Successful real world data generation and use in Latin America

Policy principles, operational framework and analytic considerations

Discussion Leaders: Daniel Luna, MD, MSc(C), PhD(C); Daniel Ferrante, MD, MSc, PhD; Gerardo Machnicki, MSc, PhD,
4th ISPOR Latin American Meeting
Buenos Aires, Argentina
September 14, 2013

Introduction and Objectives

- Analytic framework
  - Supporting different needs in healthcare
  - A framework for the analytics process:
    - Data selection/quality
    - Study design
    - Analysis
- Case study - Using real world data of HIBA in one outcomes research program
  - Irritable bowel syndrome
- The future of real world evidence generation in Latin America: how can we contribute to the agenda from an analytic perspective?
Guidelines for good database selection and use in Pharmacoepidemiology

- **Database selection**
  - Population covered
  - Relevant variables
  - Continuity of data capture
  - Record duration/latency
  - Expertise identification

- **Use of multiple resources**
  - Breadth of information
  - Numbers
  - Linkage
  - Data Storage and Analysis

- **Extraction and Analysis**
  - Specifications

- **Quality, Validation and Documentation**
  - Database
  - Population
  - Testing
  - Documentation format and specifics

**Privacy and security**

- Compliance, limited use, security, review of procedures

Source: Hall GC et al, Pharmacoepidemiology and Drug Safety, 2011
Epidemiologic Study Designs

Bias

- Any systematic error in the design, conduct or analysis of a study that results in an inaccurate estimate of an exposure’s effect on the risk of disease

**Selection**
- Inappropriate population, not well selected

**Information**
- Related to the way data are collected

**Confounding**
- Unaccounted factors that may be influencing the outcomes

**Remedies (mostly in context of secondary data)**
- When data have been collected
  - Ensure its completeness and quality beforehand
  - Conduct additional studies to address remaining issues
- Restriction
- Matching
- Stratification
- Regression methods

Source: Based on EPIC-501 Class Notes, Saint Louis University School of Public Health, Fall Semester 2005
Case I: Evaluation of Resource Utilization and Direct Medical Costs of IBS patients in a health care plan in Argentina

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¹Plan de Salud, Hosp. Italiano, Bs. As., Argentina
²Novartis Argentina

Presented at Digestive Disease Week, 2003

Introduction

- Irritable bowel syndrome (IBS) poses a considerable impact in health care costs
  - World Prevalence is variable depending on diagnostic criteria and geographic area. According to Rome I and II criteria, 3 to 20% of the adult population has IBS. In Argentina, a prevalence of 16% was estimated¹
  - Several studies in different health care systems found a consistent pattern of higher health care use of IBS patients compared to controls, although the distribution of cost in each country varies.
- Little is known about resource use and costs of IBS in Latin America

¹Drossman et al., 2000
²Mearin F et al. 2001
³Carullo, D&J, Novartis Arg, Nov 2000
Objectives

- To estimate resource utilization and health care costs of IBS patients from an insurer perspective

- To compare resource utilization and health care cost between IBS patients and controls

Study Setting: Plan de Salud, Hospital Italiano de Buenos Aires

- Placed in Buenos Aires, capital city of Argentina
- Staff model HMO associated to community health hospital
- 69981 enrolles (individual or family affiliations)
- Hospital Italiano de Buenos Aires: large (400 beds) University, full services hospital
Design and methods

- Retrospective cost analysis using computerized medical records
- Patients selected according to “irritable colon” diagnostic code (indicated by GP or specialist)
- Database validation study carried out
- Data elements collected
  - Demographics, IBS diagnosis, medication, medical visits, procedures, inpatient days
- Statistical analysis: Parametric and non parametric test (Wilcoxon, t-test and chi-2)

Study population

- IBS patients (n=946)
  - Irritable colon diagnostic code
  - Age 20yrs. or more
  - Active at march 1, 2001, continuously enrolled through 2000
  - Exclusion criteria (Coded in DB)
    • Diagnosed colon cancer
    • Family history of colon cancer
    • Weight loss
    • Anemia
    • Hematochezia
    • Inflammatory Bowel Disease
- Controls (n=69981)
  - Age and sex standardized controls
Validation Study

- Objective: to confirm accuracy of database diagnosis in relation to international standards
- 200 patients invited to participate
- Rome I and II administered to patients agreeing to answer
- 109 patients answered questionnaires

