defined using a binary indicator. In other situations, a success may be operationally defined based on meeting cutoff scores on some indicator variables. For example, alcohol consumption can be quantified as the alcohol intake per day in grams of pure alcohol (e.g., Roerecke & Rehm, 2012) to examine the relationship between alcohol use and ischemic heart disease (IHD). The average amount of alcohol consumed per day can then be categorized as less than 12 grams (one standard drink) or more than 24 grams (more than two standard drinks).

For psychological traits, however, it is more difficult to place individuals on common metrics (Curran & Hussong, 2009; Huo et al., 2014). Furthermore, the definition of a critical independent variable (e.g., intervention conditions) can be substantially different at the operational level across studies; thus, it must be made equivalent across studies before any synthesis can be conducted. In the IDA study of brief motivational interventions (BMIs) for college students (Mun et al., 2015), for example, we found that some of the intervention and control groups sharing the same labels were not equivalent across studies in terms of their intervention content, personalization, and other procedures. In the case of control groups, they differed, ranging from an assessment-only control group to a treatment-as-usual control group. In some studies, a treatment-as-usual group was closer to an educational group than to an assessment-only control group. We addressed this problem by carefully coding all intervention content materials and their delivery characteristics, which was carried out by two independent expert raters (Ray et al., 2014). Similarly, the operational definition of alcoholic parents can be slightly different across the three longitudinal studies of children of alcoholics included in the Cross Study Project (Hussong et al., 2013). Some of the between-study differences may be accounted for by adding covariates (e.g., COA and COA by study) in subsequent analytic models. When possible, however, it may be best to harmonize groups and derive equivalent measures across studies, prior to analysis, to reduce between-study heterogeneity. More important, any reported findings may be biased without the commensurate measures and groups established across component studies.

As for the selection of variables for outcome analysis, harmonization of measures is typically not required for meta-analysis using AD since the unit of analysis is already standardized. However, this is a serious challenge for IPD meta-analysis or IDA. The need for ensuring commensurate measures across studies is widely discussed as a notable barrier for IDA or meta-analysis using IPD, especially in psychological research (Cooper & Patall, 2009; Curran & Hussong, 2009). As indicated in the literature, the resources needed to establish commensurate measures for individuals within and across studies are quite extensive (Hussong et al., 2013; Mun et al., 2015, for detail). The task of establishing measurement equivalence starts from poring over codebooks and data to see if they are consistent across time within studies as well as across studies. If items are different in terms of the referent time frame, stem, or body of questions, or if response options are different across studies, they should be treated differently until these differences are resolved through harmonization processes. Some of the examples can be seen in Hussong et al. (2013) and Mun et al. (2015).

Once the demanding data preparatory work is completed, one can proceed to analyze measurement models specifically developed to meet the unique needs of each IDA study. In the field of psychological IDA research, item-level data have been analyzed via utilizing item response theory (IRT) based models or factor analysis (FA) based models. These models include a unidimensional, two-parameter logistic (2-PL) IRT analysis (Curran et al., 2008; Hussong et al., 2007), a multi-unidimensional 2-PL IRT analysis for multiple groups (Huo et al., 2014), a generalized partial credit model (Mun et al., 2015) for polytomous items, and longitudinal invariant Rasch test analysis (LIRT; McArdle, Grimm, Hamagami, Bowles, & Meredith, 2009). For other applications, moderated nonlinear factor analysis (MNLFA; Bauer & Hussong, 2009; Curran et al., 2014) has been utilized. Each analytical approach, although the goal of the task remains the same, has originated to address the unique demands of different IDA studies.

The entire process of establishing common metrics across studies, starting from checking data to estimating latent trait scores, can quickly become quite complex as the number of items in studies increases, as the number of studies increases, and as the number of observations or the observed duration increases. Liu, Liu, and Xie (2015) considered a new methodology to synthesize information from independent studies with heterogeneous designs, which may help to lessen the constraint that common design metrics exist across studies. But more research is still needed. Some of the challenging issues that arise from more complex situations include missing data, high dimensionality, and differential item functioning (DIF) (see Mun et al., 2015, for detailed discussion). Other measurement models, adaptations, and computing algorithms are expected to accommodate these challenges in the field of IDA research in the future.

Classical Meta-analysis Approaches

The earliest meta-analysis approaches combine *p*-values, which is particularly suitable for situations under which the only available data in original studies are *p*-values or *z* statistics. There are also a number of classical approaches for synthesizing discrete and, in particular, binary data from independent studies. In this section, we review these approaches.

p-Value Combination

Assume that the *p*-values from original studies test the same null hypothesis. We can use Fisher's method (Fisher, 1948), which can be traced back to the 1930s, to combine the *p*-values and provide an overall inference. Consider the case with *k* studies. Fisher's method combines the *p*-values into a X^2 test statistic using the formula

$$X_{2k}^2 = -2\sum_{i=1}^{k} \ln(p_i) \sim \chi_{2k}^2$$

where p_i is the *p*-value of study *i*. Under the null hypothesis, the test statistic X^2 has a chi-squared distribution with $2k$ degrees of freedom. We often use this combined X^2 test statistic to obtain an overall *p*-value for combined inference. Another closely related approach is Stouffer's *Z* (Stouffer, Suchman, DeVinney, Star, & Williams, 1949). This approach converts *p*-values to *Z* scores first and then combines the resulting *Z* scores. More specifically, we first let

$$Z_i \sim \Phi^{-1}(1 - p_i)$$

where Φ is the standard normal cumulative distribution function. Then, the combined *Z* score

$$Z \sim \frac{\sum_{i=1}^{k} Z_i}{\sqrt{k}}$$

follows a standard normal distribution under the null hypothesis. Other *p*-value combination methods include Tippett's (Min) method, Max method, and Sum method, etc. (Marden, 1991).

Weights can also be applied in *p*-value combination methods to account for different sample sizes across studies and to improve the efficiency of the combination methods. For instance, in Stouffer's *Z* score method, if the *Z* score for study *i* is weighted by w_i, then the combined weighted *Z* score is

$$Z \sim \frac{\sum_{i=1}^{k} w_i Z_i}{\sqrt{\sum_{i=1}^{k} w_i^2}}.$$

Along with the unweighted Stouffer's *Z* score, the weighted *Z* score follows a standard normal distribution under the null hypothesis. Note that Stouffer's *Z* score method, as well as other *p*-value combination methods, can be used also for combining results from multiple independent tests within a single study (see Donovan, Wood, Frayjo, Black, & Surette, 2012, for an example of how this method can be used in applied research).

Combining 2 × 2 Tables

Mantel-Haenszel Method

Many outcomes of interest are binary, discrete event data. There can be many important, naturally binary outcomes, such as mortality or meeting the diagnostic criteria for disorders. Whether an adverse event occurred following a pharmaceutical trial is also one example. Even with continuous numerical data, dichotomizing may be preferable in some situations (Shentu & Xie, 2010) when there are errors in measurement or when obtained data can be naturally fluctuating due to their sensitivity to internal and external stimulation (e.g., blood pressure). Furthermore, dichotomized outcomes can be more straightforward to communicate to various stakeholders (Mun, Bates, & Vaschillo, 2010).

To explain some of the methods for binary data, Table 23.2 shows model setting for 2 × 2 tables for *k* independent studies, where X_i and Y_i follow a binomial distribution with fixed numbers n_i and m_i of binary observations, respectively. We denote $X_1, X_2, \ldots, X_k$ and $Y_1, Y_2, \ldots, Y_k$ as responses for *k* studies following binomial distributions with expectations expressed as p_1 and p_2, respectively; t_i stands for the total number of events for study *i*. For discrete binary data, odds ratio or log odds ratio is often used as an effect size estimate. Some studies also consider other measures, such as risk ratio, risk difference, etc. The goal of a meta-analysis for 2 × 2 tables is to synthesize the overall effect across *k* independent studies.

The Mantel-Haenszel (MH) method (Mantel & Haenszel, 1959) estimates common parameters from 2 × 2 tables under a fixed-effects model, which assumes a common odds

TABLE 23.2 Model Setting of 2 × 2 Tables for *k* Independent Studies

	Event	Nonevent	Total
Treatment	X_i	$n_i - X_i$	n_i
Control	Y_i	$m_i - Y_i$	m_i
Total	t_i	$N_i - t_i$	N_i

ratio across studies (see Table 23.2 for the model setting used). The MH method proceeds:

- Estimate odds ratio and its variance for each individual study:

$$\hat{\pi}_i = \frac{R_i}{S_i} = \frac{\frac{X_i(m_i - Y_i)}{N_i}}{\frac{Y_i(n_i - X_i)}{N_i}} \text{ and}$$

$$\widehat{Var}(\hat{\pi}_i) = \hat{\pi}_i^2 \left(\frac{P_i}{R_i} + \frac{Q_i}{S_i} \right)$$

$$= \hat{\pi}_i^2 \left(\frac{1}{X_i} + \frac{1}{n_i - X_i} + \frac{1}{Y_i} + \frac{1}{m_i - Y_i} \right) \text{ where}$$

$$R_i = \frac{X_i(m_i - Y_i)}{N_i}, \quad S_i = \frac{Y_i(n_i - X_i)}{N_i},$$

$$P_i = \frac{X_i + m_i - Y_i}{N_i}, \text{ and}$$

$$Q_i = \frac{Y_i + n_i - X_i}{N_i}$$

- Estimate the combined odds ratio from k studies:

$$\hat{\pi}_{MH} = \frac{\sum_{i=1}^{k} R_i}{\sum_{i=1}^{k} S_i} = \frac{\sum_{i=1}^{k} \frac{X_i(m_i - Y_i)}{N_i}}{\sum_{i=1}^{k} \frac{Y_i(n_i - X_i)}{N_i}}$$

and

$$\widehat{Var}(\hat{\pi}_{MH}) = \hat{\pi}_{MH}^2 \left[\frac{\sum_{i=1}^{k} P_i R_i}{2\left(\sum_{i=1}^{k} R_i \right)^2} + \frac{\sum_{i=1}^{k} \left(P_i S_i + Q_i R_i \right)}{2\left(\sum_{i=1}^{k} R_i \right)\left(\sum_{i=1}^{k} S_i \right)} + \frac{\sum_{i=1}^{k} Q_i S_i}{2\left(\sum_{i=1}^{k} S_i \right)^2} \right]$$

The MH method provides consistent and asymptotically efficient estimates when study sizes are large or when a large number of small studies are combined (Breslow, 1981). Standard error of estimate can be obtained by using the final previous equation (Robins, Breslow, & Greenland, 1986).

Peto's Odds Ratio

Peto's odds ratio method (Yusuf et al., 1985) is also commonly used for 2 × 2 table data in meta-analysis. Similar to the MH method, it yields a weighted log odds ratio estimate under the fixed-effects model framework (see the Model-Based Approaches section). However, this method is different from the MH method in the sense that, instead of using observed odds ratios, an approximated log odds ratio is calculated for each study and then combined. Hence, it is sometimes known as the Peto's one-step method or the "O–E" method since log odds ratio is estimated by using the observed number of events (O) and the expected number of events (E).

Peto's odds ratio method can be computed as follows:

- Estimate log odds ratio and its variance for study i:

$$\hat{\theta}_i = \frac{O_i - E_i}{V_i}$$

$$\widehat{Var}(\hat{\theta}_i) = \frac{1}{V_i}$$

where $O_i = \mathrm{X}_\mathrm{i}$, $E_i = \frac{t_i n_i}{N_i}$, $V_i = \frac{t_i m_i n_i (N_i - t_i)}{N_i^2 (N_i - 1)}$

- Estimate the combined log odds ratio from all k studies:

$$\hat{\theta}_{Peto} = \frac{\sum_{i=1}^{k} O_i - \sum_{i=1}^{k} E_i}{\sum_{i=1}^{k} V_i}$$

and
$$\widehat{Var}(\hat{\theta}_{Peto}) = \frac{1}{\sum_{i=1}^{k} V_i}$$

For both the MH and Peto's methods, the confidence interval for the estimated log odds ratio can then be obtained by using the previous formula along with z critical value. The Peto's method, as well as the MH method, relies on the combined estimators approximating to a standard normal (z) distribution.

Both the MH and Peto's methods rely on large sample theory to justify the validity of the approaches. There is also an exact meta-analysis method for combining 2 × 2 tables based on Fisher's exact test and conditional likelihood inference (see, e.g., Gart, 1970). For the parameter of risk difference, Tian et al. (2009) proposed a simple procedure to combine confidence intervals of risk difference for 2 × 2 tables without assigning any arbitrary numbers to empty cells in meta-analysis, and reanalyzed the controversial data reported in Nissen and Wolski (2007). For more recent discussions of exact meta-analysis of discrete data, see Liu et al. (2014).

Data Example

To illustrate combining discrete binary data across similar studies, we utilize the intervention data reported in Wilk, Jensen, and Havighurst (1997). Wilk and colleagues examined the effectiveness of brief alcohol interventions targeted for adult heavy drinkers. They searched for brief interventions that were (1) motivational in nature, (2) as short as 10–15 minutes, and (3) aimed to reduce drinking and related harm to treat nondependent heavy or problem drinkers. Two databases, MEDLINE and PsychLIT, were searched with the following, more specific inclusion criteria: (1) focus on alcohol abuse/dependence or heavy drinking; (2) focus on intervention and outcome; (3) human subjects between the ages of 19 and 65; (4) publication in English; and (4) a randomized control trial that includes a control group. The resulting sample consisted of 3,948 heavy drinkers across 12 clinical trials. The brief interventions common to all trials were short, and all sessions included feedback, education, and advice. The intervention outcome was measured by using a binary indicator of moderated alcohol use at 6–12 months post intervention. Of the 12 trials, eight reported outcome data. Table 23.3 shows 2 × 2 tables, observed odds ratios, and their associated confidence intervals (last column) for all eight studies as well as overall estimates from the Peto's one-step method and the MH method (the bottom two rows).

For the purpose of illustration, here we use the 2 × 2 table for the second study (Study 2 in Table 23.3). Moderation in use indicates that participants reduced their heavy drinking, whereas nonmoderation indicates no change in drinking at 6–12 months post intervention. Typically, odds ratio, as a measure of association, is highly skewed and asymmetrical. Thus, log odds ratio and its standard errors are often computed instead for inference. The log odds ratio for Study 2 can be calculated using

$$\text{Log OR}_2 = \log\left(\frac{14/66}{4/70}\right) = \log\left(\frac{14 \times 70}{4 \times 66}\right) = 1.31.$$

Next, we show how to compute the corresponding 95% confidence interval. First, the standard error of the log odds ratio 1.13 is

$$se_2 = \sqrt{\frac{1}{14} + \frac{1}{66} + \frac{1}{4} + \frac{1}{70}} = 0.59.$$

Assuming the log odds ratio is approximately normally distributed, its 95% confidence interval is

$$1.31 \pm 1.96 \times 0.59 = [0.15, 2.47].$$

TABLE 23.3 Pooling Data from 2 × 2 Tables Using the Peto's Odds Ratio and the Mantel-Haenszel Method

Article	Group	Moderation	Nonmoderation	Observed odds ratio	95% CI
			Individual study estimate		
1	Intervention	201	247	2.25	[1.70, 2.97]
	Control	122	337		
2	Intervention	14	66	3.71	[1.16, 11.85[a]]
	Control	4	70		
3	Intervention	9	24	1.09	[0.38, 3.11]
	Control	10	29		
4	Intervention	391	367	1.80	[1.40, 2.33]
	Control	134	227		
5	Intervention	9	50	1.74	[0.44, 6.95]
	Control	3	29		
6	Intervention	22	27	3.26	[1.25, 8.49]
	Control	8	32		
7	Intervention	34	35	2.14	[1.05, 4.34]
	Control	20	44		
8	Intervention	34	102	1.23	[0.60, 2.54]
	Control	13	48		
			Pooled estimate		
Peto's odds ratio				1.95	[1.66, 2.30]
Mantel-Haenszel odds ratio				1.98	[1.67, 2.34]

Source: Wilk et al. (1997).

[a] = the upper limit of this *CI* is different from the text due to rounding.

This log odds ratio can then be converted back to odds ratio as follows:

$$\mathrm{OR}_2 = \exp(\mathrm{Log\ OR}_2) = \exp(1.31) = 3.71.$$

Similarly, the 95% confidence interval for the odds ratio can be obtained by exponentiation of lower and upper limits of the log odds ratio:

$$[\exp(0.15),\ \ \exp(2.47)] = [1.16, 11.82].$$

The MH estimate can be obtained by combining these odds ratios across studies via the combining equation shown previously. The MH odds ratio estimate was 1.98 with its 95% confidence interval ranging from 1.67 to 2.34.

Whereas the MH method combines observed odds ratios only, the Peto's method uses both observed and expected odds ratios (see the Peto's Odds Ratio section). Peto's log odds ratio for Study 2 can be calculated as

$$\begin{aligned}\mathrm{Log\ \ OR}_2^{\mathrm{P}} &= \frac{14 - (14+4) \times (14+66)/(14+66+4+70)}{\mathrm{V}_2}\\ &= 1.16\end{aligned}$$

and its associated standard error

$$\mathrm{V}_2 = \frac{(14+4) \times (4+70) \times (14+66) \times (66+70)}{(14+66+4+70)^2 \times (14+66+4+70-1)} = 4$$

with

$$se_{\mathrm{Log\ OR}_2^{\mathrm{P}}} = \sqrt{\frac{1}{\mathrm{V}_2}} = 0.5.$$

If we convert the Peto's log odds ratio to odds ratio, it becomes 3.19, which is different from the previous observed odds ratio 3.71 obtained using the MH method.

The combined overall odds ratio across all eight studies using the Peto's method was 1.95 with its 95% confidence interval ranging from 1.66 to 2.30. The combined overall estimate is also different from that obtained by using the MH method. However, both estimates suggest we reject the null hypothesis. Based on the size of the overall odds ratio, our interpretation is that those who participated in the brief interventions were almost twice as likely to moderate their drinking compared to controls. The results from both methods are expected to be similar given that the rate (37%) of the outcome (i.e., moderation in drinking in the combined sample) was not too severely low, and also because the two randomized groups were similar in size. In other extreme data situations, the two methods can result in different conclusions. It has been shown that for meta-analysis of rare events (e.g., 1% or less), the Peto's method is the least biased and most powerful method, according to a simulation study that evaluated several methods, including the MH method (Bradburn, Deeks, Berlin, & Russell Localio, 2007). Bradburn et al. also observed that the Peto's method can yield biased results when sample sizes substantially differ between groups (e.g., treatment and control) in 2 × 2 tables, and that it yields worse results than the MH method (conducted without any corrections for zero cells) when the rate of event is not that extreme (5% or 10% as opposed to 1% or less).

Model-Based Approaches

There are at least two major sources of variation to consider when combining statistics (e.g., mean difference) across studies. First, *sampling variability* may vary across studies. Studies with larger samples have more information and hence better precision, which can be indicated in taller and narrower distributions. In contrast, studies with smaller samples have shorter and wider distributions and less precision surrounding their means (Figure 23.6). Second, the statistics of interest can be assumed to have a common value (Figure 23.6) or to have come from an underlying distribution of study-specific values (Figure 23.7). The first source of variation refers to *within-study variability* and the latter addresses *between-study variability*.

Fixed-Effects Model

A fixed-effects model assumes that each study summary statistic, Y_i, is a realization from a population of study

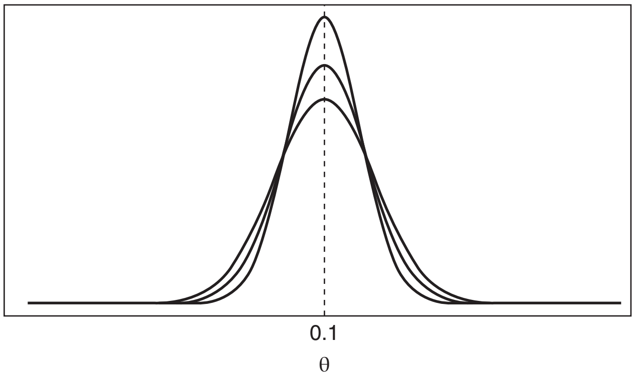


Figure 23.6 A fixed-effects model. It assumes a common underlying mean θ and different variances s_i^2 due to sampling variability for study i. This figure was drawn based on Figure 3 from Normand (1999).

