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ORIGINAL REPORT

Pharmacoepidemiology: defining the field and its core content

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ABSTRACT

Purpose Emerging interests in pharmacoepidemiology make it important to define the profession's core content. The International Society for Pharmacoepidemiology (ISPE)'s Education Committee sought to develop a consensus on its core disciplines. This report recapitulates their efforts and conclusions.

Methods The survey for skill inventories conducted characterized the field of pharmacoepidemiology by five categories of core competency/knowledge (pharmacovigilance, exposure data, epidemiology, clinical pharmacology, and medical product regulation) plus communication and leadership in these areas. It was sent to pharmacoepidemiology units within the industry, academia, and government representing the membership worldwide.

Results After three waves, 125 members responded (~10% of the membership). Respondents were from North America (61%), European Union (23%), and the remainder from Asian Pacific and South American regions, representing the full spectrum of ISPE membership. Pharmacovigilance, analysis of exposure data, epidemiologic methods, and communication skills were the competencies identified as essential. Fourteen competencies were judged to be "essential" by >80% of the respondents; a further 26 had "essential" as the most frequently rated category but represented <80% of the respondents. Six items had "desirable but not a core competency" as the most commonly selected. None of the proposed competencies scored as "not a core competency" by >25% of the respondents. Only five of the competencies were suggested as "not core" by 10% or more.

Conclusions This survey identified a wide range of content relevant to the field of pharmacoepidemiology. This list will likely evolve over time. A curriculum around these areas will help prepare the next generation of pharmacoepidemiologists. Copyright © 2012 John Wiley & Sons, Ltd.

KEY WORDS—pharmacoepidemiology; pharmacovigilance; International Society for Pharmacoepidemiology; core knowledge and functions

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INTRODUCTION

This report summarizes the current efforts and working conclusions of the International Society for Pharmacoepidemiology (ISPE) on the Core Content for the profession of Pharmacoepidemiology. We, as the Working Party, report on a multi-year membership–engagement process to study current concepts and approaches to the content of the field, develop and refine a proposed listing of that content, and finally, propose next steps.

Until now, no group has specified the core content of pharmacoepidemiology as a profession. This is not unexpected for a new and emerging discipline. Major public interest in drug safety surveillance and quantitative science surged following both the chloramphenical aplastic anemia international problem in the early 1950s and the early 1960's thalidomide disaster of unexpected and widespread teratogenicity. Industry and regulatory authorities alike created drug safety surveillance units, and major national efforts were launched to encourage/require improved and more extensive reporting of clinical adverse experiences (the spontaneous reports systems, pharmacovigilance, epidemiologic intelligence). Early efforts to study populations exposed to various therapeutic agents, including drugs, biologics, and devices, employed many of the traditional "hands-on" techniques and the population perspective of the epidemiologist.

By the late 1970s, pioneering work was in place to explore linkage of various medical data as well as to harness the potential power of automated medical

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insurance data and eventually electronic medical records. Such efforts were conducted with government support and encouragement. In the USA, in concert with the recommendation of the Joint Commission on Prescription Drug Use,[1] supported by the pharmaceutical industry association, PMA (now PhRMA), the Food and Drug Administration continued to formalize its program of multisource surveillance, and the industry recognized and supported such efforts and, itself, began to assemble staff internally to advance the efforts.

This evolution was mirrored in the European Union, particularly in the UK, France, Germany, and Sweden, where spontaneous reporting systems emerged and all, including the USA, were spurred by the activities of the International Centre for Drug Monitoring, first in Geneva and then in the late 1970s in Uppsala, Sweden, where reports from a growing number of countries were collected and available to member regulators.

With the occurrence of several drug safety issues in the late 1970s and early 1980s (e.g., phenformin,[†] propoxyphene,[‡] Bendectin/Debendox,[§] Reye's syndrome[¶]),[2–5] more structured drug safety activities evolved in industry and governments from around the world. Interest in the field led to the creation of the International Conferences in Pharmacoepidemiology in 1985 and, eventually, the founding of ISPE in 1989.

Kindred scholars from public health, the pharmaceutical industry, pharmacology, scientific computing and informatics, drug information, pharmacovigilance, and academic epidemiology convened and assisted the emerging efforts to create and name the professional field and celebrate its multidisciplinary nature. Academic units responded by training pharmacists, physicians, public health researchers, and others in pharmacoepidemiology.

Professional journals have emerged, notably *Pharmacoepidemiology and Drug Safety*, publishing scholarly work in the field.

These milestones emerged without an overall strategic plan from government, academia, or industry. Rather, this was the natural evolution of the field in response to the need to answer important public health questions that specifically related to prescription and over-the-counter (OTC) pharmaceuticals, vaccines, and other medical products. Yet, when ISPE reached its 20th anniversary, the field had not yet specified with any precision or detail the professional content, which makes up its scholarship.

