THANK YOU FOR JOINING ISMPP TODAY!

The program will begin promptly at 11:00 am EDT

November 18, 2015
ISMPP WOULD LIKE TO THANK

... the following Titanium and Platinum Corporate Sponsors for their ongoing support of the Society:

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ISMPP ANNOUNCEMENTS

• This program qualifies for 1 credit towards recertification

• Registration for the 2016 European Meeting of ISMPP is now open!

• Call for abstracts now open for the 12th Annual Meeting of ISMPP. Deadline is Friday, January 8, 2016

• Be sure to complete the 12th Annual Meeting Roundtable Survey – help us select topics YOU want to discuss. Survey closes next Tuesday, November 24th
2016 EUROPEAN MEETING OF ISMPP
19-20 January, London

• A focus on **practical** skills that drive successful publication delivery

• GPP3, RWE, data & financial transparency, guidelines & regulations, journal selection and new journal features

• Peer exchange, expert-led roundtables, member presentations, extended Q&As, interactive panel discussions

• Attendees will leave with ideas they can use the day they return to work
Day 1: Tuesday 19 January 2016 - Highlights

- **GPP3 Panel Discussion**
  - GPP3 authors & expert editors answer your questions

- **Real World Evidence and Publications**
  - With Richard White, Oxford PharmaGenesis

- **Roundtables**
  - Attendees can join **three** different tables, some eligible for CMPP credit

- **Data & Financial Transparency Reporting**
  - Representatives from EMA, EFPIA and industry

- **Evening Poster Presentation & Networking Reception**
Day 2: Wednesday 20 January 2016 - Highlights

- **Publishing & Journals: Practical Considerations in 2016**
- **SPEED Research**
  - Authors have 10 minutes to present their research
- **Parallel sessions: Other Guidelines & Regulations**
  - Attendees select two from three 45-minute sessions:
    1) Copyright
    2) Corporate Integrity Agreements
    3) EQUATOR
- **Keynote Address: Publications Pioneer Vitek Tracz on “The Future of Publications”**
CMPP™: COULD YOU BE A MENTOR?

ISMPP is seeking volunteers to provide mentorship to individuals considering sitting for the exam or who have questions related to recertification

• Must be CMPP™ certified and willing to be listed on the ISMPP website

• Please email cmpp@jsmpp.org to register your interest
FOR YOUR BEST ISMPP U EXPERIENCE . . .

To optimize your webinar experience today:

• Use a hardwired connection if available

• Use the fastest internet connection available to you

• If you are accessing the presentation over your computer, please be sure to increase the volume of your computer speakers
QUESTIONS...

• To ask a question, please type your query into the Q&A box
  • To ensure anonymity and that all panelists receive your question, please choose the drop down box option, "ALL Panelists"
  Otherwise, all audience members will be able to see your submitted question
• We will make every effort to respond to all questions

NOTE: Make sure you send your question to “ALL Panelists”
BIO-STATS PRIMER AND WORKING COLLABORATIVELY WITH STATISTICIANS FOR PUBLICATION PLANNING PROFESSIONALS
INTRODUCTIONS

• **FACULTY: Jay Hsu** earned his bachelor degree in Business Mathematics from Soochow University in Taiwan in 1983. Then he served 2 years in the army before he came to the US to receive his MS and Doctoral degree in biostatistics from The University of Alabama in Birmingham. Dr. Hsu was then a research assistance professor at University of Alabama in Birmingham for 4 years teaching biostatistics in medical school and school of public health. He also worked for the Blue Cross and Blue Shield of Alabama as a consultant to detect medical frauds in Medicare/Medicaid for 2 years. In 1999, Dr. Hsu changed his career to the pharmaceutical industry. In the past 16 years, Dr. Hsu worked for Wyeth, Novartis, and now for Sunovion since 2008.
INTRODUCTIONS

• **FACULTY: Meg Franklin** has over 10 years of experience in the health economics and outcomes research arena. She has consulted for pharmaceutical consulting companies, and spent several years in academia as an Associate Professor at the Presbyterian College School of Pharmacy in South Carolina. Over the last decade she has written numerous scientific publications, conducted retrospective database studies, developed economic models, drafted value messages, and provided strategic consulting to pharmaceutical companies. Her primary expertise is in research design and methodology, particularly retrospective analyses. She holds a PharmD and PhD from the University of South Carolina.