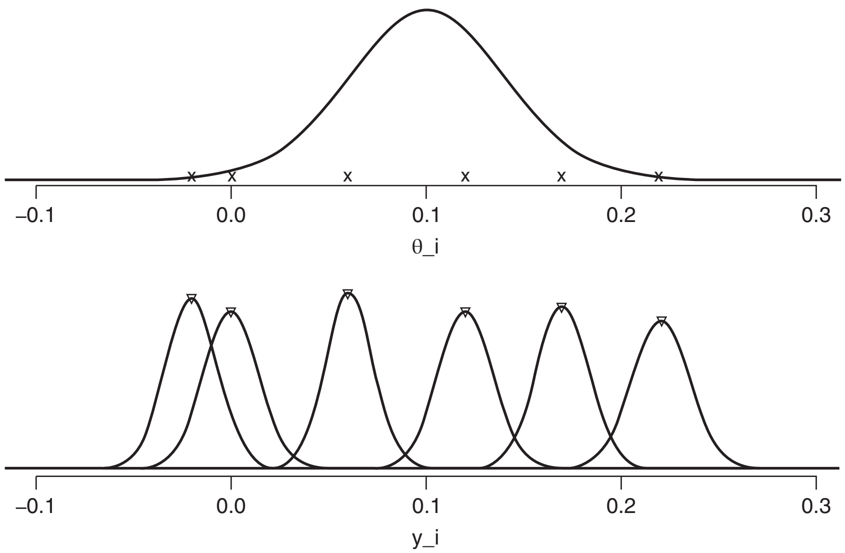


Figure 23.7 A random-effects model. It assumes a superpopulation with a mean θ and a variance τ^2 (top figure) from which distributions with different means θ_i and variances s_i^2 (bottom figure) are drawn. Figure 23.7 was drawn based on Figure 4 from Normand (1999).

estimates with a common true value θ. Let θ be the parameter of interest (e.g., mean intervention effect size) and there are $i = 1,\ 2, ..., k$ independent studies. Then, θ value quantifies the average effect size across k studies, which is assumed to be the same across studies (see Figure 23.6 for a graphic illustration) so that there is no subscript for θ. Variance of summary statistic, Y_i for study i is assumed to be known, which is denoted as s_i^2. This variance estimate can differ across studies and is indicated by subscript i. Within-study variability s_i^2 can be seen as tall and skinny (better precision) vs. short and wide (less precision) distributions in Figure 23.6.

A fixed-effects model usually takes the inverse variances (s_i^2) of the estimates as weights when pooling data. Between-study variability surrounding θ is assumed to be essentially zero or nothing more than what is expected from random errors. This can be more formally expressed as

$$Y_i \sim N(\theta,\ s_i^2) \text{ for } i = 1, 2, \ldots, k.$$

To see if this assumption holds, the test of homogeneity across studies is conducted by using the Q statistic (Cochran, 1950)

$$Q = \sum_i W_i (Y_i - \overline{Y}_w)^2$$

where W_i is the inverse of the sampling variance for study i and $\overline{Y}_W = \sum_i W_i Y_i / \sum_i W_i$ is the weighted estimator of the effect of interest (e.g., estimated mean intervention effect). Under the null hypothesis, Q follows a chi-squared distribution with $k - 1$ degrees of freedom. This test quantifies the extent of heterogeneity by examining the proportion of the total variation in point estimates that can be attributed to heterogeneity across studies. If the Q test is rejected, we can conclude that there exists significant variation across studies due to many reasons, including differences in study designs, procedures, measures, and samples. Note that this Q test suffers from low power (Sutton & Higgins, 2008), and I^2 test (Higgins & Thompson, 2002) may be an alternative. More important, it may be unrealistic and too strict to assume that there is one true common effect size across all studies and that no variability exists surrounding the true effect size (Jackson et al., 2010; Thompson & Pocock, 1991).

Random-Effects Model

A random-effects model assumes that each study summary statistic, Y_i, comes from a study-specific distribution, and that the expectations of these study-specific distributions follow a common distribution. Hence, in addition to within-study variability s_i^2, there is study-to-study variation surrounding the underlying common effect θ, which can be expressed as variance τ^2. The top figure in Figure 23.7 shows the underlying superpopulation with a mean θ and a variance τ^2, from which study-specific true effect size estimates are drawn.

These relationships can be expressed more formally as follows:

$$Y_i \mid \theta_i, s_i^2 \sim N(\theta_i, s_i^2) \text{ and } \theta_i \mid \theta, \tau^2 \sim N(\theta, \tau^2).$$

Hence, the distribution of each study summary measure, Y_i, after averaging over the study-specific effects, is normally distributed with mean θ and variance $s_i^2 + \tau^2$. The distribution of θ_i can be helpful for identifying subgroups of intervention procedures that are more effective. When between-study variability $\tau^2 = 0$, random-effects models reduce to fixed-effects models. Given that between-study variability τ^2 is typically greater than zero, fixed-effects models will almost always have narrower confidence intervals than random-effects models. Likewise, the larger the τ^2, the wider the confidence intervals for the effect of interest. This is because the underlying between-study variation of the effect is incorporated into weights in a random-effects model (DerSimonian & Laird, 1986).

Estimators of Variance

Most commonly used methods for estimating variance are the maximum likelihood estimator (MLE), restricted maximum likelihood (REML), DerSimonian and Laird (DL; DerSimonian & Laird, 1986), method of moments, and Bayesian (see Normand, 1999, for a review of estimators, including equations and detailed discussion). To obtain θ estimates in a model-based model, the MLE and Bayesian methods are used. The REML, DL, and method of moments are used to estimate between-study variance in a random-effects model. Note that both fixed-effects and random-effects models are typically based on the assumption of a normal distribution. Sensitivity to this distributional assumption or to any individual study may need to be examined (Normand, 1999). For example, leaving one study out of analysis in a series of analyses and examining the stability of the estimates across these analyses may be performed as part of sensitivity analysis. However, there may be limited options when a few studies are analyzed.

Fixed-Effects Versus Random-Effects Model

Synthesizing data from sufficiently similar studies that have some variation in measures, samples, and designs has an important benefit in that it provides new understanding about the boundaries of the effect being examined. When the evidence of a significant difference exists across studies based on the Q test of homogeneity, it is often used as the basis for choosing a random-effects model over a fixed-effects model. However, the significant Q test can also be used to imply that at least one study distinctively differs from others in the effect size estimates examined. In a meta-analysis of intervention studies, this may indicate the presence of an important subgroup in which the efficacy of intervention substantially differs from the rest. Thus, pooling these heterogeneous intervention studies into one model may not make sense when estimating the overall intervention effect size. For example, if there are outlier studies with strongly negative intervention effects, it may not be informative to include them with the rest of the studies that have clear positive intervention effects, only to yield no overall effect. Rather, it may be more useful to pool data only from *sufficiently similar* studies. Alternatively, the magnitude of heterogeneity across studies can be reduced by including informative covariates in the model. Covariates can be study-level variables for an AD meta-analysis and individual- and study-level variables for an IPD meta-analysis.

Otherwise, when heterogeneous studies are combined in a fixed-effects meta-analysis model, studies with larger samples can dominate the combined estimate in a meta-analysis, essentially throwing away studies with small samples (Al khalaf, Thalib, & Doi, 2011). Similarly, pooling data from heterogeneous studies in a random-effects model may yield findings that may shift an inverse variance weighted meta-analysis back toward an unweighted mean estimate (Al khalaf et al., 2011).

The decision of which model to use may depend on other practical considerations. When there is a sufficiently large number of similar studies with normally distributed outcome data (i.e., effect size estimates or IPD outcome variable), a random-effects model can be used, in which studies are viewed as a random sample drawn from a superpopulation of studies and, consequently, any resulting inference can be generalized back to this broad population. If there are a limited number of studies, however, one may need to be cautious about using a random-effects model, since in this case the between-study variability τ^2 may not be estimated accurately and the quality of the overall meta-analysis estimator may be affected. In such a situation, a fixed-effects model can be used not to draw broad inference but to obtain specific summary results about the pooled studies (see also Borenstein, Hedges, Higgins, & Rothstein, 2010).

Last, when the number of individual studies is finite, Claggett, Xie, and Tian (2014) proposed an alternative, resampling-based *nonparametric meta-analysis* approach that is more flexible than both random- and fixed-effects models. Note that, in the fixed-effects and random-effects models, we often assume that the underlying study-level parameters are either exactly the same across individual studies and that they are realizations of a random sample from a population (often normal), respectively. In the approach by Claggett et al., one needs to assume only that the study-level parameters are unknown fixed parameters. This approach draws inferences about, for example, the quantiles of the set of parameters using study-specific summary statistics. This nonparametric approach proposed by Claggett et al. is more flexible than the fixed-effects model method, because it allows the underlying study-level parameters to be different across different studies. It is also more flexible than the random-effects model method because it does not need to limit the underlying study-level parameters to be from a normal distribution or any other assumed known distribution, and also because it accommodates any population of the underlying study-level parameters.

Unifying Approach to Synthesize Data from Multiple Studies

Xie, Singh, and Strawderman (2011) proposed a broad, unifying approach to combining data from multiple studies. This approach can encompass all of the procedures reviewed previously, including those from model-based approaches (i.e., fixed-effects and random-effects models using MLE or Bayesian estimator) under one inclusive theoretical umbrella. This approach by Xie et al. is more comprehensive than combining point estimates (e.g., means) or p-values like Stouffer's Z or confidence interval estimates from multiple studies. When combining data, it uses the so-called confidence distribution (CD). CD is a sample-dependent distribution function that can represent confidence intervals of all levels for a parameter of interest. It uses a distribution function, instead of a point (point estimator) or an interval (confidence interval), to estimate a parameter of interest. For example, in the simple normal example with sample $x_i \sim N(\mu, 1)$, for $i = 1, \ldots, n$, the CD approach invokes the distribution function $N(\overline{x},\ 1/n)$ to estimate, instead of estimating just a point estimate, sample mean $\overline{x}$ and 95% confidence interval $(\overline{x} - 1.96/\sqrt{n},\ \overline{x} + 1.96/\sqrt{n})$, for the parameter of interest, μ. Analogous to a Bayesian posterior distribution that contains a wealth of information for Bayesian inference, CD contains rich information for constructing frequentist inference (Xie & Singh, 2013). Unlike a few point estimators or confidence intervals, CD contains information about not only important point estimators—mean, median, and mode—but also confidence intervals of all levels and p-values for various tests. Depending on the set up, the CD approach to combining data can be used to make either *approximate* (i.e., justified based on large sample theory) or *exact inference* for the parameters of interest. The CD combining approach has also been generalized for *robust meta-analysis* that is resistant to errors in data, misspecified models, and outlying or bad studies (Xie et al., 2011). An R package *gmeta* has been developed to combine data using conventional as well as robust meta-analysis approaches (Yang & Xie, 2010).

Complex Research Synthesis

Complex research synthesis, although somewhat arbitrary to define, involves models that (1) incorporate evidence on multiple related parameters (e.g., multiple intervention comparisons or multiple end points—two or more related outcome variables), (2) specifically model data from different study designs (e.g., experimental studies and observational studies), or (3) involve raw IPD (Sutton & Higgins, 2008). In other words, complex research synthesis is a collection of emerging analytical approaches that are aimed at taking full advantage of existing data to respond to research questions not easily addressed in a single individual study or in a typical AD meta-analysis.

Multivariate Meta-analysis

Multivariate meta-analysis generally refers to the joint synthesis of multiple related parameters across studies, which can be found in terms of multiple intervention conditions, covariates, or outcomes, and repeatedly observed single measures. These variables are correlated within studies by their nature and are referred to as the *within-study correlation*. In contrast, the *between-study correlation* indicates how the true estimates are related among studies. A multivariate model takes into account within-study correlations, which allows one to *borrow strength* from other related data and obtain more desirable estimates. Riley (2009) demonstrated in a simulation study that ignoring within-study correlations results in increases in the standard errors of overall effect estimates (precision) and mean-square error (between-study variance), and results in bias when nonignorable missing data exist. The diagnostic application example we discussed in the Screening and Diagnostic Tests section (i.e., Reitsma et al., 2005) utilized a bivariate meta-analysis for the joint estimation of two related estimates (i.e., sensitivity and specificity). The utilities of multivariate meta-analysis, however, extend much beyond diagnostic meta-analysis. Multivariate meta-analysis methods can be utilized for synthesizing treatment effects on multiple related outcomes (also called *multiple end points*), multiple interventions, or exposure groups (also called *network meta-analysis*; see Jackson, Riley, & White, 2011, for a review).

More formally and generally, multivariate meta-analysis can be shown as below. When multiple outcomes are synthesized using the framework of a random-effects model, we typically assume the following multivariate model:

$$\mathrm{Y}_i|\theta_i, \mathrm{S}_i \sim N(\theta_i, S_i)$$
$$\theta_i|\theta, \sum \sim N\left(\theta, \sum\right)$$

where Y_i denote the $p \times 1$ vector of outcomes of interest for study i; θ_i is the true underlying effect for study i; and S_i is the within-study covariance matrix, which is assumed to be known. N denotes the multivariate normal distribution with dimension p. We also assume that θ_i varies from study to study and follows a multivariate normal distribution with overall mean θ and between-study covariance matrix Σ. The estimate $\widehat{\theta}$ can be expressed in terms of $\widehat{\Sigma}$:

$$\widehat{\theta} = \left(\sum_{i=1}^{n}\left(S_i + \widehat{\Sigma}\right)^{-1}\right)^{-1}\left(\sum_{i=1}^{n}\left(S_i + \widehat{\Sigma}\right)^{-1}\mathrm{Y}_i\right)$$

where $\widehat{\Sigma}$ can be obtained by using the MLE, REML, method of moments, or Bayesian method. The estimated variance is

$$\mathrm{Var}(\widehat{\boldsymbol{\theta}}) = \left(\sum_{i=1}^{n}\left(S_i + \widehat{\Sigma}\right)^{-1}\right)^{-1}.$$

If some studies have missing data for the vector of interest, one way of incorporating these studies with missing data in multivariate analysis may be to replace the missing data with estimates with a negligible weight and information. This can be achieved by setting very large within-study variances to the missing data points and by constraining within-study correlations with other end points to be zeros (Jackson et al., 2010). Thus, multivariate meta-analysis methods achieve better efficiency in using all available information than univariate methods.

The idea that multivariate meta-analysis should take into account the correlated nature of data when there are multiple end points is not new, although its utilization has been rare in applied research. Jackson and colleagues (2011) summarized the following five advantages of multivariate meta-analysis over univariate methods: First, we can obtain estimates for all effects in a single modeling framework. A single integrated multivariate meta-analysis is more elegant than multiple univariate ones. Conceptually, it is analogous to conducting a multivariate analysis of variance (MANOVA) as opposed to conducting a series of analysis of variance (ANOVA) when there is a need to analyze multiple related outcomes. Second, we can utilize the relationships among the multiple effects examined when making inferences. For example, in quadratic growth curve models, linear and quadratic growth parameters are often negatively associated and this information can be interpreted and used in a multivariate analysis. Similarly, sensitivity and specificity estimates are negatively associated and this information can be used when jointly estimating the region of significance.

Third, we can obtain parameter estimates with better statistical properties. When we utilize the correlations among related end points in a multivariate analysis, each end point can borrow strength from the other related end points, resulting in smaller standard errors for the overall estimates compared to those from separate univariate models. Moreover, it also results in smaller mean square error of the between-study variance. This gain in estimation is directly related to the within-study correlation. As the within-study correlation increases, we generally obtain better estimates. Fourth, we can make potentially different clinical conclusions, compared to those from multiple univariate meta-analyses. By providing all results in a single multivariate meta-analysis, it is easier to compare the results than it is from different analyses that make different assumptions. Fifth, the multivariate methods have the potential to reduce bias due to partial reporting of data. These advantages apply to both AD and IPD analysis. With IPD, however, the implications of the multivariate meta-analysis methods significantly change. Its promise is very appealing and clear. At the very least, within-study correlations can be directly estimated using IPD. More important, data can be newly and directly analyzed using IPD with advanced analytical models.

Multivariate meta-analysis is particularly well suited for use in prevention and intervention research. Many behavioral outcome measures are highly correlated and typically not fully reported in publications. When multiple related outcome data exist in studies and when they are examined one by one (and separately at each follow-up) or selectively, it raises the possibility of chance findings, especially in studies with small samples (Tversky & Kahneman, 1971). This research practice can lead to misleading conclusions with regard to whether the intervention is efficacious overall. In some situations, investigators may selectively report some outcomes and omit others when publishing, which is a questionable research practice that should be avoided (Bakker, van Dijk, & Wicherts, 2012). Given that the average behavioral intervention effect is generally small, the likely conclusion one can make under this questionable research practice is that an intervention has an effect for some of the outcome variables but not for others.

When it comes to univariate meta-analysis using AD, multiple related outcomes are analyzed separately one by one, which can result in different samples for different analysis because not all studies report or have those outcome measures. As a consequence, each meta-analysis includes only those studies that have the measure being analyzed. Any different conclusions across different outcome measures from univariate meta-analysis methods can be attributed to different studies or samples being included, as well as to different intervention benefits for different outcomes. For a relatively understudied outcome variable, it is also possible to have just a few available studies, which seriously limits our ability to draw any firm conclusions in a typical univariate meta-analysis. Multivariate meta-analysis is a promising new approach, especially when the method is used with IPD. Below, we discuss how the multivariate meta-analysis methods can be used for comparing multiple intervention groups.

Network Meta-analysis

Network meta-analysis refers to synthesis of a network of trials connected by evidence (Jansen et al., 2011). When a multivariate meta-analysis is performed for comparing multiple intervention groups, it can be viewed as a network meta-analysis (Hoaglin et al., 2011; Jansen et al., 2011). This approach enables us to draw conclusions about relative intervention effects of different intervention approaches that have not been compared head-to-head in a trial using a network of direct and indirect evidence (Jansen et al., 2011). It takes advantage of a greater share of available evidence than a traditional meta-analysis of RCTs, which typically features comparing just two arms (i.e., intervention and control). Furthermore, when a new intervention surfaces, it is rarely compared against another, effective intervention approach. As a result, there is a dearth of evidence suggesting relative benefits when attempting to make evidence-based health decisions. Via network meta-analysis, the existing interventions can be contrasted with new ones through connected evidence, even when they were never directly compared.

To know the relative strengths of all available interventions, it may be best to include them in a large-scale study and compare them pairwise to derive estimates of relative intervention effects. However, with limited resources, this is practically impossible to carry out. In the absence of direct head-to-head comparisons of competing interventions, network meta-analysis utilizes networks of direct and indirect comparisons to derive relative intervention effect size estimates between competing interventions. Figure 23.8 illustrates the concepts of direct and indirect evidence. The solid lines between ovals indicate that direct head-to-head intervention comparisons are possible. The dotted lines indicate indirect comparisons are possible. As long as indirect pairwise comparisons can be anchored, indirect comparisons of multiple intervention conditions are possible. For example, head-to-head pairwise comparisons of intervention conditions A and B and A and C are anchored on the common condition A. With A serving as the anchor, relative effects of intervention conditions B versus C can be obtained indirectly (the figure on left). Intervention conditions B and C are connected indirectly through the condition A. This is the essence of an indirect comparison through using an anchor intervention in a network of evidence. The figure on the right shows that both direct and indirect comparisons are possible between intervention conditions B and C. Many more intervention conditions can be compared even though they are not directly compared in any trials. For example, intervention conditions B and D, B and E, C and D, C and E, and D and E are possible due to the anchor intervention A. As more intervention conditions are linked to the existing network, more interventions can be directly and indirectly compared.

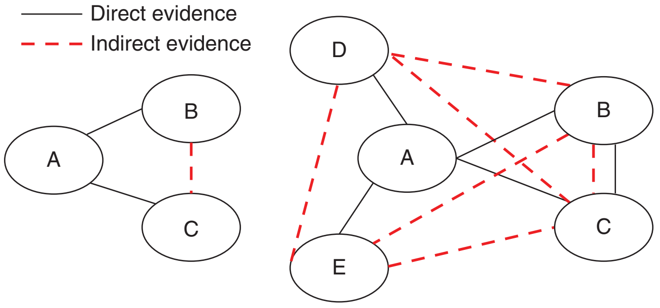


Figure 23.8 Network meta-analysis. The figure on the left shows an example of an indirect comparison between interventions B and C. The figure on the right shows mixed networks of evidence (both direct and indirect) for interventions B and C. Interventions B and C are connected via both solid and dotted lines. See footnote 1.