Indeed, as the need for a trained, qualified workforce grows, this maturing field lacks an overall approach to its development. As an essential first step, agreement on core content can provide the catalyst for this development.

This state of affairs is hardly unique to the discipline of pharmacoepidemiology. Many other areas of professional activities and practice have realized this disconnect between incremental growth and rigorous planning and accountability in professional practice. Notable among these are the recent efforts of the Association of American Medical Colleges (AAMC) to inventory the competencies expected of physicians in drug safety and those of the Public Health Foundation's Council on Linkages between Academia and Practice to delineate the Core Competencies of Public Health Professionals. The latter are particularly useful guides for pharmacoepidemiology, given the eclectic nature of public health, practiced as it is by teams of diverse professionals, united around a common workplace and professional focus.

International Society for Pharmacoepidemiology leadership charged the Education Committee with defining the core content that can serve as the basis for a curriculum to train future practitioners and leaders in the field of pharmacoepidemiology. Thus, in 2008, ISPE undertook a multi-year process to delineate the core content of the field of pharmacoepidemiology.

METHODS

Organization

The Education Committee of ISPE undertook a coordinated effort to develop the core content of the field. To do so, a working party was named to oversee the effort and two of us (J. J. and H. T.) served as principal investigators.

Initial survey of skills, knowledge, and related content in pharmacoepidemiology

The leaders of several cooperating units of Pharmacoepidemiology from the industry, academia, and government were requested to submit any formal inventories of skills, knowledge, attitudes, or other competencies used in creating or supporting their programs. They also were

[†]Phenformin was an oral antidiabetic found in the 1970s to cause lactic acidosis and removed from the market in 1979.

[‡]Propoxyphene (Darvon®) was an analgesic that was initially the subject of a petition to remove it from the market in 1979 because of misuse and overdosing, but the petition was denied; an early risk management program (restriction of prescription size) started, and the product remained a target of drug safety concern until its removal from the market in late 2010.

[§]Bendectin/Debendox was a combination product of two antihistamines (dicyclomine and doxylamine) and pyridoxine (vitamin B6) widely used for nausea and vomiting of pregnancy in the 1950s through the early 1980s. It was alleged to be associated with birth defects, resulting in many epidemiological studies and worldwide regulatory discussions. Although it was not found to be associated with birth defects, the sponsor ultimately removed it from the market in the early 1980s.

[¶]Reye's syndrome, a serious condition resulting in hepatic failure and coma, was found to be associated with exposure to aspirin in the early 1980s, resulting in the restriction of use of aspirin in children.

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invited to provide position descriptions and other specified job requirements. From these, an initial list of commonly mentioned terms describing the content of work was developed. From this, the research team developed a nominated list of functional skills, knowledge, and behavioral skills (group problem solving and communications), which one might expect a professional to possess to accomplish this work.

Nominated inventory

We selected the framework for listing competencies utilized by the AAMC [https://www.aamc.org/initiatives/54242/meded/].[6] Practice requirements were grouped according to related descriptors and listed. This inventory, in the form of a questionnaire, was then vetted and revised with members of the ISPE Education Committee for cogency, relevancy, and completeness. As a decision rule, only those descriptors of activities, which appeared to the Committee to be candidates for content, which "...every professional in the field should possess," were included in the survey. Highly specialized skills were to be reserved for subsequent (non-core) inventories.

Survey

It was proposed that the field of pharmacoepidemiology includes the following: (i) knowledge of drug safety surveillance, or pharmacovigilance; (ii) regulatory requirements; (iii) research epidemiology (particularly as applied to the study of the use and effects of drugs); (iv) clinical pharmacology (the study of effects of drugs in man); and (v) related areas such as risk management and drug utilization. Categories of types of competencies were defined as knowledge, functional competence, communications, and leadership. The categories for the specific are summarized in Table 1.

The resulting list of items nominated as potential core competencies was described, with the intent and possible role for each, in an electronic mailing to all ISPE members, along with an accompanying electronic survey. Members were invited to support or oppose inclusion of each item as a core element on a three-point continuum: "essential," "desirable but not core," or "not a core competency." Commentary and nomination of further items for the list were invited. The survey included an initial and two-wave follow-up solicitation from all members.

Membership validation

At the annual International Conference on Pharmacoepidemiolgy (ICPE) (Providence RI, August 2009), an open forum was held at which the findings from the survey were presented, and further comment was elicited from the membership.

RESULTS

One hundred twenty-five members responded to the survey sent in three waves. Characteristics of responders are shown in Tables 2 and 3. The survey elicited interest from a diverse group of members, representing the full spectrum of ISPE membership.

