

# Diffusion of Innovations model helps interpret the comparative uptake of two methodological innovations: co-authorship network analysis and recommendations for the integration of novel methods in practice

Suzanne M. Cadarette<sup>a,\*</sup>, Joann K. Ban<sup>a</sup>, Giulia P. Consiglio<sup>a</sup>, Cody D. Black<sup>a</sup>, David Dubins<sup>a</sup>,  
Alexandra Marin<sup>b</sup>, Mina Tadrus<sup>a</sup>

<sup>a</sup>Leslie Dan Faculty of Pharmacy, University of Toronto, 144 College Street, Toronto, Ontario M5S 3M2, Canada

<sup>b</sup>Department of Sociology, University of Toronto, 725 Spadina Avenue, Toronto, Ontario M5S 2J4, Canada

Accepted 1 December 2016; Published online 23 December 2016

## Abstract

**Objective:** The objective of this study was to characterize the diffusion of methodological innovation.

**Study Design and Setting:** Comparative case study analysis of the diffusion of two methods that summarize confounder information into a single score: disease risk score (DRS) and high-dimensional propensity score (hdPS). We completed systematic searches to identify DRS and hdPS papers in the field of pharmacoepidemiology through to the end of 2013, plotted the number of papers and unique authors over time, and created sociograms and animations to visualize co-authorship networks. First and last author affiliations were used to ascribe institutional contributions to each paper and network.

**Results:** We identified 43 DRS papers by 153 authors since 1981, reflecting slow uptake during initial periods of uncertainty and broader diffusion since 2001 linked to early adopters from Vanderbilt. We identified 44 hdPS papers by 147 authors since 2009, reflecting rapid and integrated diffusion, likely facilitated by opinion leaders, early presentation at conferences, easily accessible statistical code, and improvement in funding. Most contributions (87% DRS, 96% hdPS) were from North America.

**Conclusion:** When proposing new methods, authors are encouraged to consider innovation attributes and early evaluation to improve knowledge translation of their innovations for integration into practice, and we provide recommendations for consideration. © 2016 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Key Words:** Bibliometrics; Diffusion of innovation; Disease risk score; Pharmacoepidemiology; Social networks; Propensity score; Methodological innovation

## 1. Introduction

The field of postmarketing drug safety and effectiveness research (pharmacoepidemiology) has experienced rapid scientific progress and growth [1,2], particularly in the last

decade [3–6]. The rapid increase may partly relate to the emerging availability of health care utilization data [7,8] and significant funding investment [9,10]. The recent investment in pharmacoepidemiology is motivated by the recognition that drug safety and efficacy data from randomized controlled trials are limited [2], and thus, more evidence is needed for postmarketing to improve our understanding of drug benefits and harms [7]. Real-world drug safety and effectiveness data are important for patient and physician prescribing decisions, as well as for drug policy decision making. Methodological challenges in pharmacoepidemiology have required innovative solutions. Prior research has identified slow knowledge translation of statistical innovations [11,12]. We identified two statistical innovations that summarize confounder information into a single score: disease risk score (DRS [13]) and high-dimensional propensity score (hdPS [14]) to serve as

Conflict of interest: None.

Funding: No specific funding was received to support this work. This research was supported in part by unrestricted funds from an Ontario Ministry of Research and Innovation Award (ER09-06-043) to S.M.C.; Life Sciences Committee Undergraduate Research Opportunity Program Award, University of Toronto, to C.D.B.; Frederick Banting and Charles Best Canada Graduate Scholarship (GSD-11342), Canadian Institutes of Health Research, to M.T.

\* Corresponding author. University of Toronto, Leslie L. Dan Pharmacy Building, 144 College Street, Toronto, Ontario M5S 3M2, Canada. Tel.: 416-978-2993; fax: 416-978-8511.

E-mail address: [s.cadarette@utoronto.ca](mailto:s.cadarette@utoronto.ca) (S.M. Cadarette).

**What is new?**

- When proposing new methods, authors are encouraged to consider innovation attributes and early evaluation to improve knowledge translation, and thus integration of their innovation(s) into practice; and we provide recommendations for consideration.
- Co-authorship network analysis can be used to examine the diffusion of methodological innovation by visualizing the prominence of, and connections between authors that publish using novel methods.
- We propose methods to ascribe institutional credit to publications and encourage researchers to consider and comment on our approach.
- Web of Science citation and author searches are important to help find the application of innovative methods, as keyword searches are limited.

comparative case studies in the diffusion of methodological innovation. Our aim was to examine the speed (number of publications over time) and spread (across institutions) of each innovation and interpret uptake relative to innovation attributes, the social system, and communication channels described in Rogers' Diffusion of Innovations model [15].

## 2. Methods

We apply comparative case study methods with the Diffusion of Innovations model [15–18]. In brief, the Diffusion of Innovations model defines diffusion as a process by which an innovation (something perceived as new) is communicated through channels (how messages are passed between individuals) over time among members of a social system, **Box 1**. In particular, the rate of adoption of an innovation is proposed to be affected by five innovation attributes: (1) relative advantage over existing ideas or methods, (2) compatibility with the needs and values of potential adopters, (3) complexity (hereafter referred to as simplicity), (4) trialability (degree it can be tested), and (5) observability (degree its use and results are visible to others) [15].

We selected two methodological innovations in pharmacoepidemiology that cover a range of innovation attributes and time frame within a social system, according to the Diffusion of Innovations model, **Table 1**.

### 2.1. Case study 1: disease risk score

Stratification or matching by confounding variables was a common approach to control for confounding in the

1970s. However, stratification becomes inefficient as the number of strata or confounding variables to control for increases. The DRS, proposed by Miettinen in 1976 (“multivariate confounder score”) [13], summarizes all confounder information into a single summary score. Authors can then use DRS for stratification and thus reduce the number of strata. The innovation addressed an important limitation at the time and had a clear advantage over traditional stratification by individual confounding variables (relative advantage). Because the DRS is based on the baseline probability of disease risk, it can also be used to provide a meaningful scale to examine effect modification [19–21]. Despite its advantages, a recent systematic review (from 1976 to May 2011) identified that DRS initially received little attention or application in the epidemiologic literature [6]. DRS application was characterized by a bimodal distribution with a peak in 1979/1980 and resurgence since 2000 [6]. DRS was first proposed in 1976 [13], yet a simulation paper published in 1979 introduced early uncertainty in the method by concluding that it overestimates confounding and thus induces bias [22]. A subsequent simulation published in 1989 concluded that overestimation of confounders was rare [23], and more recent contributions corroborate DRS ability to control for confounding and highlight its potential advantages [19–21,24,25]. This case study thus provides an opportunity to consider the diffusion of an innovation introduced during the infancy of the field of pharmacoepidemiology and over a 40-year time span in the context of initial uncertainty.