It is important to note that there are necessary assumptions for network meta-analysis to be valid—similarity and consistency (Jansen et al., 2011). The assumption of similarity necessitates that trials included in relative comparisons should be *sufficiently similar* in terms of participant characteristics, protocols, and measures and that any between-study variation in these characteristics should not systematically modify the intervention effect across studies. The assumption of *consistency* dictates that when both direct and indirect comparisons are possible in a network of connected evidence (Figure 23.8, on the right side), the evidence from direct and indirect comparisons should be consistent. Jansen and colleagues (2011) recommended that network meta-analysis be used when the evidence base consists of more than two RCTs connecting more than two interventions.

IPD Meta-analysis and Integrative Data Analysis

As discussed thus far, IPD meta-analysis or IDA can be conducted to address whether the effect of interest exists across the board and how large the effect is at the population level. When utilized in the context of multivariate meta-analysis for multiple related parameters, IDA or IPD meta-analysis can be a particularly compelling approach because the advantages of multivariate methods can be fully exploited.

At the same time, some cautionary comments about IPD are needed. When IPD is analyzed in a large study, one can achieve much needed precision about point estimates and standard errors. In a small IDA project with a few studies, however, it is difficult to obtain such precision, especially when considerable between-study variability exists. For this reason, there should be a sufficiently large number of studies available for IPD meta-analysis and consequently greater resource, compared to AD meta-analysis (Mun et al., 2015; Steinberg et al., 1997). For any population-based inference, some researchers have suggested that 10–20 studies may be needed for its population representation and validity of parameter estimates (Hussong et al., 2013). In relation to this population based inference, it is also important to communicate how the set of studies included in IDA relates to the body of existing studies in the literature.

In this section, we focus on combining IPD for comparing multiple intervention groups across studies. Whenever there are multiple competing intervention conditions in some of the studies, data are typically combined and analyzed only from the studies that have the target intervention groups, and this analysis is repeated for all intervention pairs. However, the downside of this approach is that the studies being included in each set of analysis can be different, and any effect size estimate cannot be directly compared because uncertainty surrounding the estimates can be due to the different samples analyzed. Furthermore, it is unreasonable to assume that these interventions or multiple outcomes are independent within studies. Thus, comparing intervention conditions separately is an inefficient use of data, and can also lead to misleading and/or biased estimates.

In a multivariate meta-analysis, we can include all conditions across studies as long as they can be linked together by utilizing the correlational structure among these conditions. In the current chapter, we illustrate a new two-stage multivariate meta-analysis for IPD. We use the methodology proposed by Liu et al. (2015) but extend this method for IPD. This analysis proceeds in two stages. At the first stage, the analyst formulates a model to run for each data set based on a substantive conceptual model. This model can be flexibly designed by the analyst based on the research goals and data characteristics of the study. It can be a latent curve model with polynomials, piecewise model, or mixed-effects model. In addition, an intervention effect can be variously defined and derived. It can be derived from a model that includes baseline outcome levels. Alternatively, one can specify an intervention effect on the rate of growth of an outcome behavior. In addition, different distributions of outcome measures can also be accommodated by selecting a model of the appropriate form.

At the second stage, the vectors of estimated coefficients of the selected model across studies are analyzed to obtain the vector of overall estimates and its covariance matrix. For the second step, different estimators for the between-study covariance matrix, such as the MLE or method of moments, can be utilized. If estimates for some of the covariates are not available from the first stage analysis of individual data sets because the covariates were not assessed originally or because estimates were not identifiable (e.g., all participants were men), the coefficients for these covariates for some specific studies would be selectively omitted when estimates are combined at the second stage. For example, if there is a total of five coefficients in the formulated model, three may exist in one study but four in another. It is possible that none of the studies has all five coefficients. The design differences across studies are accommodated by applying appropriate mapping matrices (see Liu et al., 2015 for technical details). This multivariate meta-analysis approach is well suited for IPD because IPD can be analyzed separately for each study using an advanced or complex model and, consequently, resulting coefficients and their within-study covariance matrices can be directly obtained. For a multivariate meta-analysis with AD to be feasible, within-study covariance matrices should be reported in publications in the first place or made available subsequently. However, this IPD approach may not be feasible in some situations. Although there are no restrictions as to the number of coefficients that can be analyzed and combined, it can quickly become challenging as the number of coefficients or studies increases and as sparseness goes up.

To present the method more formally, we first assume that the model to be analyzed at the first stage is

$$y_{ijt} = \beta_i^T x_{ijt} + u_{ij} + \varepsilon_{ijt}$$

where y_{ijt} is the outcome score for participant j at time t in study i, x_{ijt} and β_i are the corresponding design and coefficient vectors, respectively. u_{ij} is the random intercept for participant j in study i, and ε_{ijt} is the residual error term. Each β_i is a subset of the vector β, and its estimate $\widehat{\beta}_i$ and the covariance matrix of $\widehat{\beta}_i$ denoted as $\widehat{\Sigma}_i$, are obtained separately for each study (first stage) and subsequently combined across studies (second stage).

At the second combining stage, we assume a hierarchical model with the form

$$\beta_i | \theta_i, S_i \sim N_{P_i}(\theta_i, S_i);$$
$$\theta_i | \theta, \Sigma \sim N_P(A_i\theta, A_i \Sigma A_i^T)$$

where β_i and θ_i are the observed and true parameter vectors for study i, respectively. S_i is the covariance matrix of θ_i, which is typically assumed to be known. θ and Σ are the population parameters and the corresponding covariance matrix Σ can be estimated by many estimation methods, such as the REML. A_i is the mapping matrix for study i that indicates missing data and maps θ to θ_i. The particular estimation approach utilizes the CD method (see the Unifying Approach to Synthesize Data from Multiple Studies section) and explicitly incorporates the overall structure of missing data into the model through a mapping matrix A_i. If there are no missing data points (i.e., covariates or coefficients), A_i becomes an identity matrix. The CD estimator consequently becomes equivalent to other estimation methods (see Jackson et al., 2011), which is extremely unlikely for any IPD analyses in behavioral and clinical research.

When applying the CD method, the combined estimates of θ and its covariance, denoted as $\widehat{\theta}_E^{(c)}$ and $S_{c,E}$, respectively, have the following forms:

$$\widehat{\theta}_E^{(c)} = \left(\sum_{i=1}^{n} A_i^T \left(S_i + A_i \widehat{\Sigma}_i A_i^T \right)^{-1} A_i \right)^{-1} \times \left(\sum_{i=1}^{n} A_i^T \left(S_i + A_i \widehat{\Sigma}_i A_i^T \right)^{-1} A_i A_i^T \beta_i \right)$$

and

$$S_{c,E} = Var(\widehat{\theta}_E^{(c)}) = \left(\sum_{i=1}^{n} A_i^T \left(S_i + A_i \widehat{\Sigma}_i A_i^T \right)^{-1} A_i \right)^{-1}.$$

These equations are used when combining estimates of θ and its covariance. This multivariate meta-analysis approach for comparing multiple intervention groups using IPD can be seen as a network meta-analysis application when multiple interventions are compared across studies. At the same time, this multivariate approach using IPD is more general and flexible than typical network meta-analysis methods using AD in the sense that the effects combined in the former reflect input from all available data. Furthermore, any data and model can be combined in principle. Thus, this new two-stage approach using IPD is not restricted to what has been reported by primary studies.

It is also important to note that IDA is not limited to a large number of studies. It can be conducted to pool just two or three non-RCT studies into one. When two or more non-RCT studies are pooled into one, the resulting pooled data can still enjoy many advantages of IDA. The pooled data set would be more heterogeneous in terms of samples and study characteristics, be larger in sample size, and have more follow-ups for a longer duration. Overall, combined data from two studies may be better than data from a single study, if the measurement equivalence can be established across the studies being pooled. IDA or IPD meta-analysis, regardless of the nature of its component studies, is highly innovative. Not only does it strengthen causal inference based on existing data, but more importantly it allows testing of a new set of hypotheses and mechanisms of change that may not be feasible to examine in single studies. One possibility for new analyses is to detect moderated effects and explore subgroups, which can be explored in the pooled data of RCTs or non-RCTs.

Subgroups, Moderated Effects, and New Discoveries

IPD meta-analysis or IDA can be useful for understanding subgroups because individual-level, as well as study-level, covariates can be explicitly studied in connection with different intervention effects. Subgroups in this context extend beyond subgroups of individuals to include any meaningful differences that may affect intervention outcomes, such as any differences in intervention protocols and follow-up periods. These investigations are of critical interest in intervention and prevention research, as they suggest clues for mechanisms of behavior change at the individual level. Through the use of IDA, one can conduct new analyses well suited to reveal subgroups for a large pooled sample. IPD analysis can overcome issues of *low power, publication bias,* and *ecological fallacy*.

The power advantage of IPD analysis over single studies or AD analysis is generally well known. Investigations aimed at revealing subgroups require a considerably large sample in original single studies. In comparison with AD analysis, the power to detect these effects by using the summary-level data will often be prohibitively low, and IPD analysis is necessary to detect effects of covariates at the individual level (Sutton & Higgins, 2008). However, with careful considerations, an AD meta-analysis may gain back the power even under heterogeneous designs (Liu et al., 2015).

As for publication bias, single studies lack sufficient power to detect moderated effects. Thus, statistically nonsignificant moderated effects may go unreported in many publications. Furthermore, the analytic approaches chosen for subgroup analysis in single studies vary widely, which makes it even more difficult to combine effect sizes across individual studies in AD meta-analysis. More important, there is an issue of interpretation. This applies to the relative advantage of IPD over AD. When study-level covariates are used to explain any differences in the effects of interest, this can lead to invalid statistical conclusions.

Meta-regression (via using AD; Figure 23.2) requires careful interpretation, as it is more prone to ecological bias than analysis using IPD. *Ecological fallacy* or *ecological bias* occurs when conclusions are made about the mechanism at the lower-level data (e.g., individual participants) based on the higher-level data (e.g., study-level information). For example, in the field of college alcohol intervention research, some of the studies comprise all men or all women. If gender is included as a study-level moderator of the treatment effect in a meta-regression analysis, which is then confounded with study membership, the resulting conclusion may be subject to ecological bias. Thus, IPD meta-analysis is better suited than single studies and AD meta-analysis when examining subgroups (Brown et al., 2013; Simmonds & Higgins, 2007).

Of course, IPD analysis has other advantages, such as the capabilities to check the quality of data and reanalyze data using more appropriate approaches (Curran & Hussong, 2009; Sutton, Kendrick, & Coupland, 2008). For these reasons, IPD meta-analysis is widely considered as the "gold standard" in the statistical literature (Lin & Zeng, 2010; Sutton & Higgins, 2008). At the same time, it has been echoed by many that such analyses require much more time and efforts to carry out (Cooper & Patall, 2009; Mun et al., 2015; Steinberg et al., 1997; Sutton et al., 2008).

The advantages of IDA need to be understood in the context of challenges. IDA requires the availability of data and subsequent contacts with original investigators who have conducted relevant studies. Other challenges include the need for harmonizing groups and measures across studies. These challenges go up when the number of studies increases because the number of variations to be harmonized across studies goes up along with the number of studies (see Mun et al., 2015, for some examples). In addition, as the number of studies goes up, overall percentage of missing data at the study level (i.e., did not assess or could not be harmonized) may become prohibitively huge when individual data sets are combined for a single-step integrated analysis. When one of the goals of IDA is to fully utilize available data in analysis, missing data can cause great difficulties for IDA studies throughout all stages of analysis.

Table 23.1 provides an overview of various methods discussed in this chapter. Figures 23.1, 23.2, and 23.4 graphically summarize the relationships among the source of data, type of data being pooled, analytic methods, and approaches to the univariate and multivariate methods. Figure 23.4 shows emerging directions in the field of research synthesis. Namely, future innovations may be obtained by prospectively coordinating and designing single studies as part of research networks, then channeling IPD from these sources for innovative multivariate analysis, and maximally utilizing all available data for more robust inference and new discoveries. Next, we illustrate two data examples from an IDA research project that pooled data from multiple alcohol intervention studies for college students.

DATA EXAMPLES

In the field of college alcohol intervention research, brief motivational interventions (BMIs) have received empirical support for reducing excessive alcohol use and related problems among college students at least on a short-term basis (Carey et al., 2007; Cronce & Larimer, 2011). However, there are several outstanding questions, including inconsistent intervention effects within and between studies, as well as the small intervention effect sizes reported in the literature. Furthermore, the mechanisms of behavior change remain sketchy. Project INTEGRATE (Mun et al., 2015) was a response to address these outstanding questions. More specific goals were to examine (1) whether BMIs are efficacious for bringing about changes in theory-based behavior targets, such as normative perceptions about peer alcohol use and the use of protective behavioral strategies while drinking; (2) whether positive changes in behavior targets predict greater reductions in alcohol use and negative consequences; (3) whether subsets of interventions are more promising; and (4) whether subgroups of individuals exist for whom different interventions are more efficacious.

Pooled Data

To compile data from BMIs, we contacted individual investigators in spring 2009 who had published data on BMIs. All but one agreed to share their data. In the case of the single exception, there was an ongoing project within the research team that had similar research goals. There was also a snowballing recruitment of other investigators. The unpublished data by these investigators were also compiled. Unlike a typical meta-analysis project, we did not systematically search databases or launch an exhaustive search of all eligible studies. Thus, the sample of studies we have is a convenience sample that is nonetheless broadly representative of the existing intervention studies conducted between 1990 and 2009 (published between 1998 and 2010). The combined data set was diverse in terms of original investigators, college campuses from which participants were recruited, demographic characteristics, and intervention study designs (Table 23.4; see also Mun et al., 2015).

Sample

Data were pooled from 24 independent studies (Studies 1–7, Studies 8a, 8b, and 8c, and Studies 9–22; see Table 23.4), resulting in a combined data set consisting of 12,630 participants (42% men; 58% first-year or incoming students) who were assessed two or more times from baseline up to 12 months. The majority of the sample is White (74%), with 12% Asian, 7% Hispanic, 2% Black, and 5% belonging to other or mixed ethnic groups. Approximately 15% are college students mandated to complete a university program (e.g., a BMI or educational program) as a result of alcohol-related infractions; 27% are members (or pledged to be a member) of fraternities and sororities; and 13% are varsity athletes or members of club sports. The majority of the individual studies included in Project INTEGRATE have been previously described in the published literature (see Mun et al., 2015, for more information).

Intervention Groups and Procedures

All studies included one or more BMI conditions, with the majority (21 studies) including either a control condition or other comparison condition (i.e., alcohol education). Across studies, some groups with the same intervention label were different; and several other groups with different intervention labels were actually similar when examined at the operational level. To determine which groups are equivalent to and different from others, we developed a quite detailed coding procedure to go over all published and unpublished intervention materials and quantitatively code their content and characteristics. Two content experts coded independently and any discrepancies were discussed in detail, at first between them and, if necessary, with the rest of the research team (see Ray et al., 2014 for details). We consequently relabeled intervention groups based on their intervention characteristics and content.

Newly labeled five intervention groups for Project INTEGRATE were Motivational Interview plus Personalized Feedback (MI + PF), stand-alone Personalized Feedback (PF), Group Motivational Interview (GMI), Alcohol Education (AE), and Control. There were also several unique conditions that did not fit these categories, including an MI + PF condition combined with an alcohol expectancy challenge, an MI without PF, and an MI + PF condition combined with a parent-based intervention. Participant recruitment and selection also varied across studies, ranging from volunteer students recruited with flyers to students who were required to complete an alcohol program because they violated university rules about alcohol.

In a preplanned, large multisite RCT, intervention conditions or groups can be perfectly balanced as in a factorial design, which is practically not feasible for IDA studies. For Project INTEGRATE, five intervention conditions sparsely existed across 24 studies. Table 23.5 shows the unbalanced nature of the intervention conditions in terms of their number and type for a subset of studies that were utilized in the current chapter. Studies 9 and 13/14 had all four groups (GMI excluded), but all other studies had two or three groups. Some of the studies did not have a control group (Studies 1 and 3), and only three studies had an Alcohol Education group. If these groups were to be analyzed simultaneously in one-step IDA using typical analytic approaches, it is likely that missing conditions would create estimation difficulties in analysis.

Measures

We now describe how measures were harmonized and how latent traits were estimated across studies for two of the measures used in the outcome analysis. See also Huo et al. (2014) for technical detail and Mun et al. (2015) for an accessible overview of the measurement approach taken for Project INTEGRATE.

Measures: Protective Behavioral Strategies

Protective behavioral strategies refer to specific cognitive behavioral strategies that can be employed to reduce risky drinking and limit harm from drinking (Martens et al., 2004). We identified five major questionnaires used to assess protective behavioral strategies: the 10-item Protective Behavioral Strategies (PBS) measure taken from the

TABLE 23.4 Project INTEGRATE: Study Designs (Adapted from Mun et al., 2015)*

Study	Representative reference	Intervention	First year (%)	Men (%)	White (%)	*N*	*N* at follow-up				
							1 mo.	2 mo.	3–4 mo.	6 mo.	9-12 mo.
Mandated college students											
1	White, Mun, Pugh, and Morgan (2007)	MI + PF, PF	62	60	73	348	--	--	319	--	219
2	White, Mun, and Morgan (2008)	PF, Control	63	71	69	230	--	199	--	106[1]	--
3	Barnett, Murphy, Colby, and Monti (2007)	MI + PF, AE	67	49	66	225	--	--	206	--	211
4	Cimini et al. (2009)	GMI, AE,[a] AE[a]	49	62	80	682	--	--	--	471	430
5	LaBrie, Lamb, Pedersen, and Quinlan (2006)	GMI	71	60	74	167	158	148	139	125	--
6	LaBrie, Thompson, Huchting, Lac, and Buckley (2007)	GMI	49	0	58	115	110	110	110	--	--
7.1	Fromme and Corbin (2004)	GMI,[b] Control	58	76	75	124	106	--	--	61[2]	--
Volunteer college students											
7.2	Fromme and Corbin (2004)	GMI[b], Control	38	59	59	452	332	--	--	221	--
8a	Larimer et al. (2007)	PF, Control	40	35	86	1, 486	--	--	--	--	1, 122
8b	Larimer et al. (2007)	PF, Control	37	41	64	2, 155	--	--	--	--	1, 618
8c	Larimer et al. (2007)	PF, Control	22	34	83	600	--	--	--	--	304
Volunteer first-year or incoming college students											
10.2	Baer, Kivlahan, Blume, McKnight, and Marlatt (2001)	Control	100	41	78	87	--	--	--	--	81
11	Walters, Vader, and Harris (2007)	PF, Control	100	59	64	383	--	272	288	--	--
15	LaBrie, Huchting, et al. (2008)	GMI, Control	100	0	56	263	261	260	258	--	--
16	LaBrie et al. (2009)	GMI, Control	100	0	57	287	282	277	268	250	--
17	LaBrie, Pedersen, Lamb, and Quinlan (2007)	GMI	100	100	65	120	110	105	90	56	--
22	Wood et al. (2010)	MI + PF, MI + PF + PBI,[c] Control	100	43	87	758	--	--	--	--	687
Volunteer heavy drinking college students											
9	Lee, Kaysen, Neighbor, Kilmer, and Larimer (2009)	MI + PF, PF, AE, GMI, GMI,[a] Control	100	38	71	604	--	--	504	485	--
10.1	Baer et al. (2001)	MI + PF, Control	100	46	84	348	--	--	--	--	322
12	Wood et al. (2007)	MI + PF, AE,[a,c] MI + PF + AE,[a,c] Control	4	47	91	335	276	--	257	258	--
13	Murphy, Benson, and Vuchinich (2004)	MI + PF, PF	13	32	94	54	--	--	--	51	--
14	Murphy et al. (2001)	MI + PF, AE, Control	41	46	94	84	--	--	79	--	79
21	Walters, Vader, Harris, Field, and Jouriles (2009); Walters, Vader, Harris, and Jouriles (2009)	MI + PF, PF, MI without PF[c], Control	41	35	84	288	--	--	261	252	251
Intercollegiate student athletes or fraternity, sorority, and service organization members											
18	Martens, Kilmer, Beck, and Zamboanga (2010)	PF, PF,[a] Control	32	26	85	329	289	--	--	259	--
19	LaBrie, Hummer, Neighbors, and Pedersen (2008)	GMI,[a] Control[a]	19	31	67	1, 178	966	922	--	--	--
20	Larimer et al. (2001)	MI + PF, Control	78	52	84	928	--	--	--	--	631

*N = 12,630. Studies are numbered arbitrarily. MI + PF = Motivational Interview plus Personalized Feedback; PF = Stand-alone Personalized Feedback; GMI = Group Motivational Interview; AE = Alcohol Education; PBI = Parent-based Intervention.