Dr. Franklin has worked across a myriad of therapeutic areas. Recent areas of focus include the following: oncology (pancreatic, lung, and breast cancers, multiple myeloma, melanoma, and chemotherapy induced nausea and vomiting), hepatitis, diabetes, cardiovascular disorders, epilepsy, multiple sclerosis, hemophilia, and rheumatoid arthritis. She also has experience working with rare/orphan diseases. Prior to entering the HEOR arena, she completed an ASHP accredited pharmacy practice residency and worked as a clinical pharmacist.
INTRODUCTIONS

• **MODERATOR:** Tom Drake has been involved in medical communications for over twenty-five years. He began his career in the pharmaceutical industry as a product and marketing manager, with postings in the United States, Europe and the Far East. In 1990 Tom founded and launched the healthcare marketing trade publication, *Product Management Today (PMT)*. He was publisher and editorial director for its first six years. *PMT* targeted over 10,000 healthcare marketers and helped pioneer the focus on marketing management’s professional growth and development. Tom has been involved in most areas of medical communications including: global publication planning, continuing medical education, thought leader development, HEOR and Market Access, digital and web based communications, consumer healthcare communications, market research and healthcare marketing. He has been an active member of ISMPP since 2008 and most recently was chair of the ISMPP-U committee and remains a committee member. In 2014 Tom launched the Global Outcomes Group, an independent agency supporting HEOR and Market Access communications for the bio/pharma and medical device industries.
DISCLAIMER

• Information presented reflects the personal knowledge and opinion of the presenters and does not represent the position of their current or past employers or the position of ISMPP.
At the end of this presentation, attendees should be able to:

• Gain an understanding of statistical methods for medical and life sciences
• Understand the role of biostatisticians in industry-supported clinical research
• Understand how biostatistics and medical affairs can best collaborate together
• Have knowledge of educational opportunities and/or ways to improve clinical research skills as medical publication professionals
HOW BIOSTATISTICS WORK
WITH MEDICAL AFFAIRS FOR
PUBLICATION SUPPORT

Jay Hsu, PhD
Executive Director, Biostatistics
Sunovion Pharma Inc.
OUTLINE

• Who are we? Where do we stand in company’s organization chart?
• What do we do?
• Why biostatistics and Medical Affairs (MA) need to work together?
• What are the problems?
• How much work to do?
• How do we handle it?
WHO ARE WE IN COMPANY ORGANIZATION CHART?

In my company:

CDMA

MA

Data Science

ClinOps

ClinRes

MI

MSL

HEOR

Stats

PGM

DM

...
WHAT DO BIOSTATISTICIANS DO?

- Participate study design, protocol development, & study conduct for all phase studies
- Statistical Analysis Plan (SAP) developments
- Study Tables/Listings/Figures (TLFs)
- Clinical study reports
- Regulatory submissions/Health Authority interactions
• Publication Supports
  
  — Discuss requests for post-hoc analyses with MA
  
  — Perform post-hoc analyses for posters, manuscripts, and presentations
  
  — Review and QC all MA materials are essential
• FTEs (full-time employees) for study conduct are usually accounted for
• No FTEs or limited resources in biostats and programming groups to handle Health Authority requests and publication supports
• Once a drug is approved by Health Authority, a large volume of clinical requests from MA to support the medical plan
• All requests from MA require meetings/discussions before any work performed
HOW MUCH WORK IS THERE?
AN EXAMPLE OF ONE DRUG ON MARKET

• For this specific drug on market, the company achieved the following in 2014:
  - Manuscripts: 15
  - Posters/Presentations: 146
  - Plus many PMRC (Promotional Materials Review Committee) and MSL materials and others
  - 5 Phase III studies database locked, tables/listings/figures generated, and CSR completed
  - 5 Phase III studies ongoing
  - 1 sNDA preparation
WHAT ARE THE PROBLEMS?