### 2.2. Case study 2: high-dimensional propensity score

Studies that rely on health care utilization (administrative claims) databases may be biased if important confounding information is missing. In theory, statistical adjustment for proxy variables or combinations of variables that indirectly capture information on unmeasured confounder(s) may yield better control for confounding. The hdPS is an adaptation of the commonly used propensity score [5] and uses a multistep algorithm to empirically identify candidate proxy variables based on their estimated strength of confounding. The proxy variables are then included into the hdPS [14]. The innovation paper included simple figures to help contextualize the theory around proxy variables (simplicity), compared statistical adjustment using a standard confounder model to that using the hdPS (compatibility), documented results closer to those from clinical trials when using the hdPS (advantage), and authors posted statistical code on their research website ([www.drugepi.org/dope-downloads/](http://www.drugepi.org/dope-downloads/)) to facilitate application of the innovation by other researchers (trialability). In addition, preliminary results were presented at the International Society for Pharmacoepidemiology meeting (observability and active communication channel), the first author (Schneeweiss) served as the president of the

### Box 1 Summary of Rogers' Diffusion of Innovations model [15]

The adoption of methodological innovation in pharmacoepidemiology can be described using Rogers' Diffusion of Innovations model [15]. Over 5,000 studies in a variety of disciplines have used the Diffusion of Innovations model since it was first published in 1962 [18]. The model includes four key elements that are proposed to impact the uptake of an innovation: (1) Innovation Attributes, (2) Communication Channels, (3) Time, and (4) Social System.

**i. Innovation Attributes:** An innovation is an idea, practice, or object that is perceived as new. Rogers identifies five key innovation attributes that affect its rate of uptake:

Attribute	Description
1. Relative advantage	Perceived relative advantage over existing ideas or methods
2. Compatibility	Perceived consistency with existing needs and values of potential adopters
3. Simplicity*	Degree perceived to be simple to understand or use
4. Trialability	Degree can be tested (testing reduces uncertainty)
5. Observability	Degree its use and results are visible to others

\* Rogers' model labels this attribute complexity (degree perceived to be difficult to understand or use), yet we have used simplicity so that the label corresponds with a quicker rate of adoption.

**ii. Communication Channels:** How messages are passed between individuals. Communication channels have two important components; its source, and the method of communication:

1. *Source:* An individual or an institution that originates a message.

The more similar individuals who interact are (e.g., education, beliefs, institution, region), the more likely the source will be effective. In addition, the more well known/respected (opinion leaders) the source, the more likely the recommendation will be considered for adoption.

2. *Channel:* Means by which a message gets from the source to the receiver.

The more interpersonal (vs. mass media) and active (vs. passive), the quicker it will diffuse.

- Interpersonal vs. mass media: direct communication between individuals is advantageous over mass media (e.g., one or few to reach many).

- Active vs. passive: degree more actively targeted to individual (e.g., small seminar or interpersonal email) will diffuse more quickly vs. passive communication (e.g., publication).

**iii. Time:** Adopters of an innovation are classified into one of five categories: innovators, early adopters, early majority, late majority, and laggards. Innovators are those that develop methodological innovations as well as the first members of a group to adopt the technology. Early adopters typically interact with the innovators, with early majority attending conferences and late majority and laggards learning after the method is well established. Early adopters' leadership in adopting a new technology serves to reduce the uncertainty about the innovation by other researchers.

**iv. Social System:** A social system is a group of individuals who work together toward a common goal, for example, researchers, decision makers, and funding agencies. Units in the social system may be comprised of individuals, groups, or organizations.

International Society for Pharmacoepidemiology in 2010, and several co-authors are eminent researchers in the field of pharmacoepidemiology (important communication sources as key opinion leaders). This case study thus provides an opportunity to consider the diffusion of an innovation by a number of opinion leaders, presented with several critical innovation attributes, in a short time period and during a period of growth in the field of pharmacoepidemiology.

### 2.3. Systematic literature search

We updated a recent systematic review of DRS applications [6], to identify English language papers in the field of pharmacoepidemiology through to December 2013. The original systematic review identified 97 papers (24 in the field of pharmacoepidemiology) using three search strategies: (1) MEDLINE keyword search (terms listed in Appendix A at [www.jclinepi.com](http://www.jclinepi.com)), (2) Web of Science citation search [13,22–24], and (3) Web of Science author search (Ray WA and Arbogast PG) [6]. In our update, we restricted the original search strategy to January 2011 through to the end of December 2013. We then performed an EMBASE keyword search from 1976 to December 2013, and citation searches of more recent DRS methods papers [19–21].

A new systematic search was completed to identify all English language articles on the hdPS in pharmacoepidemiology from the time of innovation (July 2009) to the end of December 2013 using (1) MEDLINE and EMBASE keyword searches (terms listed in Appendix A at [www](http://www).