[a]= These groups are quite unique despite having the same label as others without the superscript;

[b]= GMI in Study 7 provided personalized feedback, whereas other GMIs did not;

[c]= These groups represent unique intervention conditions not found in any other studies included in Project INTEGRATE.

[1] The control group (n = 119) for Study 2 received feedback at 2 months post baseline and thus their follow-up data at 6 months post baseline were excluded;

[2] Mandated students who were in the control group (n = 24) in Study 7.1 received GMI at 1 month post baseline and their follow-up data at 6 month post baseline were excluded. "--" indicates that follow-up was not administered. Follow-up sample sizes were based on selective alcohol use measures and could differ from those reported in published articles.

TABLE 23.5 Project INTEGRATE: Intervention Groups Across Studies After Removing Ineligible Studies for the Multivariate Meta-analysis Data Example

	1	2	3	8a	8b	8c	9	10	11	12	13/14	18	20	21	22
MI + PF*	X	--	X	--	--	--	X	X	--	X	X	--	X	X	X
PF	X	X	--	X	X	X	X	--	X	--	X	X	--	X	--
Alcohol Education	--	--	X	--	--	--	X	--	--	--	X	--	--	--	--
Control	--	X	--	X	X	X	X	X	X	X	X	X	X	X	X

*MI + PF = Motivational Interview plus Personalized Feedback; PF = Stand-alone Personalized Feedback. "--" indicates the intervention groups are missing by design.

National College Health Assessment survey (American College Health Association, 2001); the 15-item Protective Behavioral Strategies Scale (PBSS; Martens et al., 2005); the 37-item Self Control Strategies Questionnaire (SCSQ; Werch & Gorman, 1988); a seven-item Drinking Restraint Strategies (DRS) scale used in Wood, Capone, Laforge, Erickson, and Brand (2007); and a nine-item Drinking Strategies (DS) scale reported in Wood et al. (2010). The PBS was assessed by Studies 1, 2, 8a, 8b, 8c, and 9; the PBSS was assessed in Studies 4, 16, 18, and 21; the SCSQ by Study 3; the DRS by Studies 12 and 22; and the DS by Study 22. In these studies, items were assessed in Likert-type scales. Note that many items were similar in wording. Given that slightly differently worded items can be responded differently by responders, we initially treated them as different items. In addition, we limited item-level data only for those who reported recent drinking (i.e., past 1 to 3 months) due to the nature of the construct.

Of the compiled pool of items, items indicating abstinence from drinking (two items; *cut back on drinking* and *choose not to drink alcohol*) or manner of drinking (one item; *drink shots of liquor*) were dropped, as they do not conceptually fit the definition of protective behavioral strategies. Study 3 included an additional 16 items related to protective behavioral strategies, which were dropped from the pool because they were assessed only in Study 3 and could not be linked to any other items across studies. Study 7 assessed protective, as well as risky, behaviors (a total of 17 items) as a set of behaviors that one can engage during drinking, such as "leaving drinks unattended" or "drank lower alcohol content beverage." Participants were asked to provide the total number of times that they participated in such activities in the past month (possible values ranging from 0 to 99). Their response patterns were very different from those of other studies measured on a Likert-type scale and difficult to harmonize reasonably. We thus decided not to include these items in the pool.

A total of 58 protective behavioral strategy items assessed by 13 studies (Studies 1–4, 8a–8c, 9, 12, 16, 18, 21, and 22) were then analyzed using item response theory (IRT) analysis. Different questionnaires had different stem questions leading to specific items. Some of the major variations were as follows:

- The following set of questions asks about your drinking behavior. Please indicate how often you did the following . . . " (PBS)
- Please indicate the degree to which you engage in the following behaviors when using alcohol or "partying" . . . (PBSS)
- How often did you use each of these strategies to deliberately limit your drinking? (SCSQ)
- Do you deliberately try to . . . (DRS)
- How often do you . . . (DS)

We assumed that these stem questions did not make a difference. Of the remaining 58 items, 20 were combined into five individual items because they were very similarly worded. Examples of similarly worded questions were "avoid drinking games," "avoid or limit your participation in drinking games to drink less," and "avoid playing 'drinking games.'" Collapsing such similarly worded items may not be ideal, as participants can respond differently to slightly differently worded items or different leading (stem) questions. However, to be able to link items across studies, we made an assumption that these similarly worded items were essentially the same in eliciting responses. Many pooled items were similar, as they had been adopted or modified from other existing questionnaires included in the pool of items. If we were to take the strictest route and treat all items as different, one consequence would be to analyze only those few studies that administered exactly the same questionnaire for exactly the same time frame using exactly the same response options. For example, the PBS was administered in six studies and the PBSS was administered in four studies. If these data sets were analyzed separately, it would be difficult to draw any direct comparisons between the two sets of analyses.

In general, there is a trade-off between item coverage across studies and quality of information when harmonizing measures. The coverage of items will be greater when we accept slightly imperfect items as commensurate across studies. However, the coverage will suffer if slight variations are not tolerated across studies. This decisional balance may have to be determined individually depending on the research questions, available data, and subsequent analytic methods (to see examples in which harmonization may not be reasonable, see Mun et al., 2015).

Our subsequent analysis did not involve comparing intervention cases and control cases across studies (called *breaking randomization* or *naïve comparison*). We compared intervention cases against their own controls within studies, before their relative differences were pooled across studies. Thus, we made an assumption that this item linkage we established would not yield biased results. In situations where naïve comparisons are made, however, one cannot assume that even the same item has the same item function across studies. In other words, when participants in one study are combined with participants in another study without the nested data structure taken into consideration, item functions may differ across studies, which may result in biased inference. In such situations, DIF tests across studies and appropriate follow-up actions may be needed to demonstrate measurement equivalence across studies.

Response options were harmonized and recoded to indicate 0 = never; 1 = rarely, seldom, occasionally, or sometimes; 2 = often or usually; and 3 = always. Response options rarely, seldom, occasionally, and sometimes were originally assessed as different categories but were combined into one because endorsement rates were relatively low for these categories. Also, for protective behavioral strategies, answers in either extreme (i.e., never or always) and adjacent steps from the extremes are more important than any difference that exists in the middle of the scale (e.g., rarely vs. seldom or occasionally vs. sometimes).

A total of 43 items (38 unique and five collapsed items) were then analyzed, specifying a single, underlying dimension of protective behavioral strategies. Because we deemed it important to distinguish *often* from *always*, we used a generalized partial credit model (GPCM; Muraki, 1992) to assign partial credit for polytomous items (for more detailed explanations of the GPCM parameters, see Mun et al., 2015). We developed Markov chain Monte Carlo (MCMC) algorithms to fit several IRT models, including the GPCM model, within a hierarchical Bayesian framework. Huo et al. (2014) provided the theoretical and technical details of the IRT models and MCMC algorithms, which were written in Ox (Doornik, 2009).

Measures: Alcohol-Related Problems–Neglecting Responsibilities

Alcohol-related problems is one of the critical outcome measures and our measurement approach for this construct is described in greater detail elsewhere (see Huo et al., 2014; Mun et al., 2015). Briefly, individual items and items from well-known questionnaires for alcohol-related problems were identified from each study and compiled in a separate data set. These items mostly came from the Rutgers Alcohol Problem Index (RAPI; White & Labouvie, 1989), the Young Adult Alcohol Problems Screening Test (YAAPST; Hurlbut & Sher, 1992), the Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ; Kahler, Strong, & Read, 2005), the Alcohol Use Disorders Identification Test (AUDIT; Saunders, Aasland, Babor, De La Fuente, & Grant, 1993), the Positive and Negative Consequences Experienced questionnaire (PNCE; D'Amico & Fromme, 1997), and the Alcohol Dependence Scale (ADS; Skinner & Allen, 1982; Skinner & Horn, 1984). For each item, responses were dichotomized to indicate 1 = Yes; 0 = No, because this response format was the common denominator across studies. When someone did not drink during the time frame referenced, the score was recoded as zero.

We utilized both a unidimensional IRT model and a four-dimension IRT model for alcohol-related problems for Project INTEGRATE. In the former, a single overall, severity latent trait is assumed to give rise to item responses. In the latter, four distinct but related latent trait dimensions give rise to item responses within their dimensions, which were Neglecting responsibilities, Interpersonal difficulties, Dependence-like symptoms, and Acute heavy-drinking, respectively. Estimated correlations among the four dimensions exceeded 0.8, which indicates that these dimensions are highly correlated but still distinct. Both IRT models showed acceptable fit and parameter estimates were similar between the two models. In the current chapter, we focus on a single dimension of alcohol-related problems obtained from the four-dimensional IRT model–Neglecting responsibilities (NR) as an example in the Outcome Analysis section. Some of the example items for this dimension were "Got into trouble at work or school because of drinking" and "Missed a day (or part of a day) of school or work."

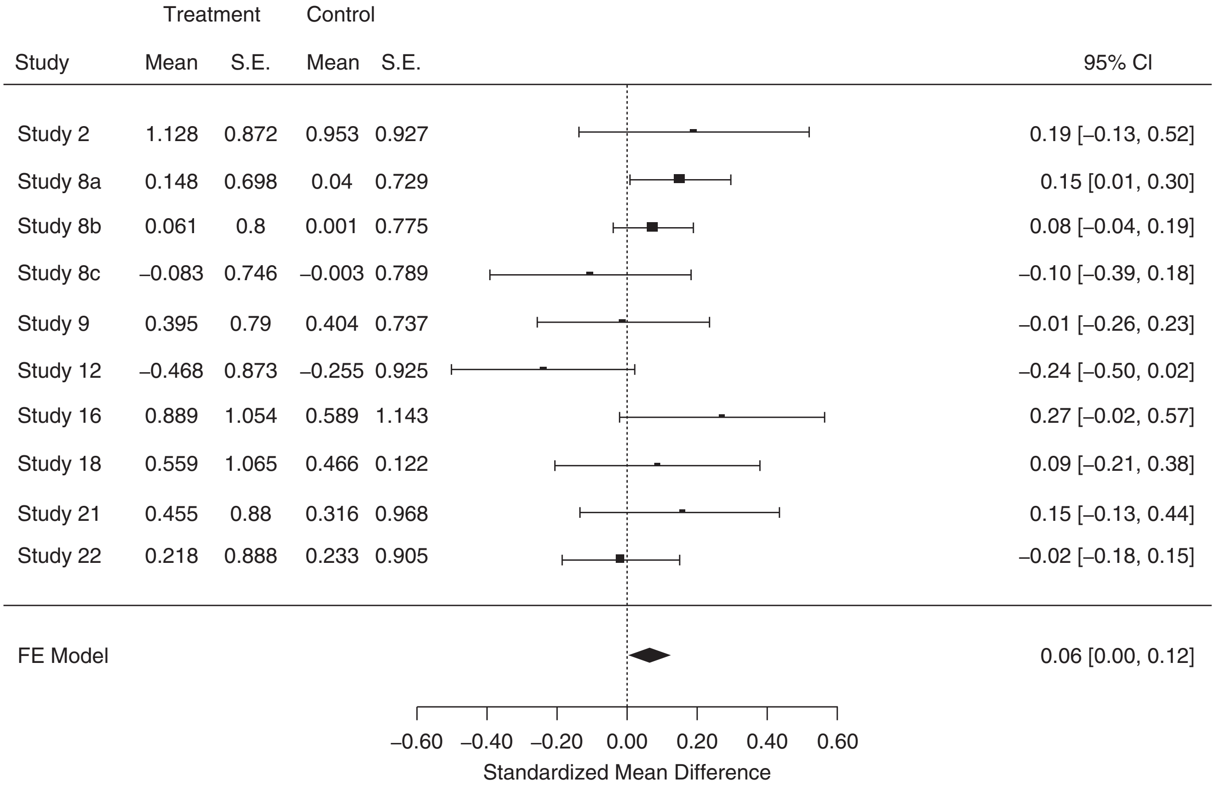
Outcome Analysis

For outcome analysis, we provide data examples for model-based meta-analysis and multivariate meta-analysis (network meta-analysis) using data for latent trait scores for protective behavioral strategies (henceforth referred to as PBS) and neglecting responsibilities (henceforth referred to as NR), respectively. For the first data example, we utilized both fixed-effects and random-effects models to examine whether college students who were assigned to a brief alcohol intervention utilized protective behavioral strategies more often their counterpart controls at the first, immediate follow-up. Protective behavioral strategies are increasingly seen as an important behavioral target of alcohol intervention efforts for college students. For the second example, we demonstrated how multiple intervention arms could be combined across studies and analyzed in a single combined, multivariate analysis using the CD approach.

Model-Based Meta-analysis

For model-based meta-analysis, we used PBS data. Of the 13 studies (Studies 1–4, 8a–8c, 9, 12, 16, 18, 21, and 22) that assessed PBS, we excluded three studies due to the lack of an equivalent control group (Studies 1, 3, and 4). Studies 9 and 21 had multiple intervention arms and we combined them into one intervention group (i.e., MI + PF, PF, and Alcohol Education were combined for Study 9; MI + PF and PF were combined for Study 21). Thus, we had a two-arm design (one intervention and one control) for a total of 10 studies, and examined their PBS data at their first follow-up. The first follow-up assessment occurred within 1–3 months for Studies 2, 9, 12, 16, 18, and 21; 9 months for Study 22; and 12 months for Studies 8a, 8b, and 8c.

Results indicated that there was no significant between-study heterogeneity, Q (df = 9) = 12.03, p = 0.21. The statistical conclusion from either a fixed-effects or a random-effects model was the same. That is, there were no significant differences between the intervention and control groups in terms of their tendency to utilize PBS at the first follow-up. The overall mean difference in PBS latent traits between the two groups was 0.05 under the fixed-effect model. The 95% confidence interval [–0.002 to 0.102] included 0. The random-effects model estimated the overall mean difference to be 0.05 and had the slightly larger 95% confidence interval [–0.008 to 0.104] to account for between-study variability, although in the present case there was no statistically significant, between-study variability in the mean differences in PBS scores. Figure 23.9 shows the results from the fixed-effects model in a forest plot. At the individual study level, only Study 8a showed a statistically significant, favorable outcome for the intervention group, compared to control.



	Treatment		Control		
Study	Mean	S.E.	Mean	S.E.	95% CI
Study 2	1.128	0.872	0.953	0.927	0.19 [–0.13, 0.52]
Study 8a	0.148	0.698	0.04	0.729	0.15 [0.01, 0.30]
Study 8b	0.061	0.8	0.001	0.775	0.08 [–0.04, 0.19]
Study 8c	–0.083	0.746	–0.003	0.789	–0.10 [–0.39, 0.18]
Study 9	0.395	0.79	0.404	0.737	–0.01 [–0.26, 0.23]
Study 12	–0.468	0.873	–0.255	0.925	–0.24 [–0.50, 0.02]
Study 16	0.889	1.054	0.589	1.143	0.27 [–0.02, 0.57]
Study 18	0.559	1.065	0.466	0.122	0.09 [–0.21, 0.38]
Study 21	0.455	0.88	0.316	0.968	0.15 [–0.13, 0.44]
Study 22	0.218	0.888	0.233	0.905	–0.02 [–0.18, 0.15]
FE Model					0.06 [0.00, 0.12]

Figure 23.9 Protective behavioral strategies at the first follow-up under the fixed-effects model for 10 studies.

Although there was no statistically significant, between-study variability in estimates, the nonsignificant Q statistic should not literally be interpreted as evidence to indicate that the effect sizes are consistent across studies, since such nonsignificance can be due to lack of power. With a small number of studies or large within-study variances in individual studies, even substantial between-study dispersion might yield a nonsignificant Q statistic (Borenstein et al., 2009). In the forest plot shown in Figure 23.9, we had narrow confidence intervals (small within-study variances) in large studies, such as Studies 8a and 8b, but in many other studies with small samples (e.g., Studies 16 and 18), the within-study variances and associated confidence intervals were large. In addition to the highly discrepant sample sizes (Table 23.4), studies varied in terms of their follow-up periods and sample characteristics, and also the interventions implemented. For example, the eligibility criteria for participation in Study 12 (Wood et al., 2007) were geared toward enrolling high-risk heavy drinkers: (1) 14 or more drinks per week for men and 10 per week for women; (2) at least one episode of heavy drinking in the past 30 days; and (3) endorsement of at least two alcohol-related consequences in the past year. Although Wood et al. excluded and referred the students who reported more than 40 drinks per week or exhibited moderate to severe dependence to the university counseling center, this sample placed on the extreme end of risk for excessive and problematic drinking, relative to other study samples (see Huh et al., 2015, for alcohol use data across studies). Furthermore, this sample was estimated to have the lowest levels of PBS at baseline across all 10 studies (Figure 23.10). For these reasons, when we excluded data from Study 12, the results from the remaining nine studies indicated a favorable outcome for the intervention group at follow-up; overall mean difference = 0.08, with 95% confidence interval ranging from 0.01 to 0.15 (Figure 23.11).

The point about this subsequent analysis without Study 12 is not to draw a conclusion that the intervention was efficacious for increasing the utilization of PBS, which was not the case for the pooled sample of 10 studies, but to suggest that the intervention's role in the utilization of PBS may differ depending on the levels of alcohol use and their PBS utilization at baseline. To test this hypothesis, however, a further investigation is required that incorporates individual-level covariates in the model. Without examining the individual level data, drawing any conclusion based on study-level data (like the one that we tentatively discussed here) may be subject to ecological fallacy, and lead to inaccurate inference about how changes occur following an intervention.

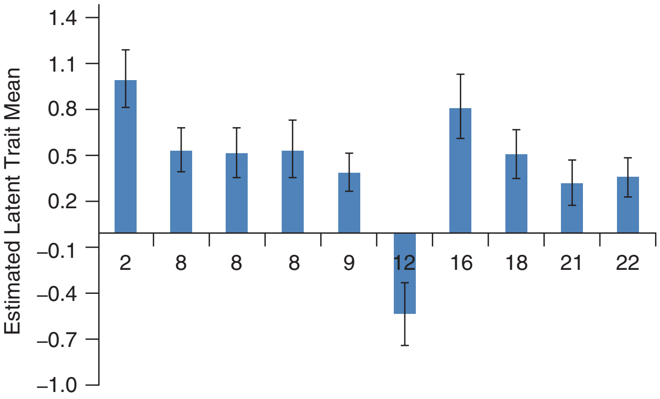
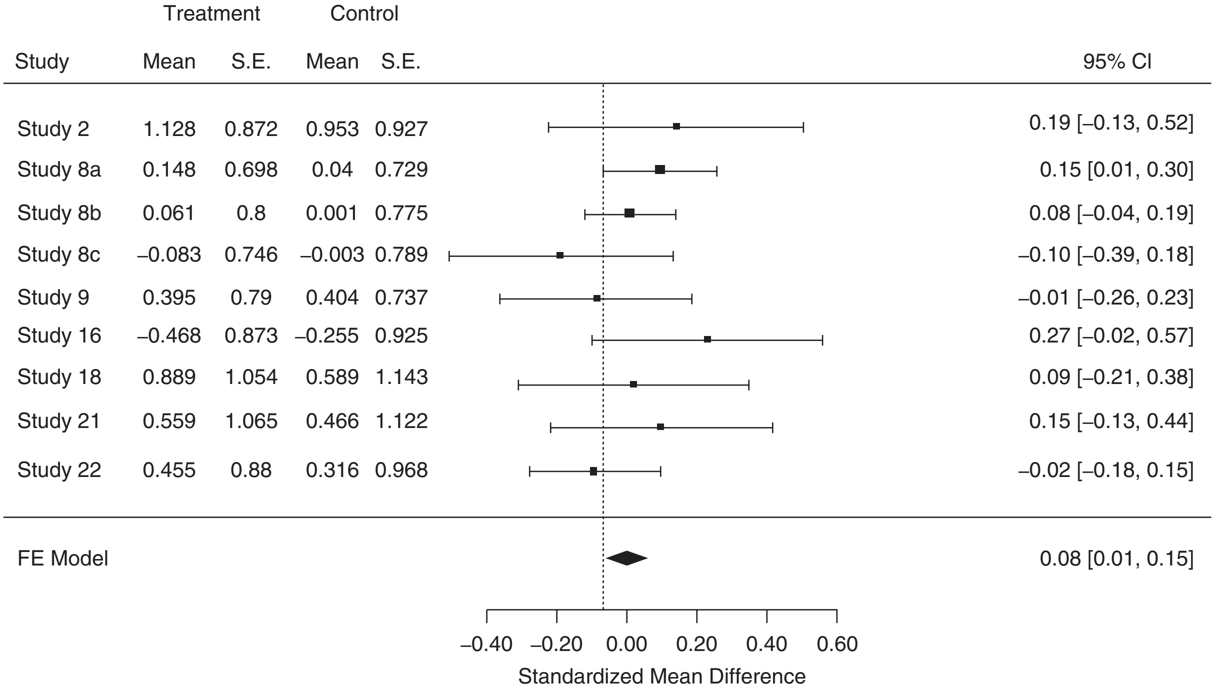


Figure 23.10 PBS latent trait means across studies estimated from the GPCM analysis. The second, third, and fourth bars indicate data from Studies 8a, 8b, and 8c, respectively. The error bars indicate two times standard errors in each direction. Participants in Studies 2 and 16 were estimated to utilize PBS more often than students in other studies. Study 12 was an outlying study—Participants in Study 12 were least likely to utilize PBS. See footnote 1.