Table 2. Country of respondents

North and South America		**76**
	Argentina	1
	Canada	2
	Colombia	1
	USA	72
Europe		**34**
	Bosnia and Herzegowina	1
	Croatia	1
	Denmark	1
	Finland	2
	France	3
	The Netherlands	5
	Spain	2
	Sweden	8
	Switzerland	3
	UK	8
Africa		**2**
	Kenya	1
	Sudan	1
Middle East		**1**
	Saudi Arabia	1
Asia		**6**
	India	1
	Japan	1
	Malaysia	1
	Singapore	1
	Taiwan	2
Australia/New Zealand		**4**
	Australia	3
	New Zealand	1

Table 1. Categories of competencies evaluated

	Core competencies			
	Knowledge	Functional	Leadership	Communication
Pharmacovigilance	X	X	X	X
Analysis of exposure data	X			
Pharmacoepidemiology	X	X	X	X
Clinical pharmacology	X			
Medical product regulation	X			

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Table 3. Characteristics of the 125 respondents*

Institutional affiliation	Percent of total
Academic	**37**%
Government	**12**%
Industry	**38**%
Consulting	**14**%
Other	**4**%
Tenure in pharmacoepidemiology?	
> 20 years	**12.8**%
11–20 years	**28.8**%
6–10 years	**25.6**%
3–5 years	**17.6**%
1–2 years	**11.2**%
< 1 year	**4**%
Level of seniority in pharmacoepidemiology	
Student	**6**%
Research associate/assistant	**2**%
Project management/research	**27**%
Supervisory in industry/consulting	**39**%
Academic associate or full professor	**24**%
Other	**8**%

*Note that some responded to more than one category, so responses do not all add up to 100% for each question.

The resulting inventory of proposed core competencies and the accompanying scores from the membership survey, as well as comments are presented fully in APPENDIX 1 and summarized in Tables 4–7.

Fourteen of the competencies listed were judged to be "essential" by >80% of the respondents. These included various functional, knowledge, and communication competencies in pharmacoepidemiology and knowledge competencies in pharmacovigilance and analysis of exposure data. An additional 26 had "essential" as the most frequently rated category, but this represented less than 80% of the respondents. Finally, six items had "desirable but not a core competency" as the most commonly selected category. None of the proposed competencies was scored as "not a core competency" by 25% or more of the respondents. Only five of the nominated competencies were suggested as "not core" by 10% or more, generally with similar proportion rating as "not core" by those with different levels of experience and among those with academic and industry affiliations

Table 4. Rating of knowledge competencies

Greater than 80% rated as "Essential"	Less than 80% rated as "Essential" but "Essential" was most frequently rated category	"Desirable but not core" was most frequently rated category	>10% Rated as "Not a Core Competency"
Pharmacovigilance			
Definitions of adverse event vs. adverse drug reaction	Common drug-associated conditions	MedDRA Coding principles and SMQs (grouping codes)	MedDRA Coding principles and SMQs (grouping codes)
Meaning/use of spontaneous reports in drug safety	Types of adverse events by mechanism		
	Definitions, uses and limitations of data mining techniques		
	Interpretation of grouped data on spontaneous reports		
Analysis of exposure data			
Knowledge of types of data on drug use (and examples)	Strengths and limitations of other measures of exposure (person-time, DDDs)	Prescription sequence analysis	Prescription sequence analysis
Strengths and limitations of cross-sectional prescription data		Analysis of drug use adherence and switching	
Epidemiology			
Knowledge of basic epidemiology study designs and their usual hierarchy	Types of data used for these studies with examples		
Strengths, limitations and selection of best designs	Examples of uses of each in pharmacoepidemiology	Quantitative approaches to benefit-risk assessment	
Clinical pharmacology			
	Knowledge of basic principles of drug actions		
	Understanding of basic pharmacokinetics/ pharmacodynamics		
	Familiarity with concepts of drug-drug interactions		
	Understanding of the information gained in the basic phases of drug development (Pre-clinical, Phases 1–3 and 4)		
Medical product regulation and decision making			
	Basic understanding of drug regulatory laws and agencies	Formulary decision making and control processes	Formulary decision making and control processes

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Table 5. Rating of functional competencies

Greater than 80% rated as "Essential"	Less than 80% rated as "Essential" but "Essential" was most frequently rated category	"Desirable but not core" was most frequently rated category	>10% Rated as "Not a Core Competency"
Pharmacovigilance			
	Evaluate seriousness, expectedness of individual spontaneous reports based upon operant regulations		Evaluate seriousness, expectedness of individual spontaneous reports based upon operant regulations
	Determine, on the basis of review of spontaneous reports (prior and recent), plus ancillary literature and related information on whether a "Signal" is likely present		
	Identify and use the range of relevant resources to qualify or eliminate a possibly signal as a strengthened hypothesis		
Epidemiology research methods			
Design an epidemiology study of both an ad hoc and database type, including:	Design an epidemiology study of both an ad hoc and database type, including:		
Cohort study	Cross-over studies		
Case–control and case-cohort studies	Registry studies		
Assure that the study designs incorporate good pharmacoepidemiology practices	Critique of meta-analysis methods of clinical trials and epidemiology studies and understand their usefulness		
Describe methods of statistical analysis and controls for confounding and biases			
Describe limitations and methods to address these limitations			
Interpretation of results in the context of public health and regulatory decision making			

(data not shown). Among these five, "desirable but not a core competency" was the most frequent rating category for all but one.