**Table 1.** Case study summary according to characteristics in the Diffusion of Innovations model

Characteristic <sup>a</sup>	Case study 1	Case study 2
	Disease risk score (DRS) [13]	High-dimensional propensity score (hdPS) [14]
Innovation type	New statistical (confounder summary score) method	Adaptation of an established [5] statistical (confounder summary score) method
Innovation year	1976	2009
Innovation field	Epidemiology	Pharmacoepidemiology
Rate of uptake	Initially slow	Rapid
Attributes <sup>a</sup>	<ul style="list-style-type: none"> <li>• Relative advantage over conventional methods               <ul style="list-style-type: none"> <li>○ Controls for several confounders by summarizing all into a single score (+A)</li> <li>○ Study effect modification by baseline disease risk (+A)</li> </ul> </li> <li>• Initial uncertainty in 1970s/80s (-A)</li> <li>• Based on conventional methods (regression and stratification, +C, +T) thus easily understood (+S)</li> <li>• Little consistency in language used to describe the method over time (-O)</li> </ul>	<ul style="list-style-type: none"> <li>• Relative advantage over propensity scores/conventional regression               <ul style="list-style-type: none"> <li>○ Identifies proxy variables to help control of unmeasured confounding (+A)</li> </ul> </li> <li>• Adaption of the propensity score method (+C, +S)</li> <li>• Sample statistical code available online for free (+T)</li> <li>• Presented at ICPE, the Annual meeting of the International Society for Pharmacoepidemiology before publication (+O)</li> </ul>
Social system when innovation introduced	Field “born” in 1970s <ul style="list-style-type: none"> <li>• 1962: Kefauver-Harris Amendment to the US Food, Drug and Cosmetic Act in response to thalidomide disaster</li> <li>• 1966: Boston Collaborative Drug Safety Research established</li> <li>• Mid-1970s: Drug Epidemiology Unit (now Slone Epidemiology Center)</li> <li>• 1976: Joint Commission of Prescription Drug Use formed</li> <li>• 1977: Computerized online Medicaid analysis and surveillance system developed</li> <li>• 1985: First International Conference on Pharmacoepidemiology (“ICPE”)</li> </ul>	Significant investment/incentives in 2000s <ul style="list-style-type: none"> <li>• 2005: AHRQ launches DEcIDE Network</li> <li>• 2006: US Medicare Part D-drug data</li> <li>• 2007: Canada calls for improved drug safety</li> <li>• 2007: US FDA Amendments Act (FDAAA) mandates “Sentinel Initiative”—drug surveillance system of electronic data from health care information holders (goal data on &gt;100 million)</li> <li>• 2008: Canada launches DSEN, commits \$32 million over five years + \$10 million annually after</li> <li>• 2010: US Patient Protection and Affordable Care Act creates PCORI and mandates development of Methodological Standards</li> </ul>
Advantage of this case study	New statistical method to control for confounding over an almost 40-year period and in the context of methodological uncertainty.	Adaptation of an established statistical method over a short period (since 2009), during a period of rapid growth in the field and innovators facilitated the uptake of the innovation through readily available statistical code.

*Abbreviations:* AHRQ, Agency for Healthcare Research and Quality; DEcIDE, Developing Evidence to inform Decisions about Effectiveness; FDA, Food and Drug Administration; DSEN, Drug Safety and Effectiveness Network; ICPE, International Conference on Pharmacoepidemiology and Therapeutic Risk Management; PCORI, Patient Centered Outcomes Research Institute.

<sup>a</sup> The rate of adoption of an innovation is proposed to be affected by its five attributes: A: advantage (relative advantage), C: compatibility (with user values), S: simplicity (in contrast to complexity), T: trialability (degree can be tested, testing reduces uncertainty), O: observability (degree results are visible to others), Box 1 [15].

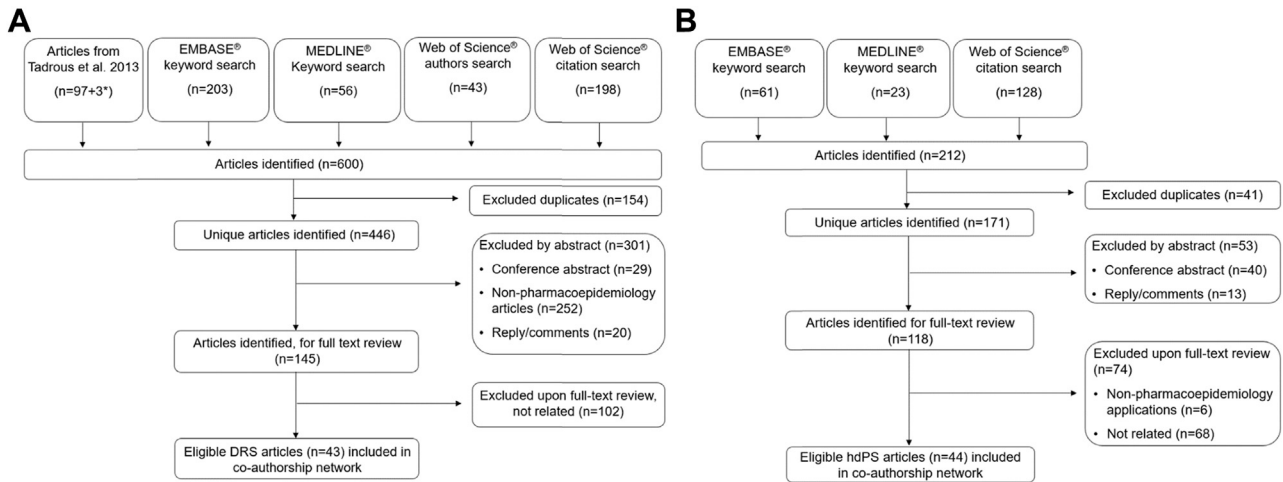
[jclinepi.com](http://jclinepi.com)) and (2) Web of Science citation search of the innovation paper [14].

Pharmacoepidemiologic empirical method and review papers were eligible. Post hoc analyses of clinical trial data were excluded to be consistent with our prior review [6]. Electronic searches were facilitated using EndNote X5 (Thomson Reuters, 2011). We created study flow diagrams to summarize results of each systematic search and Venn diagrams to illustrate search strategy yield, with circle size proportional to the number of eligible articles identified by each search strategy. We plotted the number of publications by study type (empirical, methodological, review) and the cumulative number of unique authors by calendar year to characterize the rate of adoption of each innovation over

time. As a crude way to get a sense of the general trend in pharmacoepidemiology publications, we completed a systematic literature search using PubMed only, as well as a combination of PubMed, EMBASE, and MEDLINE, from their dates of inception to 2013 using the keyword “pharmacoepidemiology.” We limited our search to English language publications on humans from 1902 to 2013 and excluded duplicate publications, commentaries, editorials, letters, and conference abstracts.

#### 2.4. Co-authorship network analysis

Author names and order were downloaded from EndNote X5 into Excel 2010. Names of authors presented



**Fig. 1.** Flow diagram of systematic search results. (A) Disease risk score (DRS) and (B) high-dimensional propensity score (hdPS). \*Three eligible articles identified in conversation with local research group outside the review [6].

inconsistently (e.g., Fireman BH and Fireman B) were collapsed into the most common presentation or in the event of a tie, the one with more initials. We generated sociograms in Cytoscape, version 3.2.0 (Harvard Analytic Technologies, 2002) [26] to examine the co-authorship network structure of each innovation. Sociograms depict authors as “nodes,” with lines or “ties” between nodes denoting co-authorship. Directed sociograms were generated to clarify network structure by only sending ties as arrows from first authors to each co-author. Node size was created proportional to the number of articles published by that author. The number of components was then identified. A component is a group of authors connected directly (co-author on the same paper), or indirectly (connected through a mutual co-author on separate papers).