Results of validation study (n=109)

- Rome I or II= 63 (58%)
- Rome I only=29 (46%)
- Rome I and II=34 (54%)
- No Rome criteria=22 (20%)
- Alarm criteria=24 (22%)
Patient Demographics: not statistically significative differences between database and validated patients

<table>
<thead>
<tr>
<th></th>
<th>IBS group (n=946)</th>
<th>Interviewed patients (n=109)</th>
<th>Rome II (n=34)</th>
<th>Rome I (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender (%)</strong></td>
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<tr>
<td>Male</td>
<td>20</td>
<td>12</td>
<td>3</td>
<td>9,4</td>
</tr>
<tr>
<td>Female</td>
<td>80</td>
<td>88</td>
<td>97</td>
<td>90,6</td>
</tr>
<tr>
<td><strong>Mean age (±SD) (years)</strong></td>
<td>57 (17)</td>
<td>62 (12)</td>
<td>62</td>
<td>62</td>
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<tr>
<td><strong>Age (%)</strong></td>
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<tr>
<td>20-39</td>
<td>20,2</td>
<td>7</td>
<td>6*</td>
<td>9,5</td>
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<tr>
<td>40-64</td>
<td>39,2</td>
<td>39</td>
<td>50</td>
<td>40</td>
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<tr>
<td>65 or more</td>
<td>40,6</td>
<td>54</td>
<td>44</td>
<td>51</td>
</tr>
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</table>

*p <0.05

Patient Demographics: not statistically significative differences between database and no-Rome validated patients

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<td>18</td>
<td>17</td>
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</tr>
<tr>
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<td>20,2</td>
<td>7,5</td>
<td>0</td>
</tr>
<tr>
<td>40-64</td>
<td>39,2</td>
<td>33,3</td>
<td>50</td>
</tr>
<tr>
<td>65 or more</td>
<td>40,6</td>
<td>59,2</td>
<td>50</td>
</tr>
</tbody>
</table>
Results

Annual Cost of IBS Per Patient* in Argentina (HMO Perspective)

*946 patients
Argentina: IBS patients have a high resource utilisation

Resource utilization in IBS Patient vs control (HIBA HMO, 2000)

Direct medical cost of different study groups
HRQoL substudy: Patients and methods

- Randomized sample of 100 patients over a total of 946 pacientes older than 20 years with a IBS diagnostic with electronic medical record (CIAP: D93)
- Inclusion criteria: Rome I or Rome II criteria
- Exclusion criteria: alarm signs

Resultados: Validación diagnóstica

- Pacientes randomizados: 100
- Completaron encuesta: 83
  - Signos de alarma: 17
  - Sin signos de alarma: 66
    - Sin criterios de Roma: 16 (24%)
    - Criterios de Roma I o II: 50 (76%)
    - Criterios de Roma II: 26 (52%)
Results: Score of patients with Rome II criteria vs general population, n:50

<table>
<thead>
<tr>
<th>Physical Component</th>
<th>Mental Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rome I-II</td>
<td>General population</td>
</tr>
<tr>
<td>42.31</td>
<td>47.69</td>
</tr>
<tr>
<td>43.25</td>
<td>50.42</td>
</tr>
</tbody>
</table>

• $p = 0.579$

• $+ p = 0.057$

Discussion: bias / limitations

- Patients identified according to diagnostic code (GP or specialist criteria)
  - Validation confirmed initial expectations of database accuracy
  - Main goal was to analyze cost according to electronic database (GP or specialist criteria), using a real insurer perspective
- The study was called a “case-control” study, as IBS was considered an outcome and costs were analyzed retrospectively. This was in some way related to the amount of data available for follow-up (a more typical option is to define an index date of diagnosis and follow cost or other outcomes from there on)
- Responder bias possible: only more worried patients may have participated in the health related quality of life sub study
- Generalizability: study population may not be representative of other health care plans
Conclusions

- Back in 2002, it was possible to document real-life utilization patterns in IBS patients using an HMO database
  - IBS patients costed 30% more than standardized controls

- A hybrid design allowed to ascertain HRQoL in this population, increasing even the value of the resources invested in the study

- The value of the information was augmented by
  - A diagnostic validation criteria