A wide range of additional comments were provided (see APPENDIX 1) in particular, providing suggestions on other areas that should be included (e.g., statistics, drug utilization studies). Notable also were a few comments and responses that reflected the view that pharmacovigilance and pharmacoepidemiology are quite separate. Another divergence was reflected in responses to the clinical pharmacology and clinical medicine topics: some opined this was essential, whereas a small group of other respondents did not view these clinical issues as "core."

DISCUSSION

This activity was undertaken to define the core content of the field of pharmacoepidemiology. The respondents to our survey identified relevance to pharmacoepidemiology of almost all of the proposed content. Few items received consistent rating as "not core" from participants. Among these, there was no uniform opposition to any. Although there was general agreement that most items were essential or desirable, only pharmacovigilance, analysis of exposure data, epidemiologic research methods, and communication skills were the knowledge competencies that were identified as essential by 80% or more respondents. Rather, many of the content areas were viewed by 20% to 60% of the respondents as being "desirable, but not core" to the field. Various functional, knowledge, and communication competencies in pharmacoepidemiology and knowledge competencies in pharmacovigilance and analysis of exposure data were the areas most strongly endorsed by the respondents.

A few items had differential ratings by those with academic affiliations as compared with industry affiliation. In general, those with academic affiliations were more likely to rate more complex scientific items as essential, whereas those with industry affiliation were more likely to rate facilitation skills and knowledge of MedDRA coding principles as essential (Table 7). This highlights a possible division in the field between those

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Table 6. Categorization of leadership and communication competencies

Greater than 80% rated as "Essential"	Less than 80% rated as "Essential" but "Essential" was most frequently rated category	"Desirable but not core" was most frequently rated category	>10% Rated as "Not a Core Competency"
Leading group problem solving in pharmacovigilance			
	Direct a group to determine if a pharmacoepidemiology study is needed and its value and limitations if done. Direct a group to identify the parameters of an identified risk, including root cause, to contribute to the design of a Risk Management plan and its evaluation	Direct a group (e.g., Labeling Committee) to consensus on whether a new adverse event requires label changes and other regulatory actions	Direct a group (e.g., Labeling Committee) to consensus on whether a new adverse event requires label changes and other regulatory actions
Leading group problem solving in pharmacoepidemiology			
	Facilitate and develop conclusions from a group's review of a critical pharmacoepidemiology study or studies to arrive at regulatory or formulary coverage decisions—including ability to summarize strengths, weaknesses, and methods to validate/refute Direct a group to the design of a Risk Management plan or REMS and its long-term evaluation		
Communications in pharmacovigilance (the ability to communicate)			
	Communicate the appropriate interpretation of a signal of a possible serious adverse event that may be confounded to clinical, regulatory, and other colleagues and also explain the pros and cons of the various actions that may follow Communicate the strengths and limitations of various interventions in a strong and/or a limited risk management plan and their long-term implications from public health, regulatory and business perspective.		
Communications in pharmacoepidemiology (the ability to communicate)			
The results of a pharmacoepidemiology study to a group of non-epidemiology scientists, placing the study and its design in context, explaining strengths and weakness, and options for interpretations and action	The design and strengths of a risk management plan to non-pharmacoepidemiology colleague to explain the value, implementations, ongoing operations, and implications for the enterprise and the product.		

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Table 7. Areas with 20% or greater difference in rating as "Essential" or "Not Core" by academia or industry affiliated respondents*

	Academic	Academic	Industry	Industry
	Percent rating as "Essential"	Percent rating as "Not Core"	Percent rating as "Essential"	Percent rating as "Not Core"
Knowledge of MedDRA coding principles	25%	16%	50%	13%
Knowledge of types of adverse events by mechanism	72%	5%	42%	13%
Understanding of basic pharmacokinetics/pharmacodynamics	61%	2%	40%	2%
Familiarity with concepts of drug–drug interactions	72%	2%	48%	0%
Understanding of the information gained in the basic phases of drug development (Pre-clinical, Phases 1–3 and 4)	80%	2%	58%	0%
Facilitate and develop conclusions from a group's review of a critical pharmacoepidemiology study or studies to arrive at regulatory or formulary coverage decisions—including ability to summarize strengths, weaknesses, methods to validate/refute	59%	9%	85%	2%

pharmacoepidemiologists who embrace and include the management and assessment of spontaneous reports (pharmacovigilance) within their purview and those who do not. This division was underscored by a single respondent who protested that he/she could not reasonably complete the survey because the pharmacovigilance items are not part of his/her experience as a pharmacoepidemiologist.