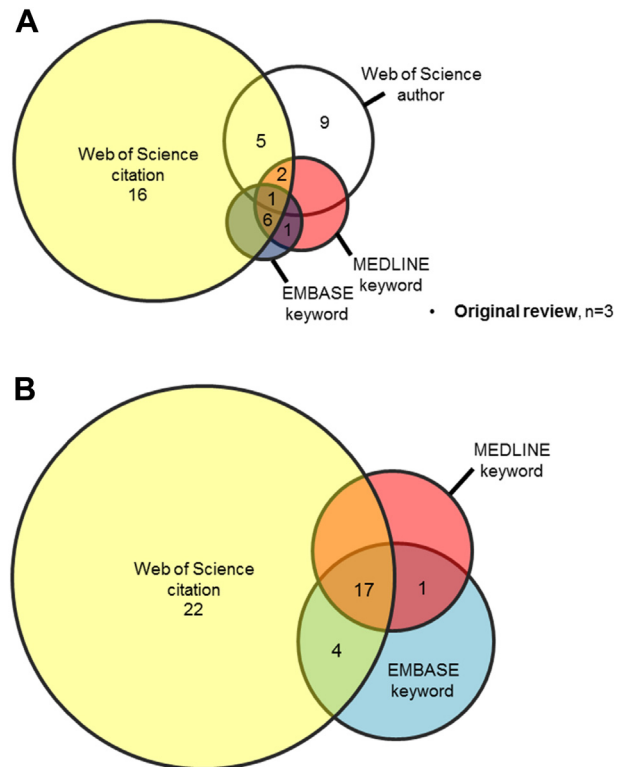
2.5. Institutional credit

Institutional affiliations of the first and last author were used to ascribe institutional credit to each paper, component, and network. Institutional credit was given proportional to the number of institutional affiliations between the first and last author. Institutional departments and divisions were collapsed into the main institution. For example, affiliation with Harvard Medical School and Harvard School of Public Health was ascribed to Harvard University. Each publication was given equal weight when determining contribution to the network. Affiliations of the first, second, and last author were considered in a secondary analysis.

3. Results

We identified 43 DRS (Appendix B at [www.jclinepi.com](http://www.jclinepi.com)) and 44 hdPS eligible articles (Appendix C at [www.jclinepi.com](http://www.jclinepi.com)), Fig. 1. The citation search strategy identified the most papers, including 30 (75%) of the 40 DRS papers identified through electronic searches, and all but the hdPS

seminal paper used as the citation in the search, Fig. 2. Three DRS papers were identified outside the electronic search, as documented previously [6]. Web of Science

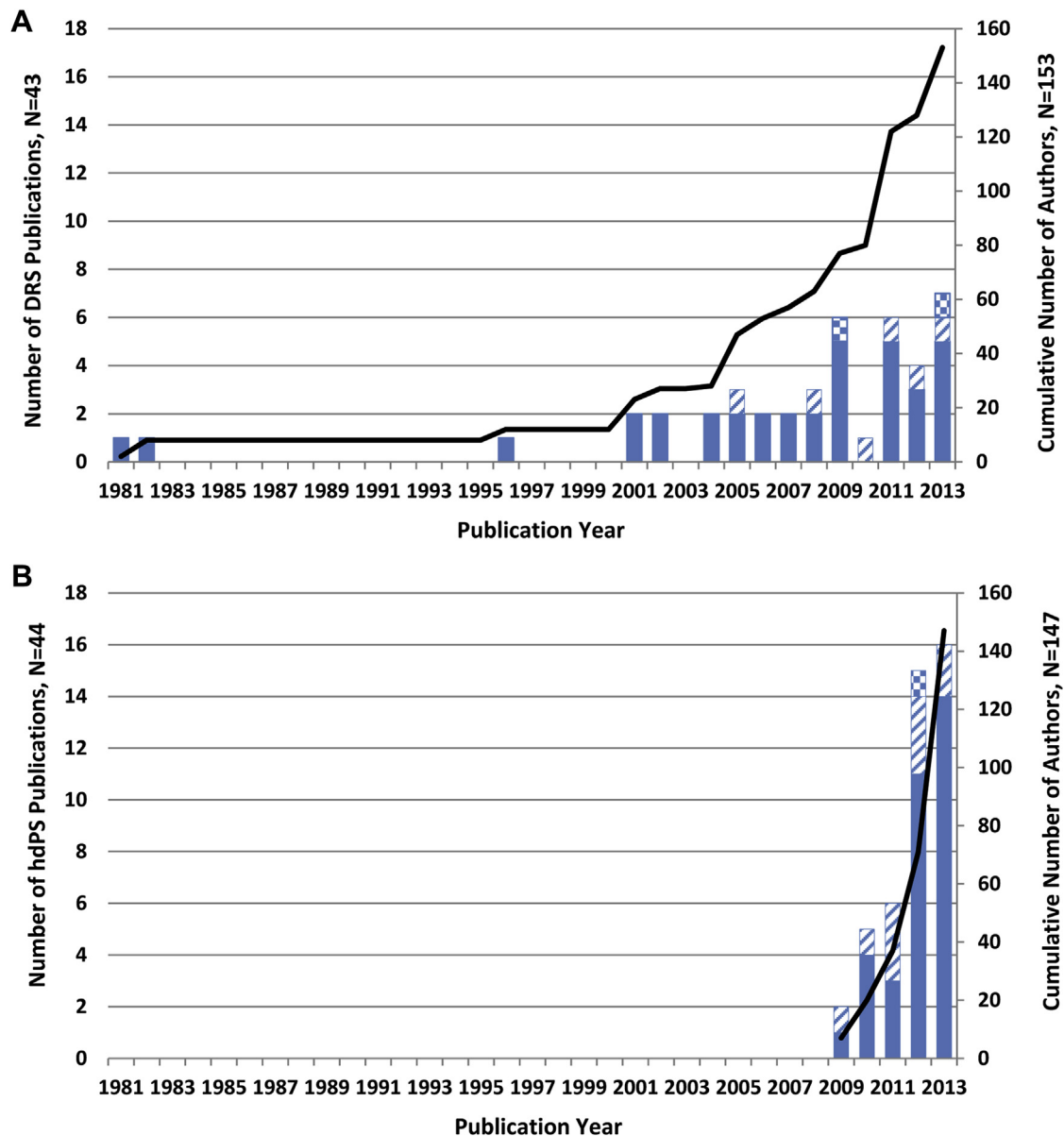


**Fig. 2.** Venn diagram of systematic search results depicting unique and overlap papers identified by each search engine. Circle size is proportional to the number of eligible papers identified by each search strategy. (A) Disease risk score electronic search yielded 40 papers: Web of Science citation (n = 30), Web of Science author (n = 17), MEDLINE keyword (n = 10), EMBASE keyword (n = 8). An additional three articles were identified outside the electronic search in our original review [6]. (B) High-dimensional propensity score search yielded 44 papers: Web of Science citation (n = 43), MEDLINE keyword (n = 18), and EMBASE keyword (n = 22).