- Competing tasks: clinical studies, regulatory submissions, and MA requests
- Requests from MA to biostats are sometimes late
  - No time for meetings and discussions
  - No time for performing analyses
WAT ARE THE PROBLEMS?

• Usually requires huge amount of time
  — To think carefully whether the requests are clinically and/or statistically sound
  — To program summaries and statistical inferences/analyses
  — To review and QC posters, presentations, and manuscripts

• Not enough time for review/comment before final documents
If enough resource in both biostats and programming in-house:

- Great, but unusual!

- Due to some special expertise and/or software availability reasons, sometimes still need help from CROs or external consultants. For example, modeling and simulation, special statistical methodologies ... etc.
• If in-house programming support is not enough:
  — Seek for external help, and the earlier, the better
    • Acceptance check or validation sometimes needed
  — Or, biostats needs to jump in and get hands dirty
    • Biostatistician’s programming capability is essential
    • Be able to produce summaries in table format (no need to be pretty) so that medical writers can easily read and understand the results.
• Validation may be a problem!
If no biostats/programming support in-house:

- A very tough situation!
- Seek for external help
- Quality! May need to 100% rely on others (external help) without any checking
- Cost! Maybe expensive
HOW DO WE HANDLE IT?

• Introduction of statistical analysis request form (SARF)
  — Requester’s info, date of request
  — Detail of the request,
  — Rationale and Hypothesis
  — Where will the data be presented or used?
  — Format of outputs
  — Deadline
  — Approval for the request
  — Biostats/programmer information
  — Completion/Delivery date
  — Programs/outputs file names and locations
• Biostatisticians are “gatekeepers”:
  — Ensure requests from MA are feasible,
  — Requests are clinically and statistically sound
  — Pre-meeting to go over each request is essential to get agreement and to make strategic decisions (prioritization) if too many requests at the same time
• Last minute request is usually not acceptable
• Validation
  — Required, but sometimes it has to be flexible based on different level of validation if resource is an issue
  — Consider CROs
• Follow up with MA/medical writer
• Review and Comment
• QC
IDEAL FLOW OF MA’S REQUESTS

Requests from MA via SARF

Meetings with Clinical/MA

Clinically and statistically sound?

Yes → Performing statistical analyses

Statistical results to MW

No → Adjustments or more analyses

Meetings with Clinical/MA

Biostats Review and QC

Biostats Review and QC

Drafts

Meetings with Clinical/MA

Final

All good

Publish

All good
HOW TO ACHIEVE THE BEST OUTCOME?

• The bottom line is
  — Send SARFs to biostats as early as possible
  — Communications and discussions are essential
  — Review and biostats QC
• Why are we here?
• What should we get out of this?

Focus on:
1. Nomenclature
2. What to report
3. Common pitfalls
Study Design

- Categories of Studies
- Example Study Designs
STUDY DESIGN

• 2 broad categories

- Study Designs
  - Experimental
  - Observational
Which category of study design do you encounter most often in your work?