It is important to understand that the breadth of pharmacoepidemiology results in a wide range of content. As with many professional fields, sub-specialization means that the content described as core to the field does not apply equally to all pharmacoepidemiologists. We have not attempted to combine these into groups defined by area of specialization nor have we defined the level of sophistication appropriate for specific core areas that are applicable to all pharmacoepidemiologists regardless of their focus. Practically, many who will work in the field may start in academia and then pursue further work in either regulatory bodies or the industry. This migration underlines the importance of a core set of terminologies and understanding. Future efforts are needed to define the content of competencies for all in contrast to more in-depth content in sub-areas for the more expert/specialized in the field. Undoubtedly, those developing curriculum and job descriptions would combine these into groups most applicable to their goals.

The purpose of this exercise was to begin to define the content that composes pharmacoepidemiology. These data, derived from a very diverse group of pharmcoepidemiologist and further discussed in a public ICPE forum, should provide guidance to those wishing to develop comprehensive curricula, certificate, and degree programs. For students considering training in pharmacoepidemiology, this document can provide an outline for self-assessment and identifying educational needs. For employers, these topics provide the outline of professional strengths around which to conduct employment interviews, build programs, and structure life-long learning and continuing education efforts.

The core content listings described in this document are not meant to be constraining or to stifle creativity and diversity within the field. Pharmacoepidemiology is a young field with rapidly evolving challenges and opportunities. Training in or hiring around the core content alone cannot assure preparation for the many and varied pathways ahead. Furthermore, this document is intended for broad application in the field. Although eventually these may contribute to considerations regarding credentialing of individuals or educational programs, we emphasize that such considerations are appropriately reserved for a future time when the field has agreed upon, established, and developed the practice around its core competencies.

LIMITATIONS

This proposed inventory should be viewed as the first, but by no means the ultimate, set of such content for Pharmacoepidemiology. The process of nomination was, perforce, limited; further and/or different nominated content will doubtless emerge as more centers and units become more familiar with them. Likewise, a relatively small proportion of membership responded to the electronic survey, and the representativeness of the respondents cannot be assured. Finally, the proposed content has not been "field tested" by those for whom their usefulness is proposed.

CONCLUSIONS

Pharmacoepidemiology remains a diverse and evolving field. This exercise has identified a wide range

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of content that is deemed relevant to the field, including knowledge, functional, leadership, and communication domains. Although these will be of immediate value to educators, students, and employers, it is anticipated that the list of content will evolve over time. Although it is unlikely that many individuals would have expertise in all of the areas described, creation of a curriculum around the range of skills and knowledge areas relevant to the field will help prepare the next generation of pharmacoepidemiologists.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

KEY POINTS

- An international survey captured opinions on key areas of knowledge and function in pharmacoepidemiology.
- Epidemiology and its research methods, pharmacovigilance, evaluation of exposure, and communications in these areas were rated "essential" by over 80% of the 125 respondents.
- This effort of gathering international opinion of pharmacoepidemiologists representing the academia, industry, and regulatory professionals in pharmacoepidemiology has provided a useful compilation of candidate topics for educational programs in pharmacoepidemiology.

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APPENDIX 1

RESULTS FROM SURVEY ON COMPETENCIES IN PHARMACOEPIDEMIOLOGY

Q 1. Are there any other competency CATEGORIES that should be included?

Answer Options	Response Count
	22
No	11
Basic statistical knowledge	1
Regulatory reporting requirements	1
Ethics	1
Administrative	1
"skills"	4
Basic understanding of health services, outcome, social epidemiology research & public health decision making	1
Experience	2
Attitude	1

*One respondent noted both skills and experience.

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2. The following Knowledge Competencies for PHARMACOVIGILANCE are (ANSWER ONLY ONE CHOICE):

	answered question			125
	skipped question			0
	1. Essential	2. Desirable but not core	3. Not a core competency	Response Count
a. Definitions of adverse event vs. adverse drug reaction	**84.2% (101)**	14.2% (17)	1.7% (2)	120
b. MedDRA Coding principles and SMQs (grouping codes)	36.4% (44)	**50.4%(61)**	13.2% (16)	121
c. Common drug-associated conditions	**63.2% (74)**	33.3% (39)	3.4% (4)	117
d. Types of adverse events (A, B, and others) by mechanism	**60.2% (71)**	33.1% (39)	6.8% (8)	118
e. Meaning/use of spontaneous reports in drug safety	**88.1% (104)**	11.0% (13)	0.8% (1)	118
f. Definitions, uses, and limitations of data mining techniques	**61.9% (73)**	36.4% (43)	1.7% (2)	118
g. Interpretation of grouped data on spontaneous reports	**70.6% (84)**	27.7% (33)	1.7% (2)	119