Multivariate Meta-analysis

For multivariate meta-analysis, we used the new two-stage approach for IPD described previously. We had the following inclusion criteria for studies: at least two intervention arms existed and participants were randomly assigned to these groups (Studies 5, 6, and 17 excluded); and the intervention utilized should not be unique (Studies 4, 7, and 19 excluded). Studies 15 and 16 were further excluded because they were exclusively for first-year female students, which represented a missing data problem (due to no variability) for two covariates (first-year student and gender) and posed a difficulty at the second stage of combining estimates. In addition, the latter two studies were small in sample size, were conducted on the same college campus by the same investigators, and utilized the same intervention (i.e., GMI). Due to the elimination of other GMI studies, these two studies became unique in the pooled data set. Of the studies that met the inclusion criteria, we further removed some conditions (e.g., alcohol expectancy challenge, parent-based intervention, or MI without PF) because they were deemed sufficiently different from other intervention conditions and/or were unique to specific studies and could not be linked to other studies. Studies 13 and 14 were combined into one study for the purpose of analysis. Study 13 included an MI + PF intervention and a stand-alone PF intervention, and Study 14 included an MI + PF intervention and an assessment-only control group. In-person MIs combined with PF in both studies were, by and large, identical (i.e., high risk samples, same PF design,



	Treatment		Control		
Study	Mean	S.E.	Mean	S.E.	95% CI
Study 2	1.128	0.872	0.953	0.927	0.19 [–0.13, 0.52]
Study 8a	0.148	0.698	0.04	0.729	0.15 [0.01, 0.30]
Study 8b	0.061	0.8	0.001	0.775	0.08 [–0.04, 0.19]
Study 8c	–0.083	0.746	–0.003	0.789	–0.10 [–0.39, 0.18]
Study 9	0.395	0.79	0.404	0.737	–0.01 [–0.26, 0.23]
Study 16	–0.468	0.873	–0.255	0.925	0.27 [–0.02, 0.57]
Study 18	0.889	1.054	0.589	1.143	0.09 [–0.21, 0.38]
Study 21	0.559	1.065	0.466	1.122	0.15 [–0.13, 0.44]
Study 22	0.455	0.88	0.316	0.968	–0.02 [–0.18, 0.15]
FE Model					0.08 [0.01, 0.15]

Figure 23.11 PBS at the first follow-up under the fixed-effects model for nine studies (Study 12 removed).

led by the same investigators, and on the same campus), and there were no baseline differences across these two groups. In addition, these two studies had very small samples. Thus, we collapsed these two studies into one combined study (i.e., Study 13/14), allowing an MI + PF group and a PF to be contrasted with a control condition.

Table 23.5 shows that only a subset of studies provides information for direct, head-to-head comparisons of intervention groups. For example, for a head-to-head, direct comparison between MI + PF and PF, data from Studies 1, 9, 13/14, and 21 can be analyzed. For a comparison between MI + PF and Alcohol Education, data from Studies 3, 9, and 13/14 can be utilized. For a comparison between MI + PF and control, Studies 9, 10, 12, 13/14, 20, 21, and 22 can be analyzed. However, for these potential subset analyses, eligible studies would be different, and the number of studies to be analyzed would be much smaller than the entire sample of eligible studies. This would be an inefficient use of available data and could also create inconsistent findings due to different data sets being analyzed for different comparisons. Furthermore, this subsetting strategy does not accommodate the fact that some of the intervention conditions are from the same studies and are hence related. Multivariate meta-analysis overcomes these data characteristics by taking advantage of all available information from all studies.

We first fit a random intercept growth model using NR latent trait scores as an outcome variable separately for each study. The regression model included a total of 15 covariate terms (Table 23.6). Alcohol outcomes following an intervention among college students typically show a pattern of an immediate decline followed by a rebound (e.g., Mun, White, & Morgan, 2009). Thus, we modeled the outcome over time by using a quadratic growth model (month post intervention as a time variable). We included three covariates to control for their differences in alcohol-related problems—being male, White, and first-year student. In addition, we included PBS scores at baseline as a covariate because it was related to dropout at follow-ups in some of the studies. To test intervention effects, we added interaction terms between each of the growth parameters (i.e., linear and quadratic growth slopes) and each of the three intervention groups (i.e., MI + PF, PF, and Alcohol Education). Naturally, three variables to contrast the three intervention groups against control were also included in the model. Note that the actual model for each study was different due to missing covariates at the study level. For example, if a study did not assess PBS, the model had a total of 14 covariates for that study (e.g., Study 13/14 in Table 23.6). Similarly, for studies that had just one follow-up, any coefficients involving a quadratic growth parameter could not be estimated. The

TABLE 23.6 Patterns of Covariates by Study for IPD Multivariate Meta-analysis*

Study	1	2	3	8a	8b	8c	9	10	11	12	13/14	18	20	21	22
Man vs. woman	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
White vs. non-White	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
First-year vs. other	X	X	X	X	X	X	--	--	--	X	X	X	X	X	--
PBS at baseline	X	X	X	X	X	X	X	--	--	X	--	X	--	X	X
Control**	--	X	--	X	X	X	X	X	X	X	X	X	X	X	X
Alcohol Education	--	--	X	--	--	--	X	--	--	--	X	--	--	--	--
PF	X	X	--	X	X	X	X	--	X	--	X	X	--	X	--
MI + PF	X	--	X	--	--	--	X	X	--	X	X	--	X	X	X
Linear slope (LS)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Quadratic slope (LS)	X	--	X	--	--	--	X	--	X	X	X	X	--	X	--
LS * Control**	--	X	--	X	X	X	X	X	X	X	X	X	X	X	X
LS * Alcohol Education	--	--	X	--	--	--	X	--	--	--	X	--	--	--	--
LS * PF	X	X	--	X	X	X	X	--	X	--	X	X	--	X	--
LS * MI + PF	X	--	X	--	--	--	X	X	--	X	X	--	X	X	X
QS * Control**	--	--	--	--	--	--	X	--	X	X	X	X	--	X	--
QS * Alcohol Education	--	--	X	--	--	--	X	--	--	--	X	--	--	--	--
QS * PF	X	--	--	--	--	--	X	--	X	--	X	X	--	X	--
QS * MI + PF	X	--	X	--	--	--	X	--	--	X	X	--	--	X	--

*"--" indicates missing by design. These include variables not assessed by study (PBS); the entire sample consisted of first-year students only (Studies 9, 10, and 11); particular intervention groups were not employed; and only one follow-up assessment available during the 12-month period, and thus their quadratic slope parameter in change could not be estimated.

**= in actual models, this group becomes a referent group for the three other intervention groups, and is not counted in the number of covariates included in the model.

overall pattern of covariates analyzed for each study is shown in Table 23.6.

The growth model was analyzed separately for each of the 15 studies (13/14 was analyzed as one study) in the first stage of the analysis using IPD. In the second stage, a vector of the estimates of regression coefficients and its covariance matrix were retrieved for each study and subsequently combined with the estimates from other studies using the formulas and the REML estimation approach shown in the IPD Meta-analysis and Integrative Data Analysis section.

The multivariate meta-analysis method utilized for this data example combines multiple estimates from multiple studies simultaneously and borrows information, when information is missing, from other studies by incorporating their correlations. This approach differs from existing multivariate meta-analysis approaches utilizing AD. This approach also differs from those combining single or bivariate estimates from multiple studies in the sense that what is integrated across studies is the entire model specified at the first stage of the multivariate meta-analysis. This IPD multivariate meta-analysis approach utilizes more data than any other existing approaches to meta-analysis. The combined model from the second stage can be interpreted and utilized for subsequent investigations.

Table 23.7 shows the IPD multivariate meta-analysis results from the combined model. With the effects of other covariates adjusted, Alcohol Education had higher levels of NR problems compared to control, reflecting their baseline difference (Figures 23.12–23.14) that was maintained throughout the follow-up period. In-person MI combined with PF (MI + PF) or PF did not differ from control. For the efficacy of these interventions, we focused on the interaction terms between growth parameters and intervention conditions. There was a statistically significant interaction effect on NR problems between the linear slope

TABLE 23.7 Parameter Estimates from IPD Multivariate Meta-analysis*

	Estimate	*SE*	*p*
Intercept	–0.907	0.150	0.000
Man (1; 0 = Woman)	0.008	0.047	0.865
White (1; 0 = Non-White)	0.045	0.034	0.182
First-year (1; 0 = Other)	0.055	0.030	0.070
PBS at baseline	–0.240	0.032	0.000
Linear slope (LS)	–0.034	0.012	0.007
Quadratic slope (QS)	0.002	0.002	0.185
Alcohol Education (vs. Control)	0.216	0.081	0.007
PF (vs. Control)	–0.011	0.031	0.733
MI + PF (vs. Control)	0.035	0.044	0.427
LS × Alcohol Education	0.010	0.026	0.684
LS × PF	0.007	0.004	0.088
LS × MI + PF	**–0.030**	**0.010**	**0.002**
QS × Alcohol Education	0.000	0.002	0.905
QS × PF	–0.001	0.001	0.552
QS × MI + PF	**0.001**	**0.001**	**0.349**

**SE* = Standard Error. PBS = Protective Behavioral Strategies. MI + PF = Motivational Interview plus Personalized Feedback. PF = Stand-alone Personalized Feedback. The efficacy of the MI + PF can be seen in Figure 23.14.

of growth and MI + PF. The interaction term between the quadratic growth parameter and MI + PF was not statistically significant. These two terms are highlighted in bold in Table 23.7 because it is impossible to evaluate any growth trends or growth-related effects in a compartmentalized, piecewise manner. In a typical growth curve model, for those whose initial levels are high, their subsequent growth trends tend to be subdued. It would be misleading to focus on one growth parameter without considering the other as the first-order polynomial term (linear) is dominated by the second-order term (quadratic) in growth models.

Thus, to demonstrate this intervention effect as a whole, we estimated the NR trait levels at two important follow-up periods—6 months and 12 months post intervention—by plugging the meta-analyzed regression coefficients into the model and calculating the estimated scores for the intervention groups. For some studies, this resulted in extrapolated estimates and for others, these were actual estimates based on observed follow-up data (Figures 23.12–23.14). Note that confidence intervals (and error bars) in Figures 23.12–23.14 were calculated by using different formulas depending on the focus of the comparisons (within-group vs. between-group). In estimation, we used the following values for covariates: male = 1, first-year = 1, White = 1, and PBS = average value. Negative NR scores were due to anchoring (of a group in IRT analysis) and shorter bars indicate more severe problems for the present data in Figure 23.12.

Since first-year students tended to have more severe problems and those with greater PBS had lower levels of problems, depending on the covariates of interest, these bar graphs could be adjusted a little lower (or longer; i.e., less serious problems) for non-first-year students and

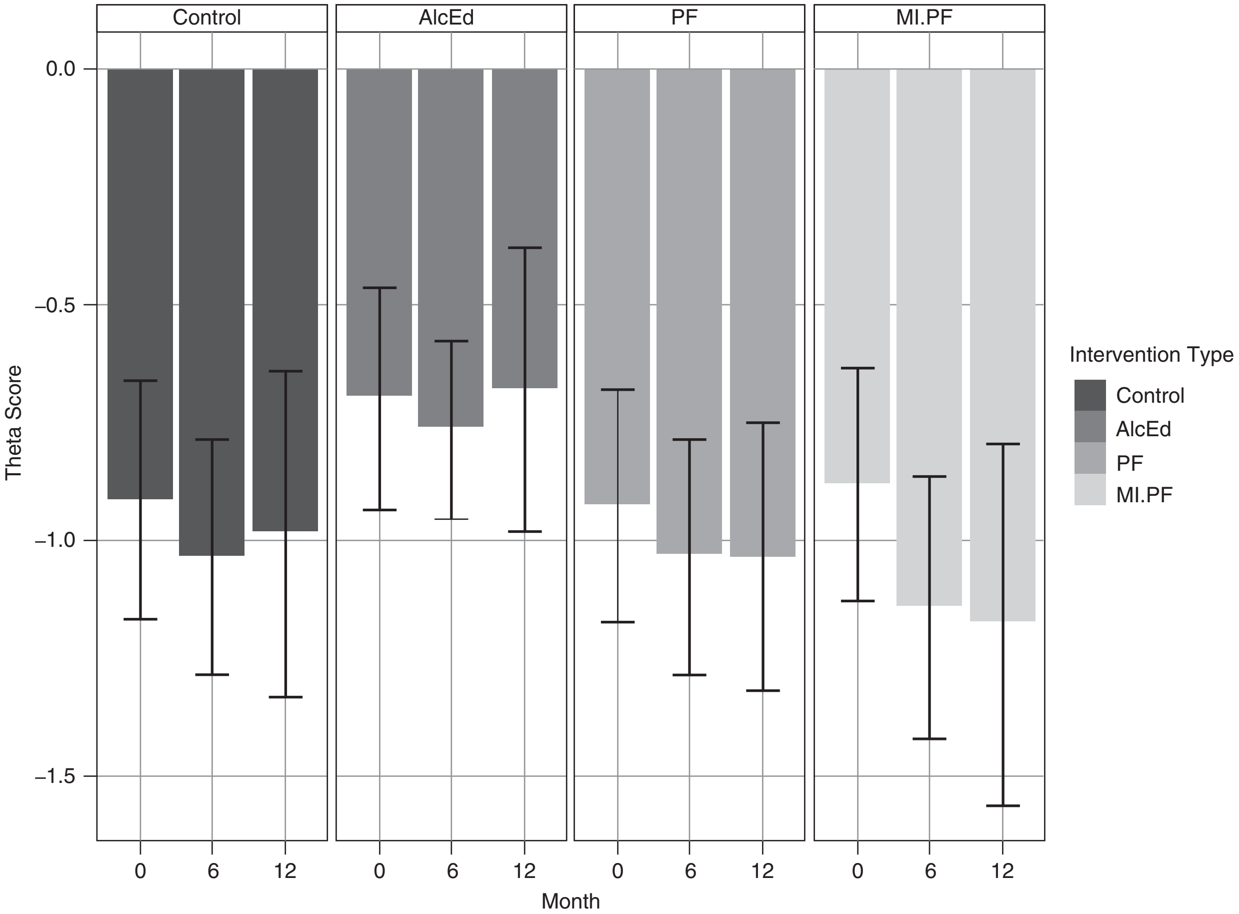


Figure 23.12 Model-based estimates of NR latent trait scores at baseline, 6 months and 12 months post intervention by group. NR = Neglecting responsibilities due to drinking; AlcEd = Alcohol Education; PF = Stand-alone Personalized Feedback; MI.PF = Motivational Interview plus Personalized Feedback (MI + PF); y-axis indicates NR scores. Higher scores (i.e., shorter bars in this figure) indicate greater severity. Error bars indicate 95% confidence intervals. Relatively speaking, there was a trend toward improving for those in the PF and MI + PF conditions.

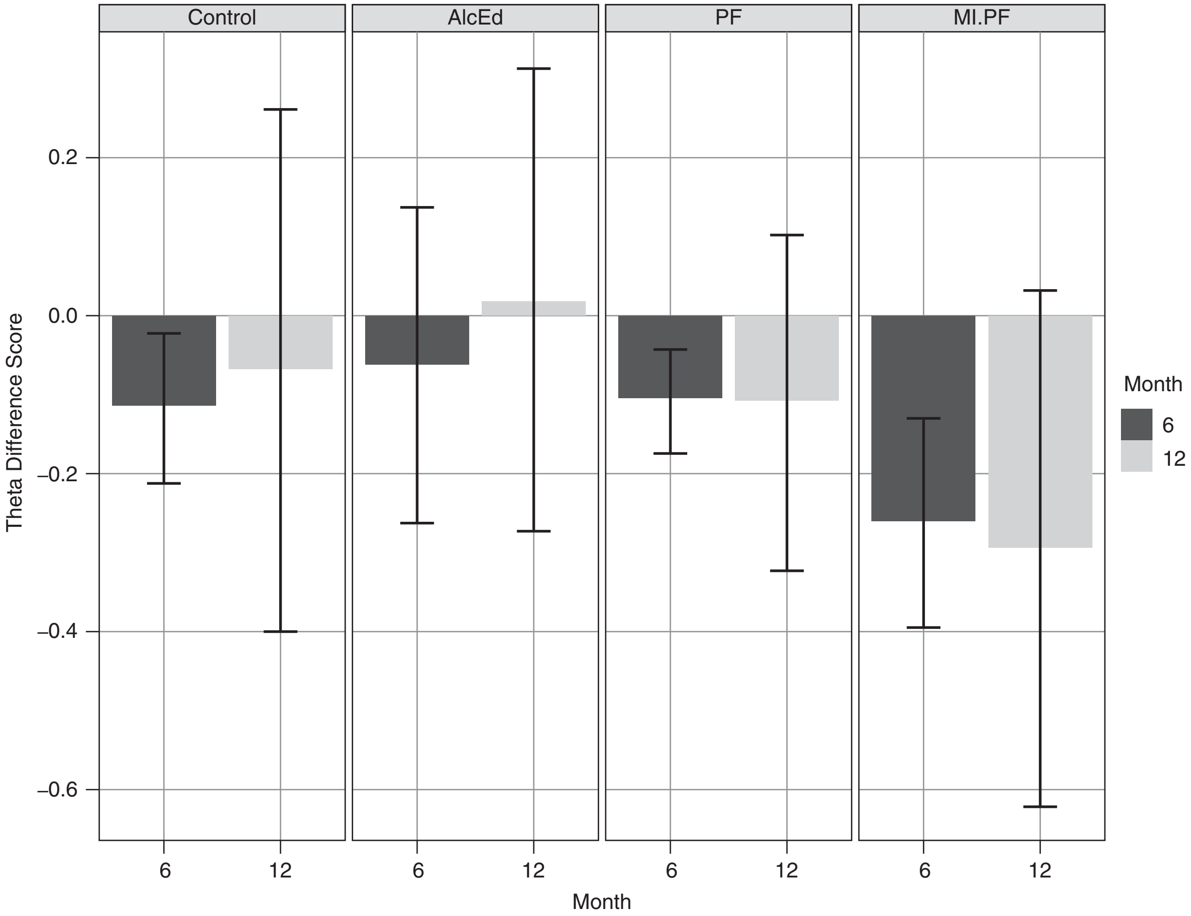


Figure 23.13 Model-based estimates of change at 6 months and 12 months post intervention by group. NR = Neglecting responsibilities due to drinking; AlcEd = Alcohol Education; PF = Stand-alone Personalized Feedback; MI.PF = Motivational Interview plus Personalized Feedback (MI + PF); y-axis indicates NR change scores. Error bars indicate 95% confidence intervals for these change scores. Confidence intervals that do not include zero indicate a statistically significant reduction at a given time point within groups. All groups with the exception of Alcohol Education showed a statistically significant reduction at 6 months. The significant reduction disappeared at 12 months for all three groups.

for those with higher levels of PBS at baseline. Relatively speaking, there was a trend toward improvement for PF and MI + PF. Figure 23.13 shows the statistically significant reductions from baseline at 6-month follow-up but not at 12-month follow-up for control, PF, and MI + PF. No evidence of change was found for Alcohol Education. Higher difference scores (positive scores on y axis) indicate higher levels of NR trait scores at follow-ups relative to their baseline levels (i.e., NR score went up; in other words, greater problems), whereas lower difference scores (negative scores on y axis) indicate reductions in NR scores at 6-month and 12-month follow-ups, compared with baseline. Given that control also significantly reduced NR at 6-month follow-up (zero not included in 95% confidence interval), the significant reductions shown by the PF and MI + PF groups could not be attributed to the interventions received. Thus, we then specifically compared the changes shown by three intervention groups against the change by control. Figure 23.14 shows the results. Compared to control, MI + PF showed significantly lower levels of NR at both 6-month and 12-month follow-ups. Those in the MI + PF condition were significantly better than those who received no intervention at both 6-month and 12-month follow-ups (zero not included in the 95% confidence intervals; Figure 23.14).