A. Experimental
B. Observational
C. Equal proportion of experimental and observational
D. Neither
E. I strive to avoid studies
• Experimental study designs
  — Parallel
  — Cross-over
  — Factorial
Observational study designs

- Cross-sectional
- Case-Control
- Cohort
- Historical Control

Adapted from Figure 2-5 in Basic & Clinical Biostatistics (4th Ed)
### Study Design

**Observational study designs**

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Definition</th>
<th>Common uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional</td>
<td>Reports data on a group of subjects at one time rather than over a period of time</td>
<td>Describes what is happening right now; hypothesis generating</td>
</tr>
<tr>
<td>Case-control</td>
<td>Begin with the absence or presence of an outcome and then look backward in time to try to detect possible causes or risk factors</td>
<td>What happened?</td>
</tr>
<tr>
<td>Cohort</td>
<td>Begins with the exposure and looks forward longitudinally for the outcome</td>
<td>What will happen?</td>
</tr>
</tbody>
</table>
**Observational study designs**

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Population size</th>
<th>Longitudinal</th>
<th>Direction of observation</th>
<th>Comparison Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross-sectional</td>
<td>Big</td>
<td>No</td>
<td>One point in time</td>
<td>No</td>
</tr>
<tr>
<td>Case-control</td>
<td>Big</td>
<td>Yes</td>
<td>Retrospective</td>
<td>Yes</td>
</tr>
<tr>
<td>Cohort</td>
<td>Big</td>
<td>Yes</td>
<td>Prospective</td>
<td>Usually</td>
</tr>
</tbody>
</table>
Types of Analyses

Metrics to Report
ANALYSES

• Unadjusted

• Adjusted
  – Regression
  – Cox Proportional Hazards Models
• Commonly reported metrics

**P values and CIs**
- If possible, report both
- Confidence intervals tell you everything you need to know
  - Significance
  - Idea of the range

**RR and ORs**
- When are they alike?
  - Risk vs Odds
  - Significance

**NNT/NNH**
- Resonate with clinicians
- Dichotomous data required
- Clinical significance vs statistical significance
### Quick Reference Formulas

<table>
<thead>
<tr>
<th></th>
<th>Disease (cases)</th>
<th>No Disease (control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk factor present (treatment)</td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td>Risk factor absent (no treatment)</td>
<td>C</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>A + C</td>
<td>B + D</td>
</tr>
</tbody>
</table>

Experimental event rate (EER) = \( \frac{A}{A + B} \)

Control event rate (CER) = \( \frac{C}{C + D} \)

Absolute risk reduction (ARR) = \( |EER - CER| \)

Number needed to treat (NNT) = \( \frac{1}{ARR} \)

Relative risk reduction (RRR) = \( \frac{|EER - CER|}{CER \times CER} \)

Relative risk (RR) = \( \frac{EER}{CER} = \frac{A/(A+B)}{C/(C+D)} \)

Odds ratio (OR) = \( \frac{A/(A+C)}{C/(A+C)} \times \frac{D/(B+D)}{B/(B+D)} = \frac{AD}{BC} \)
Common Pitfalls

• Terminology
  — Efficacy vs effectiveness

• Significance based on Cis
  — Crossing 0 or 1 (depending on measurement)

• When metrics can be calculated
  — Type of data
  — Significance
Are there other types of categories/studies that you would be interested in learning more about?

A. Cost-effectiveness Analyses
B. Economic Models
C. Decision Analysis
D. Randomized Control Trials
E. Patient Reported Outcomes
Helpful Resources

- Publications
- CE and Workshops


• [http://www.pharmacy.arizona.edu/centers/hope/training-programs](http://www.pharmacy.arizona.edu/centers/hope/training-programs)
RESOURCES (CONT.)


THANK YOU!
To ask a question, please type your query into the Q&A box

To ensure anonymity, before sending please choose the drop-down box option, "ALL PANELISTS." Otherwise, ALL audience members will be able to see your submitted question
UPCOMING ISMPP U'S

• December 2015
  • Topic: Medical Devices

• January 2016
  • Topic: Manuscript Development
THANK YOU FOR ATTENDING!

• We hope you enjoyed today's presentation. Please take a few moments to complete the survey that will appear on your screen immediately after the presentation. We depend on your valuable feedback and take it into account as we develop future educational offerings.