Other verbal replies = 10

Comments on other topics:

- FDA/WHO ADR reporting mechanism—strength and weakness;
- Assessment of causality in single cases;
- "Definitions" of ADE and ADR are not important, per se, but the concept that everything associated with a drug is not actually caused by the drug is important. I did not like the phrasing of the first question; main adverse reporting databases;
- General understanding of ascertainment of safety endpoints in clinical trials and associated labeling;
- Understand that the main purpose of pharmacovigilance is signal generation, not quantification;
- Regulatory reporting requirements in USA and EU clinical and postmarketing surveillance;
- Common definitions used for postmarketing reporting, such as challenge, dechallenge, seriousness of ADR, suspect drug, etc;
- AE reporting in observational studies;
- Ability to define and cite examples of the principles and practices of "Public Health Surveillance & Response";
- All items (a–g) are essential core competencies for all levels of pharmacoepidemiologists.

3. The Knowledge Competencies in ANALYSIS OF EXPOSURE DATA may include:

	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Knowledge of types of data on drug use (and examples)	**87.2% (109)**	12.0% (15)	0.8% (1)	125
b. Strengths and limitations of cross-sectional prescription data	**80.0% (100)**	17.6% (22)	2.4% (3)	125
c. Strengths and limitations of other measures of exposure (person-time, DDDs)	**78.4% (98)**	21.6% (27)	0.0% (0)	125
d. Prescription sequence analysis	35.2% (44)	**53.6%(67)**	11.2% (14)	125
e. Analysis of drug use adherence and switching	44.4% (55)	**53.2%(66)**	3.2% (4)	124

Comments on other topics.

- Sources and implications of misclassification of exposure; consideration of latent or induction periods or lag times in exposure definition;
- Measurements of exposure for given events and implications for risk calculations (i.e., controlling for immortal time bias);
- Understanding prescription/dispensing/taking drug distinctions; limitations of postmarketing spontaneous reporting and exposure estimates;
- Aggregate safety reports (PSURs, PADERS, IND ANNUAL, EU annual, DSURS< ISS for NDA/Bla/maa SUBMISSIONS;
- Data needed and methods to collect and estimate historical data on baseline and on-study exposure and duration of exposure in observational studies;
- Relationships, or lack thereof, between self-reported exposure and biological evidence of exposure/absorption;
- Understanding of how the underlying data are collected and limitations of these data, including knowledge of formulary reimbursed, capture of OTC drugs.

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4. The Knowledge Competencies in EPIDEMIOLOGY include:				
	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Knowledge of basic epidemiology study designs and their usual hierarchy	**96.0% (120)**	4.0% (5)	0.0% (0)	125
b. Strengths, limitations and selection of best designs	**95.2% (119)**	4.8% (6)	0.0% (0)	125
c. Knowledge of the range of epidemiological methods and databases to address several types of signals, including a potentially very rare, unusual or new event, a rare event of a known drug-associated type, a common event (e.g., myocardial infarction), and a severely confounded event (e.g., suicide) with their strengths and limitations	**86.4% (108)**	12.8% (16)	0.8% (1)	125
d. Types of data used for these studies with key examples	**72.0% (90)**	26.4% (33)	1.6% (2)	125
e. Key examples of uses of each in pharmacoepidemiology	**67.2% (84)**	32.8% (41)	0.0% (0)	125
f. Quantitative approaches to benefit-risk assessment	44.8% (56)	**51.2% (64)**	4.0% (5)	125
f. Familiarity with Good Pharmacoepidemiology Practices guideline	**77.6% (97)**	20.8% (26)	2.4% (3)	125

5. The proposed Knowledge Competencies in CLINICAL PHARMACOLOGY include:				
	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Knowledge of basic principles of Drug actions	**71.2% (89)**	27.2% (34)	2.4% (3)	125
b. Understanding of basic pharmacokinetics/pharmacodynamics	**53.6% (67)**	44.8% (56)	1.6% (2)	125
c. Familiarity with concepts of drug-drug interactions	**64.8% (81)**	34.4% (43)	0.8% (1)	125
d. Understanding of the information gained in the basic phases of drug development (Pre-clinical, Phases 1–3 and 4)	**71.2% (89)**	28.8% (36)	0.8% (1)	125

Comments on other topics.