- Findings were consistent with previous studies performed in different health care systems

<table>
<thead>
<tr>
<th>Database quality</th>
<th>Reliability of secondary central coding of medical problems in primary care by non medical coders, using the International Classification of Primary Care (ICPC).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 1</strong></td>
<td>Intrarater and inter-rater agreement and Kappa statistics at rubric level by ICPC chapter</td>
</tr>
<tr>
<td><strong>ICPC Chapter</strong></td>
<td>% Intrarater agreement (Kappa)</td>
</tr>
<tr>
<td>A-General</td>
<td>66.11 (0.81)</td>
</tr>
<tr>
<td>B-Headache</td>
<td>66.81 (0.77)</td>
</tr>
<tr>
<td>C-Digestive</td>
<td>92.3 (0.91)</td>
</tr>
<tr>
<td>D-Eyes</td>
<td>100 (1)</td>
</tr>
<tr>
<td>E-Hear</td>
<td>90 (0.67)</td>
</tr>
<tr>
<td>F-Circulatory</td>
<td>96.84 (0.84)</td>
</tr>
<tr>
<td>G-Musculoskeletal</td>
<td>67.27 (0.45)</td>
</tr>
<tr>
<td>H-Neurological</td>
<td>87.5 (0.85)</td>
</tr>
<tr>
<td>I-Psychological</td>
<td>68 (0.62)</td>
</tr>
<tr>
<td>J-Respiratory</td>
<td>95.63 (0.95)</td>
</tr>
<tr>
<td>K-Skin</td>
<td>88.11 (0.87)</td>
</tr>
<tr>
<td>L-Endocrine, Nutr</td>
<td>100 (1)</td>
</tr>
<tr>
<td>M-Urinary</td>
<td>100 (1)</td>
</tr>
<tr>
<td>N-Pregnancy</td>
<td>0 (0)</td>
</tr>
<tr>
<td>O-Female genital</td>
<td>57.14 (0.53)</td>
</tr>
<tr>
<td>P-Male genital</td>
<td>68.50 (0.64)</td>
</tr>
<tr>
<td>Q-Social problem</td>
<td>95 (0.94)</td>
</tr>
<tr>
<td>Total</td>
<td>66.33 (0.46)</td>
</tr>
</tbody>
</table>

Source: Luna D et al., Studies in Health Technology and Informatics, 2001
Real world data in Latin America – Contributing to the agenda from an analytics perspective

- Latin-American specific methodological reviews and discussions

- Promote/disseminate innovative studies and establish a continuous learning cycle

- Engage the payors, health care community and the society

Predictive ability of comorbidities SUS (Brazil)  Use of comorbidity measures to predict the risk of death in Brazilian in-patients

The SIH/SUS includes anonymous information about the following variables: demographic profile of patients (sex and age); primary and secondary diagnoses; surgical, therapeutic and diagnostic procedures; medical specialty of the case treated (general or specialized surgery and obstetrics, among others); days of stay; discharge status and hospital unit. First, 4,086,329 hospitalizations resulting from respiratory and circulatory problems, based on the International Classification of Diseases, 10th revision (ICD-10), and funded by the Sistema Único de Saúde (SUS – National Health System) in Brazil, between 2003 and 2004, were included to define the universe of study. These two health problems were

Source: Martins M, Rev Saude Publica, 2010
Predictive ability of comorbidities SUS (Brazil)

Use of comorbidity measures to predict the risk of death in Brazilian in-patients

Table 5. Discriminatory capacity and adjustment of death prediction models, according to comorbidity measures. Brazil, 2003-2004.