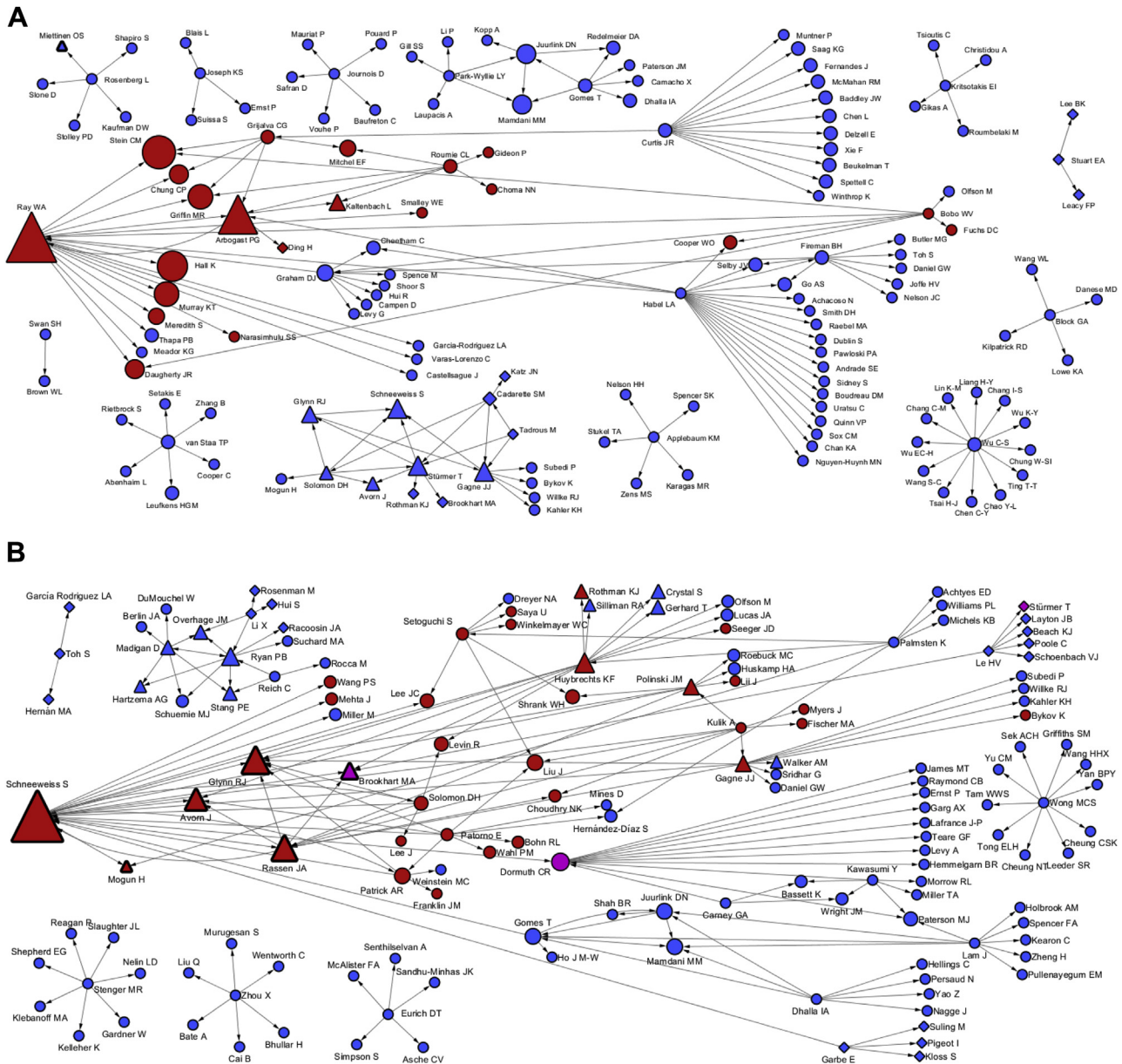
citation (DRS and hdPS) and author (DRS) searches proved critical to the identification of papers; indeed keyword searches alone would have missed half ( $n = 22$  of 44) of the hdPS papers, and three-quarters ( $n = 30$  of 40 identified in the electronic search) of DRS papers.

DRS uptake was initially slow, with few publications in the field of pharmacoepidemiology before 2001, Fig. 3A. The number of unique authors increased from 23 in 2001 to a total of 153 by the end of 2013; with 34 (79%) of the 43 papers published between 2011/01 and 2013/12. The network comprised 13 components (Fig. 4A), and as illustrated in the animated sociogram (Fig. 5A, available

in the [Online Supplemental Material at www.jclinepi.com](http://www.jclinepi.com)), diffusion did not extend from the seminal paper. Instead, Vanderbilt University led DRS diffusion starting in 2001, with initial spread facilitated by collaborations with Ray WA and Arbogast PG from Vanderbilt. Institutional credit is summarized in [Table D1, Appendix D at www.jclinepi.com](#). This largest component included 21 papers (49%) and 67 authors (44%) with primary institutions, Vanderbilt University (48%), Veteran Affairs–Tennessee Valley Healthcare System (29%), and University of Alabama at Birmingham (10%) ([Appendix B1–B21 at www.jclinepi.com](#)). The second largest component included six



**Fig. 3.** Number of publications and cumulative authors by year of publication. Cumulative number of authors represented by solid black line. Empirical application (solid), methodological contributions (striped), and review papers (checked). (A) Disease risk score, 153 authors publishing 43 (35 empirical application, 6 methodological contributions, and 2 review) papers. (B) High-dimensional propensity score, 147 authors publishing 44 (33 empirical applications, 10 methodological contributions, and 1 review) papers. DRS, disease risk score; hdPS, high-dimensional propensity score.