A few other things may be worth mentioning. Confidence intervals for 12-month outcome data were greater than those for 6-month data, which reflects greater uncertainty at 12-month follow-up, especially for PF, due to relative lack of data. Second, Alcohol Education exhibited greater problems at all three time points, reflecting their

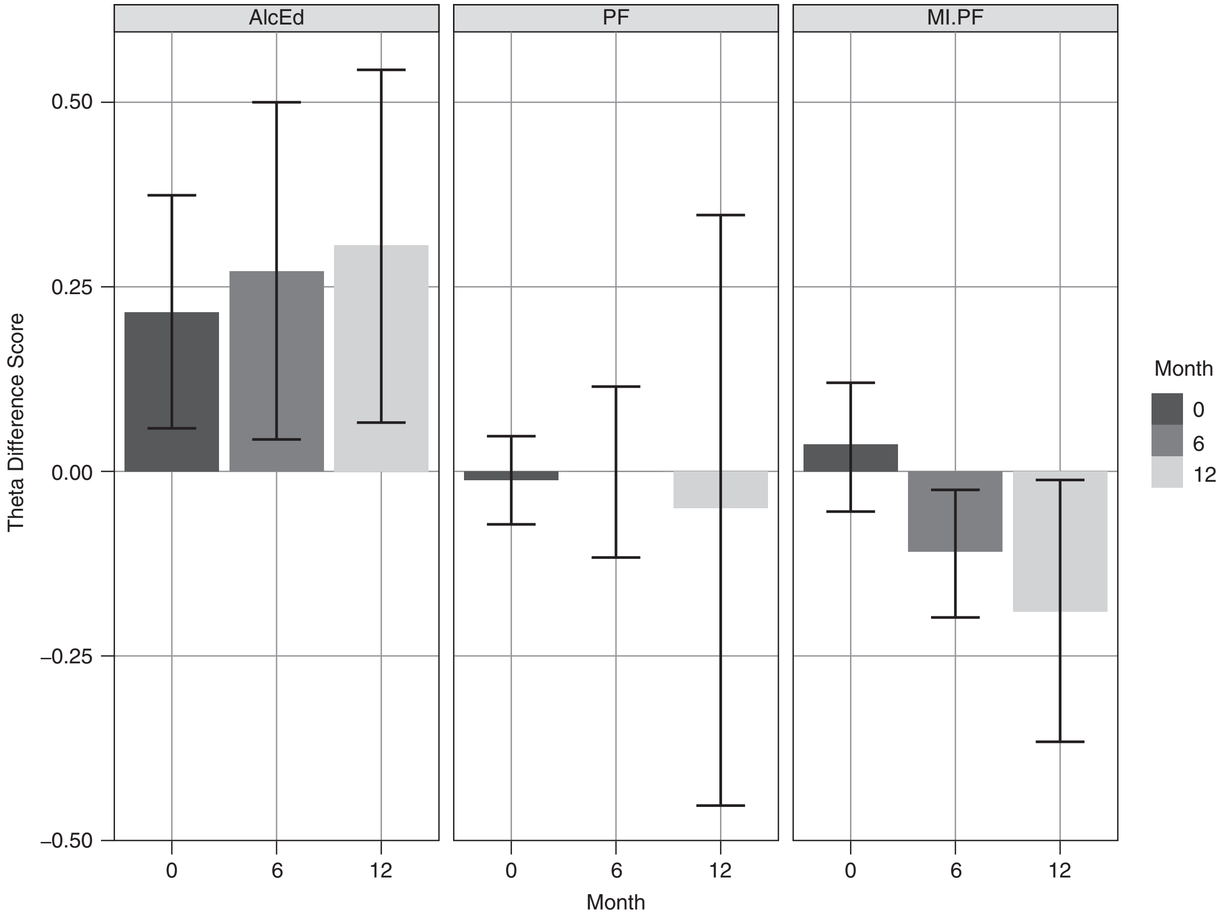


Figure 23.14 Multivariate meta-analysis of multiple intervention comparisons, showing a graphic demonstration of the significant MI + PF intervention effect compared with control. NR = Neglecting responsibilities due to drinking; AlcEd = Alcohol Education; PF = Stand-alone Personalized Feedback; MI.PF = Motivational Interview plus Personalized Feedback (MI + PF). Error bars indicate 95% confidence intervals. Confidence intervals that do not include zero indicate that the intervention condition at a given time point differed significantly in the estimated NR trait scores, compared with control. MI + PF, compared with control, showed significantly lower levels of NR trait scores at both 6 months and 12 months post intervention.

baseline differences. Combined with the data shown in Figure 23.13, we can say that Alcohol Education neither made it worse nor better for participants. The participants assigned to Alcohol Education more or less maintained their NR levels. This analysis was repeated for another dimension of alcohol-related problems and the results were largely similar (not reported). Thus, we can conclude that first, an in-person MI intervention with PF may make a difference in ameliorating alcohol-related problems among college students, at least up to 12 months; second, a stand-alone PF intervention may not be helpful for reducing alcohol-related problems, compared to control.

This finding is similar to the one reported in Huh et al. (2015) that utilized different analytic methodologies for a slightly different set of studies from Project INTEGRATE. In Huh et al., we used Bayesian multilevel overdispersed Poisson hurdle models in one-step IDA analysis to estimate intervention effects on drinks per week and peak drinking, and Gaussian models for alcohol problems in one-step IDA analysis. To overcome the unbalanced design, we utilized a three-level multilevel model, in which study-by-intervention condition was used as the highest, third level (repeated measures as the first level and individuals as the second level). To derive the overall intervention efficacy estimate (overall efficacy), as well as estimates for each of the intervention groups, we utilized posterior distributions from Bayesian analysis. The results indicated that there was no evidence of the overall intervention (BMI vs. control) effect on any of the outcomes examined but there was a small intervention effect by MI + PF on alcohol-related problems (Huh et al., 2015).

The substantive conclusion made in the current chapter is significant because the field of college alcohol interventions has embraced web-based normative feedback interventions, based on the previous findings from single studies that suggested that stand-alone PF interventions are just as efficacious as in-person MIs with PF at least for short term (e.g., see Walters & Neighbors, 2005 for a review). The current finding suggests that to reduce alcohol-related harm, an in-person MI may be needed. Although web-based interventions are easier to reach those who are in need and are attractive for their scalability, the findings from the IDA investigations reported in this chapter and in Huh et al. (2015) cautiously suggest a need to delve further into the mechanisms behind the in-person MI interventions with PF and to develop new interventions that may be more efficacious.

Note that the analytical examples shown in this chapter, as well as the one in Huh et al. (2015), are computationally demanding although the nature of the challenges is different. For the current IPD multivariate meta-analysis, the dimension of covariates was an important factor to consider. We added just four demographic covariates to the model, but the analysis required 15 × 15 covariance matrices (for 15 covariates) to be pooled across 15 separate analyses (for 15 studies with Studies 13 and 14 combined). The estimation of the between-study covariance matrix was quite challenging, especially with the embedded missing data in these matrices. Despite these challenges noted, the data examples shown in this section demonstrate new possibilities for the field of meta-analysis and IDA. Instead of focusing on qualitative or subjective interpretations of the relevant literature or counting the number of studies with a statistically significant intervention effect, IDA can be utilized using more advanced and flexible methodologies developed in recent years. It can overcome inherent limitations of single studies and AD meta-analysis. The value of fully utilizing existing data has been important and will most likely remain important in the coming years.

Software Programs and Packages

Univariate meta-analysis can be performed using commercially available software packages like Comprehensive Meta-analysis (CMA; Borenstein, Hedges, Higgins, & Rothstein, 2005) and MetAnalysis (Leandro, 2005) and other free DOS-based programs. Bax, Yu, Ikeda, and Moons (2007) reviewed their various features and different levels of usability in great detail. Table 23.8 lists available meta-analysis packages developed for R (R Core Team, 2014) and user-defined commands developed for Stata (StataCorp, 2013). For multivariate methods, *metafor* (Viechtbauer, 2010) can perform multivariate meta-analysis under fixed- and random-effects models, and the latter can be fitted through MLE or REML. In contrast, *mvtmeta* package (Chen, 2012) performs multivariate meta-analysis using the method of moments estimator for between-study covariance matrix when fitting random-effects model; *mvmeta* package (Gasparrini, Armstrong, & Kenward, 2012) uses the same method of moments estimation but allows missing data and handles meta-regression; and *metaSEM* package (Cheung, 2014) offers functions to perform fixed-effects and random-effects multivariate meta-analysis under the framework of structural equation modeling. All of these packages can handle both AD and IPD.

TABLE 23.8 Software Programs for Meta-analysis*.

	Univariate Meta-analysis	Multivariate Meta-analysis
R (packages)	epiR meta metafor rmeta gmeta	mvmeta mvtmeta metaSEM
Stata (User written commands)	metan metacum metareg	mvmeta mvmeta_make

*More information, including manuals and references, can be found at http://cran.r-project.org/web/views/MetaAnalysis.html and http://www.stata.com/support/faqs/statistics/meta-analysis.

For the multivariate meta-analysis illustrated in the present chapter, we developed our own functions to use in the R programming environment. The existing packages for multivariate meta-analysis discussed above could not be applied due to the complex data structure that we had. As indicated previously in the Multivariate Meta-analysis section, the dimension of the data estimated was high (15 × 15 covariance matrix) and this complexity was compounded with missing data. Thus, the second author wrote custom functions that were suited for the data. Essentially, the idea was to obtain the likelihood function while incorporating the missing data structure, which could not be accomplished using the existing packages. More specifically, we estimated the 15 × 15 between-study covariance matrix using REML by using the R package *optimx*. We also utilized different methods available in the *optimx* package (Nash & Varadhan, 2011) to confirm the final estimates reported in this chapter. We then calculated meta-analyzed individual coefficient estimates (reported in Table 23.7) by plugging the REML estimates into the last two equations shown in the IPD Meta-analysis and Integrative Data Analysis section. Figures 23.12–23.14 were drawn using the combined individual estimates reported in Table 23.7.

TRANSLATIONAL IMPLICATIONS OF INTEGRATIVE DATA ANALYSIS

IDA is an emerging methodological approach that is well suited for translational research. Translational research, although variously understood by different people, is generally known as the bench-to-bedside translation of knowledge from basic sciences to produce new clinical or treatment options for patients (Woolf, 2008). Through this translation, a new clinical treatment can be brought to scale to treat hard-to-treat problems and to narrow health disparities. For the successful translation of knowledge for evidence-based, bedside clinical practice, however, the integrity and validity of evidence is critical: Evidence-based practice is only as good and valid as the evidence that it is based on.

IDA, especially meta-analysis using IPD, has many promising utilities over single studies and over traditional meta-analysis utilizing summary data from published reports. More broadly, with regard to translational research, IDA may have at least three unique advantages. First, IDA studies using IPD can scrutinize existing findings in the literature and generate more robust findings and conclusions than possible based on single studies or traditional meta-analysis. Second, via IDA, one can examine mechanisms of behavior change with data that are better suited to address them. Third, through the advanced, state-of-the-art multivariate models, one can overcome compartmentalized pieces of evidence at various levels of analysis to create a more comprehensive understanding based on integrated quantitative evidence.

In terms of scrutinizing existing findings and strengthening our statistical inference, meta-analysis is increasingly seen as an important tool to shore up our confidence in evidence. In the present chapter, we suggest that traditional meta-analysis using summary statistics may be viewed as part of IDA using IPD, a broader research synthesis approach involving original raw participant-level data. Both of these approaches are expected to be relied on in the coming years; yet more advances and applications may be in store for IDA using IPD. There have been public calls to raise research standards for single studies and, in response, several stakeholders, such as editors of major journals and the National Institutes of Health (NIH), have proposed a number of changes in research practice (Collins & Tabak, 2014). According to Collins and Tabak, one of the initiatives considered by NIH is to develop a searchable data index for locating and accessing primary data. Thus, IDA using IPD may be called upon to provide a self-correcting function of science, especially for preclinical research, at more rapid pace than before.

Even for clinical research, the examples of antidepressant medications (Turner et al., 2008) and reanalysis of RCTs (Ebrahim et al., 2014) reviewed earlier in the current chapter illustrate the dangers of overly relying on data from published single studies. Therefore, from this perspective, it is promising that researchers are calling for a need to build participatory, prospective collaborative projects to tackle hallmark clinical questions such as what works (on the whole), what works for whom (subgroups or treatment modifiers), and how it works (mechanisms of behavior change) through innovative analysis of pooled data from multiple RCTs (e.g., Collaborative Data Synthesis for Adolescent Depression Trials [CDSADT]; NIMH Collaborative Data Synthesis for Adolescent Depression Trials Study Team, 2013).

In addition, it is very attractive that, via IDA, one can transcend compartmentalized pieces of evidence at various levels of analysis. In its place, one can generate a new understanding that is based on integrated quantitative evidence, which has been largely unobtainable from single studies or review studies that exclusively rely on summary data from single studies. Using IDA, similar studies can be linked to provide comparative evidence of various treatment approaches; generate evidence for treatment efficacy from multiple related outcomes; and provide clues as to the duration of treatment efficacy. Instead of subjectively interpreting and evaluating multiple coefficients obtained from multiple analyses in a piecemeal fashion, we can better grasp, for example, which treatment may be best of all available approaches in the field through the use of advanced methods well suited for IDA, as demonstrated in the data example provided in this chapter.

FUTURE DIRECTIONS AND LIMITATIONS

The research environment for IDA is ripe in many disciplines, including that of psychology. There are several thrusts behind this momentum. First, there is a great movement away from the current research practices that heavily depend on null hypothesis significance testing (NHST), toward new statistical practices that emphasize estimation of effect sizes and confidence intervals, and meta-analysis

(Cumming, 2014). The journal *Psychological Science*, a flagship journal for the Association for Psychological Science, announced new changes in publication standards and practices to be implemented starting January 2014 (Eich, 2014). To shore up the foundations of scientific inquiries, the journal's editors have proposed five broad changes: (1) remove word limits for the methods and results sections; (2) challenge researchers to clarify the what, why, and how questions of the research; (3) adopt the four-item disclosure statement aimed at making visible what goes on behind publications (i.e., undisclosed flexibility in data collection and analysis; Simmons, Nelson, & Simonsohn, 2011); (4) promote open practices by creating incentives to share data and materials when publishing and to declare full research protocols in advance; and (5) emphasize effect sizes, confidence intervals, and meta-analysis. When these changes are fully implemented, metadata repository systems that are searchable and easily accessible by others will create opportunities to quickly validate existing findings.

Second, from the perspective of exploratory, discovery-oriented investigations, data sharing can yield unexpected, serendipitous exploratory findings, which may lead to a prespecified, confirmatory study. Indeed, there are many national survey datasets that can be downloaded for public use. Moreover, in recent years, NIH has launched large, multisite projects expecting that they can serve as seed projects for other investigations. Big initiatives, such as the Human Connectome Project (HCP) and the National Consortium on Alcohol and Neurodevelopment in Adolescence (NCANDA), take advantage of improved computing capability, easier access to the web for storing and searching information, and convenient use of biological indices to better understand a complex phenomenon across different time scales and across different domains.

A third important thrust is the development of innovative methods for research synthesis. As this chapter demonstrates, there has been an explosion of more flexible, efficient, and powerful research methods to accommodate various needs, and these developments will likely continue. With the improvement in computing capability, we can run computationally demanding models, such as Bayesian models that were unthinkable not long ago. Elucidating the complex developmental processes that we see in developmental psychopathology requires a transdisciplinary systems prospective that cuts across scale and time, which has also been the guiding vision at NIH to promote scientific breakthroughs (Mabry, Olster, Morgan, & Abrams, 2008). IDA is a promising new approach in the era of big data to build a knowledge base that is more robust and cumulative and to move us forward toward more integrated and innovative research.

Despite our enthusiasm for IDA, some cautionary caveats are in order. Controlled, multisite, large studies do not always yield the same results as those from meta-analysis studies. In addition, different meta-analysis approaches—IPD or AD and different models—can lead to different estimates or conclusions (e.g., Haines & Hill, 2011). Recall, in the case of Avandia illustrated previously, the FDA restricted marketing of the drug based on findings from several meta-analysis studies showing greater heart attack risk while simultaneously offering a disclaimer stating that large-scale RCTs did not show a statistically significant risk elevation (Finkelstein & Levin, 2012). Thus, this case demonstrates that there is a need to evaluate all available evidence as a whole, and to be cautious about overly relying on one approach.

In addition, the time and resources required for IDA are considerable and one needs to carefully weigh the benefits of IDA relative to the resources needed. Data processing for IDA can be as intensive as collecting original data (Hussong et al., 2013) because of the need to examine and scrutinize all aspects of the pooled data prior to harmonizing and conducting further analysis to establish measurement invariance across important groups. Missing data resulted from combining data from multiple studies also pose a huge challenge to overcome for studies utilizing IPD. However, as the overall research environment is moving toward preregistration of a trial, reporting of all outcome variables, and better disclosure of methods and results, the environment may become more favorable for IDA studies in the future. Even for nonexperimental studies, similar, more open research practices are likely to follow, which may make it easier to conduct IDA studies.

CONCLUSIONS

Systematic research synthesis, particularly IDA involving original IPD from multiple sources, provides exciting new capabilities. IDA is well suited to address unmet needs in the field of developmental psychopathology and critical challenges in the current research environment. At the same time, there is a need to further develop research methods intended for research synthesis and to bridge our knowledge gaps in implementing these methods for IDA. Despite its many challenges, IDA is expected to be utilized more often in the future as a means to strengthen our research practice and lead to new discoveries.

REFERENCES

Al khalaf, M. M., Thalib, L., & Doi, S. A. R. (2011). Combining heterogenous studies using the random-effects model is a mistake and leads to inconclusive meta-analyses. *Journal of Clinical Epidemiology, 64*(2), 119–123. doi: 10.1016/j.jclinepi.2010.01.009

American College Health Association (2001). *National College Health Assessment ACHA- NCHA reliability and validity analyses*. Baltimore, MD: American College Health Association.

American Psychological Association Publications and Communications Board Working Group on Journal Article Reporting Standards (2008). Reporting standards for research in psychology: Why do we need them? What might they be? *American Psychologist, 63*(9), 839–851. doi: 10.1037/0003-066X.63.9.839

Atkins, D. C., Baldwin, S. A., Zheng, C., Gallop, R. J., & Neighbors, C. (2013). A tutorial on count regression and zero-altered count models for longitudinal substance use data. *Psychology of Addictive Behaviors, 27*(1), 166–177. doi: 10.1037/a0029508

Baer, J. S., Kivlahan, D. R., Blume, A. W., McKnight, P., & Marlatt, G. A. (2001). Brief intervention for heavy-drinking college students: 4-year follow-up and natural history. *American Journal of Public Health, 91*(8), 1310–1318.