- This should either be expanded or create a new category: knowledge of disease area (although this might be how to gain the knowledge and understand if no clinical training background).
- Too much emphasis on the math when approaching these studies.
- I sometimes fail to see how someone without clinical training can even perform pharmacoepidemiology studies—never seen a patient, understanding standard of care, really grasping what these data mean other than just a set of variables.
- Question d is not a component of Clinical pharmacology. It is a question for another category such as methods to ascertain the safety and efficacy of a medical product. An additional understanding of how these trial designs might differ progressing through the phases, etc. Too many epidemiologists do not understand that all clinical trials are not randomized.
- Half life is only a component to understanding medicines and the temporal relationship of the AE. Can all of this be related to pharmacodynamics or are you only discussing the pharmacodynamics of the effectiveness outcome?
- Also, understanding the potential role of genetics in drug reactions; systemic toxicology; Consider changing title of 5 to clinical development because of the inclusion of information gained in phase i–iv;
- Knowledge of basic toxicology principles and studies; understanding of PK/PD in pregnancy and lactation; basic concepts of teratogenicity; basic understanding of the normal physiology, and most common lab tests (purpose, type) and other diagnostics procedures;
- ADRS by body system typical with drug induced disease;
- The ability to carry out a critical assessment of literature, and a knowledge of resources like the "Cochrane Collaboration" for systematic reviews of literature.

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6. Knowledge Competency in MEDICAL PRODUCT REGULATION AND DECISION MAKING include:				
	answered question			125
	skipped question			0
	Essential	Desirable but not essential	Not a core competency	Response Count
a. Basic understanding of drug regulatory laws and agencies	**70.4% (88)**	25.6% (32)	4.0% (5)	125
b. Formulary decision making and control processes	28.2% (35)	**54.8% (68)**	16.9% (21)	124

Comments on other topics:

- Risk Management Plan guidance and REMS;
- What is a label? What data are in a newly approved label and quality of the data? What is a dear doctor letter? What information is added after drug approval, quality of data and types of sources. location of information in a label, etc etc.
- How about advisory committees and role. NDA, BLA, amendments;
- Up-to-date familiarity with risk management (REMS) regulations, policies and landscape; decision analytic models, policy analysis; safety reporting requirements;
- I would say more than basic understanding of regulations. a full command of regulations is essential; regulation is jurisdiction specific—but also important to recognize how one impacts the other.

7. The proposed FUNCTIONAL COMPETENCIES in PHARMACOVIGILANCE include the ability to:				
	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Evaluate seriousness, expectedness of individual spontaneous reports based upon operant regulations	**64.0% (80)**	21.6% (27)	14.4% (18)	125
b. Determine, on the basis of review of spontaneous reports (prior and recent), plus ancillary literature and related information on whether a "Signal" is likely present	**72.0% (90)**	24.0% (30)	4.0% (5)	125
c. Identify and use the range of relevant resources to qualify or eliminate a possibly signal as a strengthened hypothesis	**68.0% (85)**	31.2% (39)	1.6% (2)	125

Comments re other topics.

- PSURs, updates, REMS, RiskMaps, etc.
- Who provides information for spontaneous information, quality of the data, missingness, numerator and denominator issues, reporting rates as influenced by various factors;
- Conduct systematic review and analysis of spontaneous data that includes description of data, search strategies, case definitions, adjudication process and findings; missed all about clinical safety surveillance phase 1-3 and evaluating ICSRs premarketing and during clinical development.
- Knowing sources of postmarketing reports, literature, ADR evaluation, and so on.. this section needs to be more robust; these are core competences for a drug safety scientist, not for pharamacoepidemiologists; and add: Ability to communicate effectively the conclusions and implications of pharmacovigilance analyses. Ability to go beyond regulatory reporting requirements to medical and scientific inference. **Finally, three technical comments**: don't understand distinction between b and c; don't understand what 7a means; these are core competences for a drug safety scientist, not for pharmacoepidemiologist; 'c'—not clear what it means.

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8. The proposed Core Functional Competencies in PHARMACOEPIDEMIOLOGY include:

	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Design an epidemiology study of both an ad hoc and database type, including:	**93.0% (106)**	7.0% (8)	0.0% (0)	114
o Cohort study with suitable comparison groups	**94.3% (115)**	4.1% (5)	1.6% (2)	122
o Efficient sampling designs: Case-control and Case-cohort studies	**89.4% (110)**	8.9% (11)	1.6% (2)	123
o Cross-over studies	**62.3% (76)**	36.1% (44)	1.6% (2)	122
o Registry studies	**73.8% (90)**	23.8% (29)	2.5% (3)	122
b. Assure that the study designs incorporate Good Pharmacoepidemiology Practices	**85.4% (105)**	13.0% (16)	1.6% (2)	123
c. Describe methods of statistical analysis and controls for confounding and biases	**85.6% (107)**	13.6% (17)	0.8% (1)	125
d. Describe limitations and methods to address these limitations	**88.8% (111)**	10.4% (13)	0.8% (1)	125
e. Interpretation of results in the context of public health and regulatory decision making	**80.6% (100)**	20.2% (25)	0.0% (0)	124
f. Critique of meta-analysis methods of clinical trials and epidemiology studies and understand their usefulness	**69.9% (86)**	30.1% (37)	0.8% (1)	123

Comments:

- Not sure how registry studies differ from cohort studies;
- Describe the methods of early post-marketing surveillance, including cohort event monitoring; selection of drugs to monitor; expectations; strengths and weaknesses; not only describe limitations but how about its actual impact on study results. Without excellent study design the power means nothing. Interpretation of a RR of clinical importance (say RR of 2) and a CI crossing 1. Do we ignore it?; design of studies properly is a senior competence; I would not encourage those with basic knowledge to be able to design studies without oversight from an experienced person; basic knowledge of pregnancy registries and data collection on drug exposure during pregnancy; and add: Ability to communicate effectively the conclusions and implications of epidemiologic analyses. Defend, as appropriate observational research for the discovery of drug effects in a corporate and regulatory culture dominated by RCTs.