**Fig. 4.** Directed sociograms. Authors of the seminal paper for each method are distinguished by a thicker node border. Arrows are directed from first author to co-authors of each paper. Node size is proportional to the number of published articles. Circles represent authors who have only published articles applying each innovation, diamonds represent authorship of innovation reviews or methods papers, triangles represent authorship of both application and review or methods papers. Red nodes represent authors with institutional affiliation with the early adopters (DRS, Vanderbilt University) and innovators (hdPS, Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women’s Hospital), that drove the diffusion of each innovation. Purple nodes denote authors that had a prior affiliation with the groups that drove innovation and since moved to other institutions. Please refer to [Online Supplemental Material at www.jclinepi.com](http://www.jclinepi.com) for animated versions of each figure. (A) Disease risk score, 13 components, 43 eligible papers plus the seminal DRS paper [13]. (B) High-dimensional propensity score, 7 components, 44 papers. DRS, disease risk score; hdPS, high-dimensional propensity score (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article).

papers (13%), and 16 authors (11%) from Harvard University (39%), Brigham and Women’s Hospital (39%), University of Toronto (19%), and University of North Carolina (3%) ([Appendix B22–B27 at www.jclinepi.com](http://www.jclinepi.com)). The third largest component included four papers (9%) ([Appendix B28–B31 at www.jclinepi.com](http://www.jclinepi.com)) and 12 authors (8%) with 100% of contributions from institutions in Toronto, Canada.

The remaining 10 components included only one or two articles each ([Appendix B32–B43 at www.jclinepi.com](http://www.jclinepi.com)).

hdPS uptake was characterized by a steep slope reflecting rapid diffusion from publication in July 2009 to December 2013, [Fig. 3B](http://www.jclinepi.com). The steep hdPS slope is consistent with the dramatic general increase in pharmacoepidemiology publications since 2011, [Appendix E at www.jclinepi.com](http://www.jclinepi.com).

jclinepi.com. The 44 hdPS papers by 147 authors comprised seven components (Fig. 4B), and as illustrated in the animation (Fig. 5B, available in the [Online Supplemental Material](#) at [www.jclinepi.com](http://www.jclinepi.com)), innovators led its diffusion. Institutional credit is summarized in [Table D2, Appendix D](#) at [www.jclinepi.com](http://www.jclinepi.com). The largest component included 34 papers (77%) and 96 authors (65%) with primary institutions, Harvard University (36%), Brigham and Women's Hospital (34%), and University of British Columbia (7%) ([Appendix C1–C34](#) at [www.jclinepi.com](http://www.jclinepi.com)). The second largest component contained five papers (11%), and 16 authors (11%), with primary institutions, National Institutes of Health (28%) and Johnson and Johnson (19%) ([Appendix C35–C39](#) at [www.jclinepi.com](http://www.jclinepi.com)). The remaining five components included one paper each ([Appendix C40–C44](#) at [www.jclinepi.com](http://www.jclinepi.com)), with contributions largely from the United States.

Overall, 87% of DRS contributions were from North America (14% from Canada, 73% from United States; 24% from Vanderbilt University), with some credit attributed to France, Greece, Netherlands, Spain, Taiwan, and the United Kingdom; and 96% of hdPS contributions were from North America (17% from Canada, 79% from United States; 29% from Harvard University, 27% from Brigham and Women's Hospital) with some credit attributed to China, Germany, Saudi Arabia, and the United Kingdom. Almost 90% of publications using each innovation were attributed to academic institutions (86% DRS, 90% hdPS), with some contribution by industry (10% DRS, 6% hdPS) and least by government (4%

DRS, 5% hdPS), [Table 2](#). Including the second author in addition to the first and last author in the secondary analysis had little impact on institutional credit assigned to each innovation.

#### 4. Discussion

Our systematic search identified a similar number of DRS and hdPS articles published in pharmacoepidemiology through to the end of 2013, yet the rate of diffusion of each method differed considerably. The stark contrast in the rate of adoption of these two methodological innovations may be explained by concepts in the Diffusion of Innovations model [15]. DRS adoption was slow. The widely accepted seminal paper was published in the broad field of epidemiology in 1976 [13], yet early controversy over its merits (advantage) stifled its adoption, and inconsistent use of language made it less observable [6]. Indeed, as indicated in our prior review, our systematic search may have missed some DRS applications. In fact, even the 1976 seminal methodological article by Miettinen uses an earlier application that considers coffee drinking and myocardial infarction [27], to explain and review the relative advantage of the DRS method. Another early application outside the field of pharmacoepidemiology [28] citing an even earlier source [29] was brought to our attention after presentation of our work in August 2016 [30]. We thus acknowledge the challenge when studying methodological innovation to pin point the original publication.

**Table 2.** Institutional affiliations by country and institution type for DRS and hdPS networks

Institutional affiliation	DRS network credit (%)		hdPS network credit (%)	
	First and last author	First, second, and last author	First and last author	First, second, and last author
Country				
Canada	14.2	14.1	17.4	17.7
China	<sup>a</sup>	0.6	2.3	2.3
France	2.3	2.4	<sup>a</sup>	<sup>a</sup>
Germany	<sup>a</sup>	<sup>a</sup>	0.8	1.1
Greece	2.4	2.3	<sup>a</sup>	<sup>a</sup>
Netherlands	3.1	2.1	<sup>a</sup>	<sup>a</sup>
Saudi Arabia	<sup>a</sup>	<sup>a</sup>	0.4	0.3
Spain	0.8	0.5	<sup>a</sup>	0.5
Taiwan	3.8	3.5	<sup>a</sup>	<sup>a</sup>
United Kingdom	0.8	1.2	0.6	0.5
United States	72.6	74.0	79.0	77.9
Institution type				
Academia	86.5	87.7	89.6	89.6
School	57.5	60.8	58.2	58.9
Hospital	29.0	26.9	31.4	30.7
Government	3.6	3.2	4.7	4.1
Industry	9.9	9.1	5.7	5.8
Pharmaceutical company	0.8	1.3	4.7	4.7
Health insurance plan	7.0	6.0	<sup>a</sup>	<sup>a</sup>
Clinical research organization <sup>b</sup>	2.1	1.8	1.0	1.6

Abbreviations: DRS, disease risk score; hdPS, high-dimensional propensity score.

<sup>a</sup> No credit based on authors used to ascribe credit.

<sup>b</sup> One clinical research organization was a non-for-profit organization.



Nonetheless, we anticipate that few if any applications were in the field of pharmacoepidemiology before what we have identified as the original (seminal) methodological DRS contribution [13].