Bakker, M., van Dijk, A., & Wicherts, J. M. (2012). The rules of the game called psychological science. *Perspectives on Psychological Science, 7*(6), 543–554. doi: 10.1177/1745691612459060

Barnett, N. P., Murphy, J. G., Colby, S. M., & Monti, P. M. (2007). Efficacy of counselor vs. computer-delivered intervention with mandated college students. *Addictive Behaviors, 32*(11), 2529–2548. doi: 10.1016/j.addbeh.2007.06.017

Bauer, D. J., & Hussong, A. M. (2009). Psychometric approaches for developing commensurate measures across independent studies: Traditional and new models. *Psychological Methods, 14*(2), 101–125. doi: 10.1037/a0015583

Bax, L., Yu, L.-M., Ikeda, N., & Moons, K. (2007). A systematic comparison of software dedicated to meta-analysis of causal studies. *BMC Medical Research Methodology, 7*(1), 40. doi: 10.1186/1471-2288-7-40

Begg, C. B., & Mazumdar, M. (1994). Operating characteristics of a rank correlation test for publication bias. *Biometrics, 50*(4), 1088–1101. doi: 10.2307/2533446

Begley, C. G., & Ellis, L. M. (2012). Drug development: Raise standards for preclinical cancer research. *Nature, 483*(7391), 531–533. doi: 10.1038/483531a

Bergman, L. R., & Magnusson, D. (1997). A person-oriented approach in research on developmental psychopathology. *Development and Psychopathology, 9*(2), 291–319. doi: 10.1017/S095457949700206X

Berman, N., & Parker, R. (2002). Meta-analysis: Neither quick nor easy. *BMC Medical Research Methodology, 2*(1), 10. doi: 10.1186/1471-2288-2-10

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2005). *Comprehensive Meta-Analysis (Version 2)* [Computer software]. Engelwood, NJ: Biostat.

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2009). *Introduction to meta-analysis*. West Sussex, UK: Wiley.

Borenstein, M., Hedges, L. V., Higgins, J. P. T., & Rothstein, H. R. (2010). A basic introduction to fixed-effect and random-effects models for meta-analysis. *Research Synthesis Methods, 1*(2), 97–111. doi: 10.1002/jrsm.12

Borenstein, M., & Higgins, J. P. T. (2013). Meta-analysis and subgroups. *Prevention Science, 14*(2), 134–143. doi: 10.1007/s11121-013-0377-7

Bradburn, M. J., Deeks, J. J., Berlin, J. A., & Russell Localio, A. (2007). Much ado about nothing: A comparison of the performance of meta-analytical methods with rare events. *Statistics in Medicine, 26*(1), 53–77. doi: 10.1002/sim.2528

Breslow, N. (1981). Odds ratio estimators when the data are sparse. *Biometrika, 68*(1), 73–84. doi: 10.2307/2335807

Brown, C. H., Sloboda, Z., Faggiano, F., Teasdale, B., Keller, F., Burkhart, G., ... Perrino, T. (2013). Methods for synthesizing findings on moderation effects across multiple randomized trials. *Prevention Science, 14*(2), 144–156. doi: 10.1007/s11121-011-0207-8

Brown, L. D., Cai, T. T., & DasGupta, A. (2001). Interval estimation for a binomial proportion. *Statistical Science, 16*(2), 101–117. doi: 10.2307/2676784

Carey, K. B., Scott-Sheldon, L. A., Carey, M. P., & DeMartini, K. S. (2007). Individual-level interventions to reduce college student drinking: A meta-analytic review. *Addictive Behaviors, 32*(11), 2469–2494. doi: 10.1016/j.addbeh.2007.05.004

Carey, K. B., Scott-Sheldon, L. A., Elliott, J. C., Garey, L., & Carey, M. P. (2012). Face-to-face versus computer-delivered alcohol interventions for college drinkers: A meta-analytic review, 1998 to 2010. *Clinical Psychology Review, 32*(8), 690–703. doi: 10.1016/j.cpr.2012.08.001

Chalmers, I. (2003). Trying to do more good than harm in policy and practice: The role of rigorous, transparent, up-to-date evaluations. *ANNALS of the American Academy of Political and Social Science, 589*(1), 22–40. doi: 10.1177/0002716203254762

Chalmers, I., & Matthews, R. (2006). What are the implications of optimism bias in clinical research? *The Lancet, 367*(9509), 449–450. doi: 10.1016/S0140-6736(06)68153-1

Chalmers, T. C., Smith Jr., H., Blackburn, B., Silverman, B., Schroeder, B., Reitman, D., & Ambroz, A. (1981). A method for assessing the quality of a randomized control trial. *Controlled Clinical Trials, 2*(1), 31–49. doi: 10.1016/0197-2456(81)90056-8

Chassin, L., Rogosch, F., & Barrera, M. (1991). Substance use and symptomatology among adolescent children of alcoholics. *Journal of Abnormal Psychology, 100*, 449–463. doi: 10.1037/0021-843X.100.4.449

Chen, H. (2012). *mvtmeta: Multivariate meta-analysis* (R package version 1.0). Available from http://cran.r-project.org/web/packages/mvtmeta/mvtmeta.pdf

Cheung, M. W.-L. (2014). Fixed- and random-effects meta-analytic structural equation modeling: Examples and analyses in R. *Behavior Research Methods, 46*, 29–40. doi:10.3758/s13428-013-0361-y

Cicchetti, D., & Toth, S. L. (2009). The past achievements and future promises of developmental psychopathology: The coming of age of a discipline. *Journal of Child Psychology and Psychiatry, 50*(1–2), 16–25. doi: 10.1111/j.1469-7610.2008.01979.x

Cimini, M. D., Martens, M. P., Larimer, M. E., Kilmer, J. R., Neighbors, C., & Monserrat, J. M. (2009). Assessing the effectiveness of peer-facilitated interventions addressing high-risk drinking among judicially mandated college students. *Journal of Studies on Alcohol and Drugs, Supplement*, *16*, 57–66.

Claggett, B., Xie, M., & Tian, L. (2014). Meta analysis with fixed, unknown, study-specific parameters. *Journal of the American Statistical Association*, *109*, 1667–1671. doi: 10.1080/01621459.2014.957288

Cochran, W. G. (1950). The comparison of percentages in matched samples. *Biometrika, 37*(3–4), 256–266. doi:10.1093/biomet/37.3-4.256

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences*. Hillsdale, NJ: Erlbaum.

Collins, F. S., & Tabak, L. A. (2014). NIH plans to enhance reproducibility. *Nature, 505*, 612–213.

Cooper, H., & Patall, E. A. (2009). The relative benefits of meta-analysis conducted with individual participant data versus aggregated data. *Psychological Methods, 14*(2), 165–176. doi: 10.1037/a0015565

Cronce, J. M., & Larimer, M. E. (2011). Individual-focused approaches to the prevention of college student drinking. *Alcohol Research & Health, 34*(2), 210–221.

Cumming, G. (2014). The new statistics: Why and how. *Psychological Science, 25*(1), 7–29. doi: 10.1177/0956797613504966

Cumming, G., & Maillardet, R. (2006). Confidence intervals and replication: Where will the next mean fall? *Psychological Methods, 11*(3), 217–227. doi: 10.1037/1082-989X.11.3.217

Curran, P. J. (2009). The seemingly quixotic pursuit of a cumulative psychological science: Introduction to the special issue. *Psychological Methods, 14*(2), 77–80. doi: 10.1037/a0015972

Curran, P. J., & Hussong, A. M. (2009). Integrative data analysis: The simultaneous analysis of multiple data sets. *Psychological Methods, 14*(2), 81–100. doi: 10.1037/a0015914

Curran, P. J., Hussong, A. M., Cai, L., Huang, W., Chassin, L., Sher, K. J., & Zucker, R. A. (2008). Pooling data from multiple longitudinal studies: the role of item response theory in integrative data analysis. *Developmental Psychology, 44*(2), 365–380. doi: 10.1037/0012-1649.44.2.365

Curran, P. J., McGinley, J. S., Bauer, D. J., Hussong, A. M., Burns, A., Chassin, L., . . . Zucker, R. (2014). A moderated nonlinear factor model for the development of commensurate measures in integrative data analysis. *Multivariate Behavioral Research, 49*(3), 214–231. doi: 10.1080/00273171.2014.889594

D'Amico, E. J., & Fromme, K. (1997). Health risk behaviors of adolescent and young adult siblings. *Health Psychology, 16*(5), 426–432. doi: 10.1037/0278-6133.16.5.426

Davey, J., Turner, R. M., Clarke, M. J., & Higgins, J. P. (2011). Characteristics of meta-analyses and their component studies in the Cochrane Database of Systematic Reviews: A cross-sectional, descriptive analysis. *BMC Medical Research Methodology, 11*(1), 160. doi: 10.1186/1471-2288-11-160.

Doornik, J. A. (2009). *Object-oriented matrix programming using Ox (Version 3.1)* [Computer software]. London, UK: Timberlake Consultants.

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials, 7*(3), 177–188. doi: 10.1016/0197-2456(86)90046-2

Donovan, E., Wood, M., Frayjo, K., Black, R. A., & Surette, D. A. (2012). A randomized, controlled trial to test the efficacy of an online, parent-based intervention for reducing the risks associated with college-student alcohol use. *Addictive Behaviors, 37*(1), 25–35. doi: 10.1016/j.addbeh.2011.09.007

Duval, S., & Tweedie, R. (2000). Trim and fill: A simple funnel-plot–based method of testing and adjusting for publication bias in meta-analysis. *Biometrics, 56*(2), 455–463. doi: 10.1111/j.0006-341X.2000.00455.x

Ebrahim, S., Sohani, Z. N., Montoya, L., Agarwal, A., Thorlund, K., Mills, E. J., & Ioannidis, J. P. A. (2014). Reanalyses of randomized clinical trial data. *Journal of American Medical Association, 312*(10), 1024–1032. doi: 10.1001/jama.2014.9646

Egger, M., Smith, G. D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal, 315*(7109), 629–634. doi: 10.1136/bmj.315.7109.629

Eich, E. (2014). Business not as usual. *Psychological Science, 25*(1), 3–6. doi: 10.1177/0956797613512465

Ferguson, C. J., & Brannick, M. T. (2012). Publication bias in psychological science: Prevalence, methods for identifying and controlling, and implications for the use of meta-analyses. *Psychological Methods, 17*(1), 120–128. doi: 10.1037/a0024445

Finkelstein, M. O., & Levin, B. (2012). Meta-analysis of "sparse" data: Perspectives from the Avandia cases. *Jurimetrics, 52*(2), 123–153.

Fisher, R. A. (1948). Questions and answers #14. *The American Statistician, 2*(5), 30–31. doi: 10.2307/2681650

Ford, D. H., & Lerner, R. M. (1992). *Developmental systems theory*. Newbury Park, CA: SAGE.

Fromme, K., & Corbin, W. (2004). Prevention of heavy drinking and associated negative consequences among mandated and voluntary college students. *Journal of Consulting and Clinical Psychology, 72*(6), 1038–1049. doi: 10.1037/0022-006X.72.6.1038

Gart, J. J. (1970). Point and interval estimation of the common odds ratio in the combination of 2 × 2 tables with fixed marginals. *Biometrika, 57*(3), 471–475. doi: 10.1093/biomet/57.3.471

Gasparrini, A., Armstrong, B., & Kenward, M. G. (2012). Multivariate meta-analysis for non-linear and other multi-parameter associations. *Statistics in Medicine, 31*(29), 3821–3839. doi: 10.1002/sim.5471

Haines, T. P., & Hill, A.-M. (2011). Inconsistent results in meta-analyses for the prevention of falls are found between study-level data and patient-level data. *Journal of Clinical Epidemiology, 64*(2), 154–162. doi: 10.1016/j.jclinepi.2010.04.024

Herbison, P., Hay-Smith, J., & Gillespie, W. J. (2006). Adjustment of meta-analyses on the basis of quality scores should be abandoned. *Journal of Clinical Epidemiology, 59*(12), 1249.e1241-1249.e1211. doi: 10.1016/j.jclinepi.2006.03.008

Higgins, J. P. T., & Green, S. (Eds.). (2011). *Cochrane handbook for systematic reviews of interventions (ver 5.1.0)*. Available from www.cochrane-handbook.org: The Cochrane Collaboration.

Higgins, J. P. T., & Thompson, S. G. (2002). Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine, 21*(11), 1539–1558. doi: 10.1002/sim.1186

Hoaglin, D. C., Hawkins, N., Jansen, J. P., Scott, D. A., Itzler, R., Cappelleri, J. C., . . . Barrett, A. (2011). Conducting indirect-treatment-comparison and network-meta-analysis studies: Report of the ISPOR Task Force on indirect treatment comparisons good research practices: Part 2. *Value in Health, 14*(4), 429–437. doi: 10.1016/j.jval.2011.01.011

Huh, D., Mun, E.-Y., Larimer, M. E., White, H. R., Ray, A. E., Rhew, I., . . . Atkins, D. C. (2015). Brief motivational interventions for college student drinking may not be as powerful as we think: An individual participant-level data meta-analysis. *Alcoholism: Clinical and Experimental Research, 39*(5), 919–931. doi: 10.1111/acer.12714

Huo, Y., de la Torre, J., Mun, E.-Y., Kim, S.-Y., Ray, A. E., Jiao, Y., & White, H. R. (2014). A hierarchical multi-unidimensional IRT approach for analyzing sparse, multi-group data for integrative data analysis. *Psychometrika. Advance online publication.* doi: 10.1007/s11336-014-9420-2

Hurlbut, S. C., & Sher, K. J. (1992). Assessing alcohol problems in college students. *Journal of American College Health, 41*(2), 49–58. doi: 10.1080/07448481.1992.10392818

Hussong, A. M., Curran, P. J., & Bauer, D. J. (2013). Integrative data analysis in clinical psychology research. *Annual Review of Clinical Psychology, 9*(1), 61–89. doi: 10.1146/annurev-clinpsy-050212-185522

Hussong, A. M., Huang, W., Curran, P. J., Chassin, L., & Zucker, R. A. (2010). Parent alcoholism impacts the severity and timing of children's externalizing symptoms. *Journal of Abnormal Child Psychology, 38*(3), 367–380. doi: 10.1007/s10802-009-9374-5

Hussong, A. M., Wirth, R. J., Edwards, M. C., Curran, P. J., Chassin, L. A., & Zucker, R. A. (2007). Externalizing symptoms among children of alcoholic parents: Entry points for an antisocial pathway to alcoholism. *Journal of Abnormal Psychology, 116*(3), 529–542. doi: 10.1037/0021-843X.116.3.529

Ioannidis, J. P. A. (2005). Why most published research findings are false. *PLoS Med, 2*(8), e124. doi: 10.1371/journal.pmed.0020124

Ioannidis, J. P. A. (2012). Why science is not necessarily self-correcting. *Perspectives on Psychological Science, 7*(6), 645–654. doi: 10.1177/1745691612464056

Ioannidis, J. P. A., Gwinn, M., Little, J., Higgins, J. P. T., Bernstein, J. L., Boffetta, P., . . . , & The Human Genome Epidemiology Network and the Network of Investigator Networks (2006). A road map for efficient and reliable human genome epidemiology. *Nature Genetics, 38*(1), 3–5. doi: 10.1038/ng0106-3

Jackson, D., Riley, R., & White, I. R. (2011). Multivariate meta-analysis: Potential and promise. *Statistics in Medicine, 30*(20), 2481–2498. doi: 10.1002/sim.4172

Jackson, D., White, I. R., & Thompson, S. G. (2010). Extending DerSimonian and Laird's methodology to perform multivariate random effects meta-analyses. *Statistics in Medicine, 29*(12), 1282–1297. doi: 10.1002/sim.3602

Jansen, J. P., Fleurence, R., Devine, B., Itzler, R., Barrett, A., Hawkins, N., . . . Cappelleri, J. C. (2011). Interpreting indirect treatment comparisons and network meta-analysis for health-care decision making: Report of the ISPOR Task Force on indirect treatment comparisons good research practices: Part 1. *Value in Health, 14*(4), 417–428. doi: 10.1016/j.jval.2011.04.002

Kahler, C. W., Strong, D. R., & Read, J. P. (2005). Toward efficient and comprehensive measurement of the alcohol problems continuum in college students: The Brief Young Adult Alcohol Consequences Questionnaire. *Alcoholism: Clinical and Experimental Research, 29*(7), 1180–1189. doi: 10.1097/01.alc.0000171940.95813.a5

Kraemer, H., Mintz, J., Noda, A., Tinklenberg, J., & Yesavage, J. A. (2006). Caution regarding the use of pilot studies to guide power calculations for study proposals. *Archives of General Psychiatry, 63*(5), 484–489. doi: 10.1001/archpsyc.63.5.484

Kuntsche, E., Rossow, I., Simons-Morton, B., Bogt, T. T., Kokkevi, A., & Godeau, E. (2013). Not early drinking but early drunkenness is a risk factor for problem behaviors among adolescents from 38 European and North American countries. *Alcoholism: Clinical and Experimental Research, 37*(2), 308–314. doi: 10.1111/j.1530-0277.2012.01895.x

LaBrie, J. W., Huchting, K. K., Lac, A., Tawalbeh, S., Thompson, A. D., & Larimer, M. E. (2009). Preventing risky drinking in first-year college women: Further validation of a female-specific motivational-enhancement group intervention. *Journal of Studies on Alcohol and Drugs, Suppl*(16), 77–85.

LaBrie, J. W., Huchting, K., Tawalbeh, S., Pedersen, E. R., Thompson, A. D., Shelesky, K., . . . Neighbors, C. (2008). A randomized motivational enhancement prevention group reduces drinking and alcohol consequences in first-year college women. *Psychology of Addictive Behaviors, 22*(1), 149–155. doi: 10.1037/0893-164X.22.1.149

LaBrie, J. W., Hummer, J. F., Neighbors, C., & Pedersen, E. R. (2008). Live interactive group-specific normative feedback reduces misperceptions and drinking in college students: A randomized cluster trial. *Psychology of Addictive Behaviors, 22*(1), 141–148. doi: 10.1037/0893-164X.22.1.141

LaBrie, J. W., Lamb, T. F., Pedersen, E. R., & Quinlan, T. (2006). A group motivational interviewing intervention reduces drinking and alcohol-related consequences in adjudicated college students. *Journal of College Student Development, 47*(3), 267–280.

LaBrie, J. W., Pedersen, E. R., Lamb, T. F., & Quinlan, T. (2007). A campus-based motivational enhancement group intervention reduces problematic drinking in freshmen male college students. *Addictive Behaviors, 32*(5), 889–901. doi: 10.1016/j.addbeh.2006.06.030

LaBrie, J. W., Thompson, A., Huchting, K., Lac, A., & Buckley, K. (2007). A group motivational interviewing intervention reduces drinking and alcohol-related negative consequences in adjudicated college women. *Addictive Behaviors, 32*(11), 2549–2562. doi: 10.1016/j.addbeh.2007.05.014

Larimer, M. E., & Cronce, J. M. (2007). Identification, prevention, and treatment revisited: Individual-focused college drinking prevention strategies 1999–2006. *Addictive Behaviors, 32*(11), 2439–2468. doi: 10.1016/j.addbeh.2007.05.006

Larimer, M. E., Lee, C. M., Kilmer, J. R., Fabiano, P. M., Stark, C. B., Geisner, I. M., . . . Neighbors, C. (2007). Personalized mailed feedback for college drinking prevention: A randomized clinical trial. *Journal of Consulting and Clinical Psychology, 75*(2), 285–293. doi: 10.1037/0022-006X.75.2.285

Larimer, M. E., Turner, A. P., Anderson, B. K., Fader, J. S., Kilmer, J. R., Palmer, R. S., & Cronce, J. M. (2001). Evaluating a brief alcohol intervention with fraternities. *Journal of Studies on Alcohol, 62*(3), 370–380.

Leandro, G. (2005). *Meta-analysis in medical research*. Malden, MA: BMJ Books.