9. Competencies in Leading GROUP PROBLEM SOLVING IN PHARMACOVIGILANCE

	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Direct a group (e.g., Labeling Committee) to consensus on whether a new adverse event requires label changes and other regulatory actions	42.4% (53)	**43.2% (54)**	14.4% (18)	125
b. Direct a group to determine if a pharmacoepidemiology study is needed and its value and limitations if done.	**55.2% (69)**	40.0% (50)	4.8% (6)	125
c. Direct a group to identify the parameters of an identified risk, including root cause, to contribute to the design of a Risk Management plan and its evaluation	**49.6% (62)**	43.2% (54)	7.2% (9)	125

Comments:

- Collaborate with a group of clinicians, statisticians, and others to design / conduct / publish pharmaoepidemiology studies;
- Leadership, negotiation and influencing skills are key to success in an industry setting. They are not essential at hire and can be developed if there is desire and a basic aptitude;
- Whether or not directing a group is a core competency may depend on the level of the position (e.g., staff position vs. administrative/leadership position).
- **And, technical comments**: not sure of the definition of "leading"; NOTE: These are not usually tasks for the pharmacoepidemiologists in my company - done by medical product specialists; I would restate b and c. Direct a group in the design, implementation and evaluation of risk mitigation strategies for confirmed safety risks for a spectrum of interventions ranging from label changes to pharmacoepidemiologic studies.

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10. Competencies in Leading GROUP PROBLEM SOLVING IN PHARMACOEPIDEMIOLOGY				
	answered question			125
	skipped question			0
	Essential	Desirable but not core	Not a core competency	Response Count
a. Facilitate and develop conclusions from a group's review of a critical pharmacoepidemiology study or studies to arrive at regulatory or formulary coverage decisions-including ability to summarize strengths, weaknesses, methods to validate/refute	**67.2% (84)**	26.4% (33)	6.4% (8)	125
b. Direct a group to the design of a Risk Management plan or REMS and its long-term evaluation	**48.8% (61)**	43.2% (54)	8.0% (10)	125

Comments:

- Must be clear on what validation means. Too many say that the physician review of codes is "validation" vs case reviews in some manner; NOTE: We participate, but don't lead for RMPs-REMS development - so ability to contrubute epidemiology expertise is essential, ability to lead process is not; direct a group in the review and evaluation of integrated safety data from pre-clinical, clinical and post-market settings;
- Understanding who the key stakeholders are, and include them in the discussion; this leadership requires experience; this may be core, but it depends on the level of the position (e.g., Pharmacoepidemiologist vs. Sr. Director of Pharmacoepidemiology and Risk Management.

11. Proposed Competencies in COMMUNICATIONS IN PHARMACOVIGILANCE include the ability to:				
	answered question			125
	skipped question			0
	Essential	Desirable but not a core competency	Not a core competency	Response Count
a. Communicate the appropriate interpretation of a signal of a possible serious adverse event that may be confounded to clinical, regulatory and other colleagues and also explain the pros and cons of the various actions that may follow	**77.6% (97)**	22.4% (28)	0.8% (1)	125
b. Communicate the strengths and limitations of various interventions in a strong and/or a limited risk management plan, and their long-term implications from public health, regulatory and business perspective.	**66.4% (83)**	28.0% (35)	5.6% (7)	125

Comment. a. should not call out confounding. There are many limitations to data that require careful interpretation.

12. The proposed Core Competencies in COMMUNICATIONS IN PHARMACOEPIDEMIOLGY include the ability to communicate:				
	answered question			125
	skipped question			0
	Essential	Desirable but not a core competency	Not a core competency	Response Count
a. The results of a pharmacoepidemiology study to a group of non-epidemiology scientists, placing the study and its design in context, explaining strengths and weakness, and options for interpretations and action	**84.0% (105)**	14.4% (18)	1.6% (2)	125
b. The design and strengths of a risk management plan to non-pharmacoepidemiology colleague to explain the value, implementations, ongoing operations and implications for the enterprise and the product.	**62.4% (78)**	30.4% (38)	7.2% (9)	125

Comment: Essential, relates to the "influencing" or educating skills described above. Goes beyond explaining to non-epi scientists but also non-scientists.

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