The DRS co-authorship network started to expand in 2001 with a publication by authors from Vanderbilt University. Researchers from this group were “early adopters” of the DRS in pharmacoepidemiology and early DRS use then spread to other institutions by collaboration with authors from Vanderbilt University. The relatively recent uptake in usage of the DRS in pharmacoepidemiology may also be partially explained by the change in the social system, with significant investment in funding opportunities not only to complete drug safety and effectiveness studies, yet also to examine methods to improve the validity of pharmacoepidemiologic applications. Indeed, several recent papers underscore the comparative advantages of DRS over existing methods to adjust for confounding variables [19–21,24,25]. General increase in use of the propensity score method may have also improved perception of the benefits of confounder summary score methods [5] and thus

indirectly improved perceived compatibility of DRS in pharmacoepidemiology.

In contrast, hdPS experienced immediate and rapid diffusion over a short four and a half year period. Much of the strength of diffusion may relate to innovation attributes, how the method was presented, authors, and timing. Indeed, all five key innovation attributes were maximized: (1) evidence provided of distinct advantages over the existing methods (advantage), (2) adaptation of the well-established propensity score method (compatibility), (3) presentation in preliminary form at conferences (observability), (4) paper included figures to simplify concepts with step-by-step approach to execute the method (simplicity), and (5) free statistical code was posted on a web site (trialability). In addition, authors included several key opinion leaders (well known and respected communication sources), and hdPS was launched during a period of government investment and incentives for interinstitutional research collaboration (congruent social system). We must also acknowledge a general increase in the publication of pharmacoepidemiology papers, reflecting social system advances.

**Table 3.** Recommendations to improve the diffusion of methodological innovation

5 Innovation Attributes					Recommendations
A	C	S	T	O	
✓	✓	✓			1. Clearly describe using foundational principles (simple language)
✓	✓				Clearly articulate the methodological gap and thus need for the innovation
✓	✓				Clearly articulate relative advantage over existing methods
	✓	✓			Use standard (foundational) biostatistics and epidemiologic language; avoid technical jargon; simplify according to information or selection bias
		✓			Consider using simple figures to walk the reader through concepts
		✓			Leverage language used in foundational principles and established methods when naming the innovation
✓	✓				2. Consider comparing results to established method(s)
✓	✓				Consider comparing results achieved using the innovation methods to established method(s) in the context of known effects (e.g., known safety or effectiveness of drug), or suspected null findings (e.g., do not expect to see drug-outcome association)
	✓	✓	✓		3. Provide sample data, code or calculation examples, and instructions
		✓	✓		Create macros or provide example statistical code in the seminal publication (e.g., appendices) or on a research website
	✓	✓	✓		Provide example data set(s) and code or calculation examples for easy manipulation and trialability
		✓	✓		Publish guidance for utilization (e.g., when is the method appropriate vs. inappropriate) and clear instructions for how to implement the methods and interpret results
✓	✓	✓	✓	✓	4. Early communication, support, and testing
✓	✓	✓		✓	Present at research conferences and obtain feedback on the method, language, and approach before publication in full form
✓	✓	✓	✓	✓	Consider creating workshops to support innovation use and understanding
		✓	✓	✓	Consider creating webinars or open source content to facilitate access and understanding
		✓		✓	Consider using social media (e.g., Twitter) to showcase the innovation and highlight or comment on its use
		✓		✓	Continue to apply and test/challenge innovation merits and encourage others to do the same
✓	✓	✓		✓	5. Provide methodological and reporting guidance
✓	✓	✓		✓	Make clear recommendations for when the method may be appropriate (strengths) or inappropriately (limitations) applied
✓	✓				Identify future areas of methodological development and testing
✓	✓	✓		✓	Make recommendations for reporting standards, for example, language to describe, data display, supplemental information to present in appendices
✓	✓	✓		✓	Encourage future applications to cite the seminal innovation paper

Abbreviations: A, advantage; C, compatibility; S, simplicity; T, trialability; O, observability.

In contrast to DRS, where the innovator Miettinen was not readily engaged in its application, Schneeweiss and co-authors helped to push hdPS adoption through collaboration. For example, collaboration with hdPS seminal authors helped to bring the method to the University of North Carolina (i.e., hdPS seminal author Brookhart moved institutions), and Canada (e.g., Dormuth trained with hdPS seminal author Schneeweiss). Our results are also consistent with a recent survey of researchers and statisticians that identified lack of awareness of the new method or its relative benefits over existing methods, expertise, software, and time as key barriers to the implementation of new statistical methods [11]. Even among those with expertise to implement new statistical methods, lack of time to learn and implement new methods, as well as concerns about translating nonstandard methods, was identified as key barriers [11]. Providing statistical code for implementing new methods clearly facilitates the adoption of methodological innovation.

Our review is complete through to the end of 2013, providing a comparative case analysis of the diffusion of DRS and hdPS. For the purposes of considering the relative uptake of these innovations in the field of pharmacoepidemiology, this timeline is sufficient by providing comparative evidence of the benefits of the Diffusion of Innovations model in launching statistical innovations. Nonetheless, it is important to consider the lifecycle of these innovations. It is possible that new information about the relative advantage of these methods or the introduction of newer methods may impact future applications.

In our primary analysis, we ascribed institutional credit to the first and last author. Traditionally, the first (principal) author contributes most and receives the most credit. However, in pharmacoepidemiology as in biomedical sciences, the last (often senior) author often gets as much, or even more credit than the first author. This is because the senior author is assumed to be the driving force, both intellectually and financially, behind the research [31]. However, this may not always be the case and indeed some other authors may drive use of statistical methods. The last author may also not always be the senior author, as is the case in our paper; yet authors often strategically consider authorship order based on contributions, seniority, or relative benefit to career stage. We note little change in institutional credit when ascribing credit to first and last only vs. first, second, and last author. To our knowledge, we are the first to attempt to ascribe institutional credit to a methodological innovation, and future research in the area may help to develop methodological standards.

Based on our findings and the Diffusion of Innovations model, we summarize recommendations for authors of methodological innovations to consider (Table 3). In brief, we encourage authors to remain mindful of the five innovation attributes, and propose five principles that collectively tap into the five innovation attributes: (1) clearly describe using foundational principles; (2) consider comparing

results to established methods; (3) provide sample data, code, or calculation examples and instructions; (4) early communication, support, and testing; and (5) provide methodological and reporting guidance. We encourage authors to consider and comment on our recommendations to facilitate the knowledge translation of innovations for rapid integration into practice. A key part of the integration of novel methods includes evaluation. It is through application and testing that the relative merits and shortcoming of novel methods are identified.

## Acknowledgments

Authors thank Patrick R. Edwards, PharmD, for initial work with the disease risk score co-authorship analysis and use of the Diffusion of Innovations model; Gina Matesic, MLIS, for help with search strategies; and Alison Thompson, PhD, for an introduction to comparative case study analysis.