Lee, C., & White, H. R. (2012). Effects of childhood maltreatment on violent injuries and premature death during young adulthood among urban high-risk men. *Archives of Pediatrics & Adolescent Medicine, 166*(9), 814–820. doi: 10.1001/archpediatrics.2012.244

Lee, C. M., Kaysen, D. L., Neighbor, C., Kilmer, J. R., & Larimer, M. E. (2009). *Feasibility, acceptability, and efficacy of brief interventions for college drinking: Comparison of group, individual, and web-based alcohol prevention formats.* Unpublished manuscript, Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA.

Lin, D. Y., & Zeng, D. (2010). On the relative efficiency of using summary statistics versus individual-level data in meta-analysis. *Biometrika, 97*(2), 321–332. doi: 10.1093/biomet/asq006

Liu, D., Liu, R. Y., & Xie, M. (2014). Exact meta-analysis approach for discrete data and its application to 2 × 2 tables with rare events. *Journal of the American Statistical Association*, *109*, 1450–1465. doi: 10.1080/01621459.2014.946318

Liu, D., Liu, R. Y., & Xie, M. (2015). Multivariate meta-analysis of heterogeneous studies using only summary statistics: Efficiency and robustness. *Journal of the American Statistical Association, 110*, 326–340. doi: 10.1080/01621459.2014.899235

Loeber, R., Pardini, D., Homish, D. L., Wei, E. H., Crawford, A. M., Farrington, D. P., . . . Rosenfeld, R. (2005). The prediction of violence and homicide in young men. *Journal of Consulting and Clinical Psychology, 73*(6), 1074–1088. doi: 10.1037/0022-006X.73.6.1074

Mabry, P. L., Olster, D. H., Morgan, G. D., & Abrams, D. B. (2008). Interdisciplinarity and systems science to improve population health: A view from the NIH Office of Behavioral and Social Sciences Research. *American Journal of Preventive Medicine, 35*(2, Supplement), S211–S224. doi: 10.1016/j.amepre.2008.05.018

Magnusson, D. (2000). The individual as the organizing principle in psychological inquiry: A holistic approach. In L. R. Bergman, R. B. Cairns, L.-G. Nilsson, & L. Nystedt (Eds.), *Developmental science and the holistic approach* (pp. 33–48). Mahwah, NJ: Erlbaum.

Mantel, N., & Haenszel, W. (1959). Statistical aspects of the analysis of data from retrospective studies of disease. *Journal of the National Cancer Institute, 22*, 719–748.

Marden, J. I. (1991). Sensitive and sturdy p-values. *The Annals of Statistics, 19*(2), 918–934. doi: 10.2307/2242091

Marszalhk, J. M., Barber, C., Kohlhart, J., & Holmes, C. B. (2011). Sample size in psychological research over the past 30 years. *Perceptual & Motor Skills, 112*(2), 331–348. doi: 10.2466/03.11.pms.112.2.331-348

Martens, M. P., Ferrier, A. G., Sheehy, M. J., Corbett, K., Anderson, D. A., & Simmons, A. (2005). Development of the Protective Behavioral Strategies Survey. *Journal of studies on alcohol, 66*(5), 698–705.

Martens, M. P., Kilmer, J. R., Beck, N. C., & Zamboanga, B. L. (2010). The efficacy of a targeted personalized drinking feedback intervention among intercollegiate athletes: A randomized controlled trial. *Psychology of Addictive Behaviors, 24*(4), 660–669. doi: 10.1037/a0020299

Martens, M. P., Taylor, K. K., Damann, K. M., Page, J. C., Mowry, E. S., & Cimini, M. D. (2004). Protective behavioral strategies when drinking alcohol and their relationship to negative alcohol-related consequences in college students. *Psychology of Addictive Behaviors, 18*(4), 390–393. doi: 10.1037/0893-164X.18.4.390

McArdle, J. J., Grimm, K. J., Hamagami, F., Bowles, R. P., & Meredith, W. (2009). Modeling life-span growth curves of cognition using longitudinal data with multiple samples and changing scales of measurement. *Psychological Methods, 14*(2), 126–149. doi: 10.1037/a0015857

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & The PRISMA Group (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PLoS Med, 6*(7), e1000097. doi: 10.1371/journal.pmed.1000097

Moreno, S. G., Sutton, A. J., Turner, E. H., Abrams, K. R., Cooper, N. J., Palmer, T. M., & Ades, A. E. (2009). Novel methods to deal with publication biases: Secondary analysis of antidepressant trials in the FDA trial registry database and related journal publications. *BMJ, 339*, b2981. doi: 10.1136/bmj.b2981

Mun, E.-Y., Bates, M. E., & Vaschillo, E. (2010). Closing the gap between person-oriented theory and methods. *Development and Psychopathology, 22*(2), 261–271. doi: 10.1017/S0954579410000039

Mun, E.-Y., de la Torre, J., Atkins, D. C., White, H. R., Ray, A. E., Kim, S.-Y., . . . , & The Project INTEGRATE Team (2015). Project INTEGRATE: An integrative study of brief alcohol intervention trials for college students. *Psychology of Addictive Behaviors, 29*(1), 34–48. doi: 10.1037/adb0000047

Mun, E.-Y., White, H. R., & Morgan, T. J. (2009). Individual and situational factors that influence the efficacy of personalized feedback substance use interventions for mandated college students. *Journal of Consulting and Clinical Psychology, 77*(1), 88–102. doi: 10.1037/a0014679

Muraki, E. (1992). A generalized partial credit model: Application of an EM algorithm. *Applied Psychological Measurement, 16*(2), 159–176. doi: 10.1177/014662169201600206

Murphy, J. G., Benson, T. A., & Vuchinich, R. E. (2004). A comparison of personalized feedback for college student drinkers delivered with and without a motivational interview. *Journal of Studies on Alcohol, 65*(2), 200–203.

Murphy, J. G., Duchnick, J. J., Vuchinich, R. E., Davison, J. W., Karg, R. S., Olson, A. M., . . . Coffey, T. T. (2001). Relative efficacy of a brief motivational intervention for college student drinkers. *Psychology of Addictive Behaviors, 15*(4), 373–379. doi: 10.1037/0893-164X.15.4.373

Nash, J. C., & Varadhan, R. (2011). Unifying optimization algorithms to aid software system users: Optimx for R. *Journal of Statistical Software, 43*(9), 1–14.

NIMH Collaborative Data Synthesis for Adolescent Depression Trials Study Team (2013). Advancing science through collaborative data sharing and synthesis. *Perspectives on Psychological Science, 8*(4), 433–444. doi: 10.1177/1745691613491579

Nissen, S. E., & Wolski, K. (2007). Effect of rosiglitazone on the risk of myocardial infarction and death from cardiovascular causes. *New England Journal of Medicine, 356*(24), 2457–2471. doi: 10.1056/NEJMoa072761

Normand, S.-L. T. (1999). Meta-analysis: formulating, evaluating, combining, and reporting. *Statistics in Medicine, 18*(3), 321–359. doi: 10.1002/(sici)1097-0258(19990215)18:3<321::aid-sim28>3.0.co;2-p

Nosek, B. A., Spies, J. R., & Motyl, M. (2012). Scientific utopia: II. Restructuring incentives and practices to promote truth over publishability. *Perspectives on Psychological Science, 7*(6), 615–631. doi: 10.1177/1745691612459058

Nuzzo, R. (2014). Scientific method: Statistical errors. *Nature, 506*, 150–152. doi: 10.1038/506150a

Open Science Collaboration. (2012). An open, large-scale, collaborative effort to estimate the reproducibility of psychological science. *Perspectives on Psychological Science, 7*(6), 657–660. doi: 10.1177/1745691612462588

O'Rourke, K. (2007). An historical perspective on meta-analysis: Dealing quantitatively with varying study results. *Journal of the Royal Society of Medicine, 100*(12), 579–582. doi: 10.1258/jrsm.100.12.579

Pashler, H., & Wagenmakers, E. J. (2012). Editors' introduction to the special section on replicability in psychological science: A crisis of confidence? *Perspectives on Psychological Science, 7*(6), 528–530. doi: 10.1177/1745691612465253

R Core Team. (2014). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing.

Ray, A. E., Kim, S.-Y., White, H. R., Larimer, M. E., Mun, E. Y., Clarke, N., . . . , & The Project INTEGRATE Team. (2014). When less is more and more is less in brief motivational interventions: Characteristics of intervention content and their associations with drinking outcomes. *Psychology of Addictive Behaviors, 28*, 1026–1040. doi: 10.1037/a0036593

Reitsma, J. B., Glas, A. S., Rutjes, A. W. S., Scholten, R. J. P. M., Bossuyt, P. M., & Zwinderman, A. H. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology, 58*(10), 982–990. doi: 10.1016/j.jclinepi.2005.02.022

Riley, R. (2009). Multivariate meta-analysis: The effect of ignoring within-study correlation. *Journal of the Royal Statistical Society: Series A, 172*(4), 789–811. doi: 10.1111/j.1467-985X.2008.00593.x

Robins, J., Breslow, N., & Greenland, S. (1986). Estimators of the Mantel-Haenszel variance consistent in both sparse data and large-strata limiting models. *Biometrics, 42*(2), 311–323. doi: 10.2307/2531052

Roerecke, M., & Rehm, J. (2012). The cardioprotective association of average alcohol consumption and ischaemic heart disease: A systematic review and meta-analysis. *Addiction, 107*(7), 1246–1260. doi: 10.1111/j.1360-0443.2012.03780.x

Saunders, J. B., Aasland, O. G., Babor, T. F., De La Fuente, J. R., & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on early detection of persons with harmful alcohol consumption-II. *Addiction, 88*(6), 791–804. doi: 10.1111/j.1360-0443.1993.tb02093.x

Scheidler, J., Hricak, H., Yu, K. K., Subak, L., & Segal, M. R. (1997). Radiological evaluation of lymph node metastases in patients with cervical cancer: A meta-analysis. *Journal of the American Medical Association, 278*(13), 1096–1101. doi: 10.1001/jama.1997.03550130070040

Schulz, K. F., Altman, D. G., & Moher, D. (2010). CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. *PLoS Med, 7*(3), e1000251. doi: 10.1371/journal.pmed.1000251

Schumann, G., Coin, L. J., Lourdusamy, A., Charoen, P., Berger, K. H., Stacey, D., . . . Elliott, P. (2011). Genome-wide association and genetic functional studies identify autism susceptibility candidate 2 gene (AUTS2) in the regulation of alcohol consumption. *Proceedings of the National Academy of Sciences, 108*(17), 7119–7124. doi: 10.1073/pnas.1017288108

Shadish, W. R., Cook, T. D., & Campbell, D. T. (2002). *Experimental and quasi-experimental designs for generalized causal inference*. New York, NY: Houghton Mifflin.

Shentu, Y., & Xie, M. (2010). A note on dichotomization of continuous response variable in the presence of contamination and model misspecification. *Statistics in Medicine, 29*(21), 2200–2214. doi: 10.1002/sim.3966

Simmonds, M. C., & Higgins, J. P. T. (2007). Covariate heterogeneity in meta-analysis: Criteria for deciding between meta-regression and individual patient data. *Statistics in Medicine, 26*(15), 2982–2999. doi: 10.1002/sim.2768

Simmons, J. P., Nelson, L. D., & Simonsohn, U. (2011). False-positive psychology: Undisclosed flexibility in data collection and analysis allows presenting anything as significant. *Psychological Science, 22*, 1359–1366. doi: 10.1177/0956797611417632

Skinner, H. A., & Allen, B., A. (1982). Alcohol dependence syndrome: Measurement and validation. *Journal of Abnormal Psychology, 91*(3), 199–209.

Skinner, H. A., & Horn, J. L. (1984). *Alcohol Dependence Scale: Users guide*. Toronto, Canada: Addiction Research Foundation.

Sroufe, L. A., & Rutter, M. (1984). The domain of developmental psychopathology. *Child Development, 55*(1), 17–29. doi: 10.2307/1129832

StataCorp. (2013). *Stata statistical software (version 13)* [Computer software]. College Station, TX: StataCorp LP.

Steenkamp, J.-B. E. M., & Baumgartner, H. (1998). Assessing measurement invariance in cross-national consumer research. *Journal of Consumer Research, 25*, 78–107. doi: 10.1086/209528

Steinberg, K. K., Smith, S. J., Stroup, D. F., Olkin, I., Lee, N. C., Williamson, G. D., & Thacker, S. B. (1997). Comparison of effect estimates from a meta-analysis of summary data from published studies and from a meta-analysis using individual patient data for ovarian cancer studies. *American Journal Epidemiology, 145*(10), 917–925.

Sterba, S. K., & Bauer, D. J. (2010). Matching method with theory in person-oriented developmental psychopathology research. *Development and Psychopathology, 22*(2), 239–254. doi: 10.1017/S0954579410000015

Stewart, L. A. (1995). Practical methodology of meta-analyses (overviews) using updated individual patient data. *Statistics in Medicine, 14*(19), 2057–2079. doi: 10.1002/sim.4780141902

Stouffer, S. A., Suchman, E. A., DeVinney, L. C., Star, S. A., & Williams, Jr., R. M. (1949). *The American soldier: vol. 1. Adjustment during army life*. Princeton, NJ: Princeton University Press.

Substance Abuse and Mental Health Services Administration (SAMHSA) (2012). *National Survey on Drug Use and Health (NSDUH)*. Retrieved from http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/DetTabs/NSDUH-DetTabsSect5peTabs1to56-2012.htm#Tab5.31b

Supplee, L. H., Kelly, B. C., MacKinnon, D. P., & Barofsky, M. Y. (2013). Introduction to the special issue: Subgroup analysis in prevention and intervention research. *Prevention Science, 14*(2), 107–110. doi: 10.1007/s11121-012-0335-9

Sutton, A. J., & Higgins, J. P. T. (2008). Recent developments in meta-analysis. *Statistics in Medicine, 27*(5), 625–650. doi: 10.1002/sim.2934

Sutton, A. J., Kendrick, D., & Coupland, C. A. (2008). Meta-analysis of individual- and aggregate-level data. *Statistics in Medicine, 27*(5), 651–669. doi: 10.1002/sim.2916

Thompson, S. G., & Pocock, S. J. (1991). Can meta-analyses be trusted? *The Lancet, 338*(8775), 1127–1130.

Tian, L., Cai, T., Pfeffer, M. A., Piankov, N., Cremieux, P.-Y., & Wei, L. J. (2009). Exact and efficient inference procedure for meta-analysis and its application to the analysis of independent 2 × 2 tables with all available data but without artificial continuity correction. *Biostatistics, 10*(2), 275–281. doi: 10.1093/biostatistics/kxn034

Tse, T., Williams, R. J., & Zarin, D. A. (2009). Reporting "basic results" in ClinicalTrials.gov. *Chest, 136*(1), 295–303. doi: 10.1378/chest.08-3022

Turner, E. H., Matthews, A. M., Linardatos, E., Tell, R. A., & Rosenthal, R. (2008). Selective publication of antidepressant trials and its influence on apparent efficacy. *New England Journal of Medicine, 358*(3), 252–260. doi: 10.1056/NEJMsa065779

Tversky, A., & Kahneman, D. (1971). Belief in the law of small numbers. *Psychological Bulletin, 76*(2), 105–110. doi: 10.1037/h0031322

Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, *36*, 1–48.

Walters, S. T., & Neighbors, C. (2005). Feedback interventions for college alcohol misuse: What, why and for whom? *Addictive Behaviors, 30*(6), 1168–1182. doi: 10.1016/j.addbeh.2004.12.005

Walters, S. T., Vader, A. M., & Harris, T. R. (2007). A controlled trial of web-based feedback for heavy drinking college students. *Prevention Science, 8*(1), 83–88. doi: 10.1007/s11121-006-0059-9

Walters, S. T., Vader, A. M., Harris, T. R., & Jouriles, E. N. (2009). Reactivity to alcohol assessment measures: An experimental test. *Addiction, 104*(8), 1305–1310. doi: 10.1111/j.1360-0443.2009.02632.x

Walters, S. T., Vader, A. M., Harris, T. R., Field, C. A., & Jouriles, E. N. (2009). Dismantling motivational interviewing and feedback for college drinkers: A randomized clinical trial. *Journal of Consulting and Clinical Psychology, 77*(1), 64–73. doi: 2009-00563-015 [pii]10.1037/a0014472

Weiss, B., & Garber, J. (2003). Developmental differences in the phenomenology of depression. *Development and Psychopathology, 15*(2), 403–430. doi: 10.1017/S0954579403000221

Werch, C. E., & Gorman, D. R. (1988). Relationship between self-control and alcohol consumption patterns and problems of college students. *Journal of Studies on Alcohol, 49*(1), 30–37.

White, H. R., & Labouvie, E. W. (1989). Towards the assessment of adolescent problem drinking. *Journal of Studies on Alcohol, 50*(1), 30–37.

White, H. R., Lee, C., Mun, E.-Y., & Loeber, R. (2012). Developmental patterns of alcohol use in relation to the persistence and desistance of serious violent offending among African American and Caucasian young men. *Criminology, 50*(2), 391–426. doi: 10.1111/j.1745-9125.2011.00263.x

White, H. R., Mun, E.-Y., & Morgan, T. J. (2008). Do brief personalized feedback interventions work for mandated students or is it just getting caught that works? *Psychology of Addictive Behaviors, 22*(1), 107–116. doi:10.1037/0893-164x.22.1.107

White, H. R., Mun, E.-Y., Pugh, L., & Morgan, T. J. (2007). Long-term effects of brief substance use interventions for mandated college students: Sleeper effects of an in-person personal feedback intervention. *Alcoholism: Clinical and Experimental Research, 31*(8), 1380–1391. doi: 10.1111/j.1530-0277.2007.00435.x

Wilk, A. I., Jensen, N. M., & Havighurst, T. C. (1997). Meta-analysis of randomized control trials addressing brief interventions in heavy alcohol drinkers. *Journal of General Internal Medicine, 12*(5), 274–283. doi: 10.1046/j.1525-1497.1997.012005274.x

Wood, M. D., Capone, C., Laforge, R., Erickson, D. J., & Brand, N. H. (2007). Brief motivational intervention and alcohol expectancy challenge with heavy drinking college students: A randomized factorial study. *Addictive Behaviors, 32*(11), 2509–2528. doi: 10.1016/j.addbeh.2007.06.018

Wood, M. D., Fairlie, A. M., Fernandez, A. C., Borsari, B., Capone, C., Laforge, R., & Carmona-Barros, R. (2010). Brief motivational and parent interventions for college students: A randomized factorial study. *Journal of Consulting and Clinical Psychology, 78*(3), 349–361. doi: 10.1037/a0019166

Woolf, S. H. (2008). The meaning of translational research and why it matters. *Journal of the American Medical Association, 299*(2), 211–213. doi: 10.1001/jama.2007.26

Xie, M., & Singh, K. (2013). Confidence distribution, the frequentist distribution estimator of a parameter: A review. *International Statistical Review, 81*(1), 3–39. doi: 10.1111/insr.12000

Xie, M., Singh, K., & Strawderman, W. E. (2011). Confidence distributions and a unifying framework for meta-analysis. *Journal of the American Statistical Association, 106*(493), 320–333. doi: 10.1198/jasa.2011.tm09803

Yamaguchi, Y., Sakamoto, W., Goto, M., Staessen, J. A., Wang, J., Gueyffier, F., & Riley, R. D. (2014). Meta-analysis of a continuous outcome combining individual patient data and aggregate data: a method based on simulated individual patient data. *Research Synthesis Methods, n/a-n/a.* doi: 10.1002/jrsm.1119

Yang, G., & Xie, M. (2010). *gmeta: An R package unified meta-analysis methods through combining confidence distributions*. Piscataway, NJ: Department of Statistics, Rutgers, The State University of New Jersey.

Yusuf, S., Peto, R., Lewis, J., Collins, R., & Sleight, P. (1985). Beta blockade during and after myocardial infarction: An overview of the randomized trials. *Progress in Cardiovascular Diseases, 27*, 335–371.

Zucker, R. A., Fitzgerald, H. E., Refior, S. K., Puttler, L. I. Pallas, D. M., & Ellis, D. A. (2000). The clinical and social ecology of childhood for children of alcoholics: Description of a study and implications for a differentiated social policy. In H. E. Fitzgerald, B. M. Lester, & B. S. Zuckerman (Eds.), *Children of addiction: Research, health and policy issues* (pp. 174–222). New York, NY: Garland Press.