A Decision Analysis Model for estimating Latent Therapeutic Demand for Immunoglobulin therapy in Primary Immune Deficiencies

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Survival in PID has been improved by IG therapies.
IgG levels and risk of pneumonia

Orange – MA 2010

Quinti – 5 year prospective study 2011
Ig demand – National variations

- Canada: 140.1
- USA: 137.5
- Australia: 120.7
- France: 97.4
- Spain: 69.6
- UK: 58.3
- Italy: 56.5
- Germany: 41.5
- Japan: 26.5
- Turkey: 12.5
- Brazil: 9.4
- China: 7.8
- Russia: 4.0
Latent therapeutic demand (LTD) is the underlying demand that represents how physicians would prescribe treatment and how patients would follow or comply with the prescribed treatment if ample supplies of drugs were available and affordable (in this case grams of Ig per 1000 population)
Methodology based decision analysis to estimate LTD for primary immune deficiency (PID).

(1) Focus on Common Variable Immunodeficiency (CVID) and X-Linked Agammaglobulinemia (XLA).

(2) Identified and defined the variables impacting LTD for PID through a literature review of PID disease epidemiology and its treatment and discussions with experts.

(3) Constructed an influence diagram to model the variables impacting LTD for PID and their interrelationships.

(4) Obtained range estimates for each variable from published articles.

(5) Conducted sensitivity analysis using a tornado diagram to order variables in terms of their impact on LTD for PID.

(6) Modeled the uncertainty surrounding the most sensitive variables.
Model variables and their integration model

**Epidemiology Related Variables**

- Diagnosed Prevalence (per 100,000 population)
- Age Group of Patients
- Patient Gender
- Patient Weight
- Population

**Treatment Related Variables**

- Treatment Rate
- Administration IVIG vs. SCIG
- Compliance Rate
- Treatment Dosage
- Treatment Interval

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[Image of network diagram with nodes and arrows indicating relationships between variables.]
The extended Swanson-Megill (ESM) approximation was used to account for the uncertainty of continuous random variables.

Continuous Random Variable $X$

Underlying Cumulative Distribution Function of $X$:

Discrete Approximation of $X$ using the ESM

10th percentile $X_{10}$

50th percentile $X_{50}$

90th percentile $X_{90}$


Model inputs and outputs.

INPUTS

Latent Therapeutic Demand (LTD) Model

OUTPUT

Tornado Diagram

Probability Distribution
LTD Model – Results for CVID

- Diagnosed Prevalence
- IVIG Treatment Dose
- Treatment Rate
- Patient Weight
- IVIG Treatment Interval
- SCIG Treatment Interval
- SCIG Treatment Dose
- IVIG Compliance Rate
- Administration
- SCIG Compliance Rate
- Age Group of Patients
- Patient Gender

Latent Therapeutic Demand for CVID (grams per 1,000 inhabitants)
Diagnosed prevalence (per 100,000 inhabitants) of CVID.

<table>
<thead>
<tr>
<th>CVID Diagnosed Prevalence</th>
<th>Low</th>
<th>Base</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>15</td>
<td>30</td>
</tr>
</tbody>
</table>

Assumptions & Sources for Estimates

**Low Estimate**
- National Registries
- Beauté et al. (2010), Gathmann et al. (2009)

**Base Estimate**
- Population-based study, Omsted County MN
- Joshi, et al. (2009)

**High Estimate**
- Telephone survey
- Boyle and Buckley (2007)
Besides diagnosed prevalence, another driver of growth is IVIG/SCIG dosage and frequency.

A “snap-shot” of treatment-related data were obtained from the ESID Registry
- 2,065 patients with CVID
- 4,016 patient records/entries for CVID patients
Total number of CVID patients treated with IVIG: 748 (78.7%)
Total number of CVID patients treated with SCIG: 203 (21.3%)

Data Source: European Society for Immunodeficiencies (ESID) Registry, 2011
The probability distribution of latent therapeutic demand for CVID is skewed right with a mean of **44 grams per 1,000 inhabitants**.
Result for CVID
Using base case prevalence (Joshi et al)

- By centering the prevalence around the population-based study (Joshi, et al. 2009), the probability distribution becomes bell-shaped and the mean remains **44 grams per 1,000 inhabitants**.

A similar approach was used to derive a LTD for XLA of **48 grams per 1,000 inhabitants**.
The IG latent therapeutic demand (LTD) for the treatment of CVID alone is larger than most countries’ IG consumption across all disease indications.

Mean = 44
80% confidence range: 20-74
Conclusions

- Decision analysis has been used to construct a LTD model for IG usage in CVID and XLA
- Data from the literature were used to populate the model
- Prevalence estimates were adjusted to a base case to result in a normal probability distribution of LTD
- Using this model, the usage of IG for PIDS should exceed the total IG consumption of most countries
- These results have implications for demand planning for the treatment of PID patients