Dr. Cadarette acknowledges contributions through conversations with researchers (in alphabetical order) from McGill University (Michal Abrahamowicz, Olli Miettinen, Robert Platt), University of British Columbia (Colin Dormuth, Malcolm Maclure), and University of North Carolina (M. Alan Brookhart, Til Stürmer)—thanks for getting this research out of “death valley,” that is, the floor of my office.

## Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.jclinepi.2016.12.006>.

## References

- [1] Hartzema AG, Tilson HH, Chan KA. *Pharmacoepidemiology and therapeutic risk management*. Cincinnati: Harvey Whitney Books; 2008.
- [2] Strom BL, Kimmel SE, Hennessy S. *Pharmacoepidemiology*. West Sussex: Wiley-Blackwell; 2011.
- [3] Consiglio GP, Burden AM, Maclure M, McCarthy L, Cadarette SM. Case-crossover study design in pharmacoepidemiology: systematic review and recommendations. *Pharmacoepidemiol Drug Saf* 2013; 22:1146–53.
- [4] Jandoc R, Burden AM, Mamdani M, Lévesque LE, Cadarette SM. Interrupted time series analysis in drug utilization research is increasing: systematic review and recommendations. *J Clin Epidemiol* 2015;68:950–6.
- [5] Stürmer T, Joshi M, Glynn RJ, Avorn J, Rothman KJ, Schneeweiss S. A review of the application of propensity score methods yielded increasing use, advantages in specific settings, but not substantially different estimates compared with conventional multivariable methods. *J Clin Epidemiol* 2006;59:437–47.
- [6] Tadrous M, Gagne JJ, Stürmer T, Cadarette SM. Disease risk score as a confounder summary method: systematic review and recommendations. *Pharmacoepidemiol Drug Saf* 2013;22:122–9.
- [7] Schneeweiss S. Developments in post-marketing comparative effectiveness research. *Clin Pharmacol Ther* 2007;82:143–56.

- [8] Schneeweiss S, Avorn J. A review of uses of health care utilization databases for epidemiologic research on therapeutics. *J Clin Epidemiol* 2005;58:323–37.
- [9] Suissa S, Henry D, Caetano P, Dormuth CR, Ernst P, Hemmelgarn B, et al. CNODES: the Canadian Network for Observational Drug Effect Studies. *Open Med* 2012;6:e134–40.
- [10] Selby JV, Beal AC, Frank L. The patient-centered outcomes research institute (PCORI) national priorities for research and initial research agenda. *JAMA* 2012;307:1583–4.
- [11] Pullenayegum EM, Platt RW, Barwick M, Feldman BM, Offringa M, Thabane L. Knowledge translation in biostatistics: a survey of current practices, preferences, and barriers to the dissemination and uptake of new statistical methods. *Stat Med* 2016;35:805–18.
- [12] Altman DG, Goodman SN. Transfer of technology from statistical journals to the biomedical literature. Past trends and future predictions. *JAMA* 1994;272:129–32.
- [13] Miettinen OS. Stratification by a multivariate confounder score. *Am J Epidemiol* 1976;104:609–20.
- [14] Schneeweiss S, Rassen JA, Glynn RJ, Avorn J, Mogun H, Brookhart MA. High-dimensional propensity score adjustment in studies of treatment effects using health care claims data. *Epidemiology* 2009;20:512–22.
- [15] Rogers EM. Diffusion of innovations. Toronto: Free Press; 2003.
- [16] Stake RE. Qualitative case studies. 3rd ed. Thousand Oaks, CA: SAGE Publications; 2005.
- [17] Yin RK. Applications of case study research. 2nd ed. Thousand Oaks, CA: SAGE Publications; 2003.
- [18] Haider M, Kreps GL. Forty years of diffusion of innovations: utility and value in public health. *J Health Commun* 2004;9(Suppl 1): 3–11.
- [19] Cadarette SM, Gagne JJ, Solomon DH, Katz JN, Stürmer T. Confounder summary scores when comparing the effects of multiple drug exposures. *Pharmacoepidemiol Drug Saf* 2010;19:2–9.
- [20] Arbogast PG, Ray WA. Performance of disease risk scores, propensity scores, and traditional multivariable outcome regression in the presence of multiple confounders. *Am J Epidemiol* 2011;174: 613–20.
- [21] Glynn RJ, Gagne JJ, Schneeweiss S. Role of disease risk scores in comparative effectiveness research with emerging therapies. *Pharmacoepidemiol Drug Saf* 2012;21:138–47.
- [22] Pike MC, Anderson J, Day N. Some insights into Miettinen's multivariate confounder score approach to case-control study analysis. *J Epidemiol Community Health* 1979;33:104–6.
- [23] Cook EF, Goldman L. Performance of tests of significance based on stratification by a multivariate confounder score or by a propensity score. *J Clin Epidemiol* 1989;42:317–24.
- [24] Stürmer T, Schneeweiss S, Brookhart MA, Rothman KJ, Avorn J, Glynn RJ. Analytic strategies to adjust confounding using exposure propensity scores and disease risk scores: nonsteroidal anti-inflammatory drugs and short-term mortality in the elderly. *Am J Epidemiol* 2005;161:891–8.
- [25] Wyss R, Lunt M, Brookhart MA, Glynn RJ, Stürmer T. Reducing bias amplification in the presence of unmeasured confounding through out-of-sample estimation strategies for the disease risk score. *J Causal Inference* 2014;2:131–46.
- [26] Arbogast PG, Kaltenbach L, Ding H, Ray WA. Adjustment for multiple cardiovascular risk factors using a summary risk score. *Epidemiology* 2008;19:30–7.
- [27] Saito R, Smoot ME, Ono K, Ruscheinski J, Wang PL, Lotia S, et al. A travel guide to Cytoscape plugins. *Nat Methods* 2012;9:1069–76.
- [28] Jick H, Miettinen OS, Neff RK, Shapiro S, Heinonen OP, Slone D. Coffee and myocardial infarction. *N Engl J Med* 1973;289:63–7.
- [29] Rothman KJ, Monson RR. Epidemiology of trigeminal neuralgia. *J Chronic Dis* 1973;26:3–12.
- [30] Miettinen O, Neff RK. Computer processing of epidemiologic data. *Hart Bull* 1971;2:98–103.
- [31] Tschardt T, Hochberg ME, Rand TA, Resh VH, Krauss J. Author sequence and credit for contributions in multi-authored publications. *Plos Biol* 2007;5:e18.