<table>
<thead>
<tr>
<th>Model</th>
<th>R² model</th>
<th>Hosmer-Lemeshow Test</th>
<th>C statistic 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline model: primary diagnosis, age and sex</td>
<td>64015.16</td>
<td>1427.99</td>
<td>0.685</td>
</tr>
<tr>
<td>(g) 12, p = 0.001i</td>
<td>(p = 0.000)</td>
<td>(p = 0.000)</td>
<td>(0.664;0.687)</td>
</tr>
<tr>
<td>Baseline model + CCI</td>
<td>64570.68</td>
<td>1641.16</td>
<td>0.688</td>
</tr>
<tr>
<td>(g) 16, p = 0.001i</td>
<td>(p = 0.000)</td>
<td>(p = 0.000)</td>
<td>(0.687;0.689)</td>
</tr>
<tr>
<td>Baseline model + Elixhauser comorbidities</td>
<td>65416.16</td>
<td>1466.15</td>
<td>0.687</td>
</tr>
<tr>
<td>(g) 13, p = 0.001i</td>
<td>(p = 0.000)</td>
<td>(p = 0.000)</td>
<td>(0.666;0.689)</td>
</tr>
<tr>
<td>Baseline model + presence of comorbidity</td>
<td>68139.95</td>
<td>1122.12</td>
<td>0.691</td>
</tr>
<tr>
<td>(g) 13, p = 0.001i</td>
<td>(p = 0.000)</td>
<td>(p = 0.000)</td>
<td>(0.690;0.693)</td>
</tr>
</tbody>
</table>

*a* Likelihood ð‘ only for the intercept = 694735.46
CCI: Charlson Comorbidity Index

Source: Martins M, op cit

Innovation: National registry analysis

Factores Predictores para presentar obstrucciones coronarias significativas en pacientes adultos del Uruguay

**Modelo de regresión logística binaria; lesiones > 50 %**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (IC 95 %)</th>
<th>Valor P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edad &gt; 50</td>
<td>5.3 (2.1-13.2)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Sexo masculino</td>
<td>3.0 (2.5-3.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Usuarios Sector Privado</td>
<td>1.6 (1.2-2.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Antecedentes Personales CI.</td>
<td>2.0 (1.2-2.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.9 (1.4-2.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Situación Clínica IAM comis</td>
<td>9.0 (2.5-32)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Estudio funcional por imágenes radionado</td>
<td>2.0 (1.5-2.8)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Source: Morales M et al, Latin American ISPOR 2011
Engaging the health care community: a potential agenda

Incorporating Observational Data into the Formulary Decision-Making Process—Summary of a Roundtable Discussion

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Summary of Suggested Improvements for Integration of Observation Studies in Decision Making</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Collection</strong></td>
<td><strong>Research</strong></td>
</tr>
<tr>
<td>• Investment in data quality and quality control</td>
<td>• Transparency models as a standard—continuous improvement procedures</td>
</tr>
<tr>
<td>• Database design improved for RWD analysis</td>
<td>• Long-term follow-up studies for chronic diseases</td>
</tr>
<tr>
<td>• Guidelines based on IOM evidence</td>
<td>• RWD data used to identify best long-term outcomes (public health/奥林)</td>
</tr>
<tr>
<td>• Routine procedures:</td>
<td></td>
</tr>
<tr>
<td>• Prospective or concurrent look at patient safety and management</td>
<td></td>
</tr>
<tr>
<td>• Practice pattern analysis for drug evaluation</td>
<td></td>
</tr>
<tr>
<td>• Analysis of appropriateness of drug decisions</td>
<td>Transparency and collaboration lead to higher robustness</td>
</tr>
</tbody>
</table>

Improved data lead to more reliability of predictions (models) | |

Source: Holtorf A et al, JMPC 2008

Engaging society: dissemination

WHAT’S POSSIBLE FOR HEALTH CARE?

USE INFORMATION TECHNOLOGY MORE EFFECTIVELY

Clinicians and patients should have real-time access to medical records and use technology to streamline administrative tasks.

IN HEALTH CARE...

50%

Almost 50% of patients report that information necessary to their care was not available when needed.

IN OTHER INDUSTRIES...

25%

25% of patients said their health care provider has had to re-order tests to have accurate information for diagnosis.

ONLINE BANKING

Allows customers to view their entire financial history and conduct transactions in seconds.

Source: IOM Infographic, Revised March 2013
Conclusions

- Back more than 10 years ago, it was possible to generate outcomes research information out of an electronical clinical record in an HMO affiliated with a university hospital
- The project involved a phase of database selection, and also design, analysis and reporting aspects
- Nowadays, it is even more important to generate and use real world data in Latin America.
- In order to succeed in this endeavor, multidisciplinary and multi dimensional strategies and programs are needed
  - At international and national level: promoting the development of HC information infrastructure
  - At national, regional and local levels: continuing to generate research around real world data generation (both fundamental and applied)
- This include a important contribution from the analytics perspective
Thank you!

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