The House of Cards....

Graylands Medical Group
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The Pharmaceutical Industry

- 12 Pharmaceutical companies in US Fortune 500
  - Combined revenue last year US$310 billion
  - Combined profit US$50 billion
  - Profit greater other 488 combined

- Australian medicines industry turnover 2009/10 AUS$22 billion
  - Contribution to Australian economy 2008/09 AUS$8.7 billion
  - Medicines export 2010/11 AUS$3.8 billion
  - R & D investment 2009/10 AUS$1.0 billion
  - Employment 2009/10 13,400

The Pharmaceutical Benefits Scheme

- Government expenditure in 2012 was $9.2 billion 83% of cost of PBS

- Remainder patient contributions $1.5 billion

- Overall expenditure on prescription medicines 2009/10 was $14 billion [includes DVA, public & private hospitals, health insurance funds, etc]
In 2012, 4 of the top 20 PBS drugs in terms of cost were:

- Olanzepine (7th) PBS $160M, Total $168M
- Quetiapine (11th) PBS $114M, Total $123M
- Venlafaxine (15th) PBS $91M, Total $131M
- Risperidone (19th) PBS $78M, Total $82M

Combined expenditure these 4 - PBS $443M and Total $504M

2010-11 MBS payments to private psychiatrists $272M
Second Generation Antipsychotics in PBS top 50

Top 50 ranking
- Olanzepine
- Risperidone
- Quetiapine

Graph showing the ranking of second-generation antipsychotics from 2003 to 2012.
Second Generation Antidepressants in PBS top 50

- Sertraline
- Venlafaxine
- Paroxetine
- Citalopram
- Fluoxetine
- Desvenlafaxine
Why my interest…?

  - 9 Principles to GC – 4 approved, 5 business case/further consultation

- Controversy over article by Ian Hickie & Naomi Rodgers –

- “Debate” ANZJPsych –
  - “For richer, for poorer, in sickness and in health: the entanglement of science and marketing” [June 2012]
The Hickie – Rodgers controversy ….

- 6 letters to Editor Lancet criticising alleged bias -
  - Interpretation of data on efficacy and safety agomelatine [Servier]
  - Transparency of relationship with company [launch Valdoxan]

- Article cited 105 references – almost 1/3 related to Agomelatine
  - Able access 16 [50%] on line
  - All had some form of financial arrangement with Servier
  - Special supplement of Journal of Psychopharmacology [Servier funded]
Gabapentin [Neurontin] FDA approved epilepsy
- Promoted for off-label use BP, migraine, diabetic neuropathy, ++
- 2001 US$1.8 billion sold – 80% off label
- Pfizer [Park Davis] fined $430M in 2004

Glaxo Smith Kline fined $3B [2012]
- Promoting off-label use of Paroxetine and Bupropion to children
- Revenue from sales antidepressants $17.5B


AstraZeneka fined $520M [2010] – Quetiapine [children and elderly]

J and J – $181M states + ongoing Federal litigation – Risperidone

Abbott fined $1.5B [2012] – Valproate [agitation in dementia]
Opening the ‘black box’ …..

- Internal documents released through litigation
- Revealed comprehensive, multifaceted approach that industry uses to market their drugs:
  - Drug reps – 1:15 doctors in USA
  - Gifts – small to large [2009 Australia Wyeth sponsored $1M ‘antidepressant weekend meeting to launch Pristiq (Desvenlafaxine]
  - Drug samples – very strong influence on prescribing [2005 in US 11.2% of sales]
  - Key Opinion Leaders – specialist clinicians & senior academics
  - Continuing medical education [not have ‘educational’ but ‘marketing’ budget]
  - Medical Journal advertising [reprints and supplements]
  - Research funding
  - Ghost writing
  - Disease awareness campaigns [Hickie and Beyondblue]
  - Consumer and community advocacy groups [e.g. MHCA]
Opening the ‘black box’ …… further

Eli Lilly fined $1.4B [2009] – off-label use Olanzepine

'The fact we are now talking to child psychs and peds and others about Strattera means that we must seize the opportunity to expand our work with Zyprexa in this same child-adolescent population' Eli-Lilly CEO John Lechleiter

The “life-plan” for Zyprexa changes as “Year-X” (expiration of Prozac patent in 2001) approaches.

The company is betting the farm on Zyprexa … the ability of Eli Lilly to remain independent and emerge as the fastest growing pharma company of the decade depends solely on our ability to achieve world class commercialization of Zyprexa

If we succeed, Zyprexa will be the most successful pharmaceutical product ever … we will have made history

Bipolar Vision of Product Evolution
To be a leader in the bipolar market, Zyprexa will need to be viewed as true mood stabilizer

Regarding peer-to-peer,
we've just completed the second of two speaker training programs and have unleashed more than 130 psychs and PCP's who are chomping at the bit to help you sell Zyprexa.

Source: What do the “Zyprexa (and other) Documents” say about industry sponsored CME? RANZCP Congress 2009 Dr Peter Parry, Flinders University, SA and A/Prof Glen Spielmans, Metropolitan State University, Minnesota
Opening the ‘black box’ …… further

Sophisticated market research is applied to “customers”
– mainly psychiatrists and primary care physicians

Segmentation – type casting of physicians and tailoring information to personality styles to maximise sales.

**Insights:**
Know your customers *Personally*
- Better understand how & why your customers react to your style
- Determine ways to build relationships

**Segmentation:**
Know your customers *Professionally*
- Better understand how your physicians approach neuroscience treatments
- Determine appropriate neuroscience programs

Both help you…
- Pre-call plan
- Better understand your customers
- SELL MORE!!!!!
Opening the ‘black box’ …… further

**Skeptical Experimenter: Psych Only**

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<th>Marketing Objectives</th>
<th>How We Want Them to Think and Act</th>
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<td>Programs (promotional and non-promotional)</td>
<td>Programs not specifically planned for this physician segment (most similar to High Flyer needs with a higher degree of skepticism for marketing programs)</td>
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<td>Let them demonstrate their expertise</td>
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<td>• Advisory Boards</td>
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<td>• Round Table / P2P (but not with Rule Bounds)</td>
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<td>• Key segment to learn from via CFF’s and RCFF’s</td>
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<td>• Consultants website where they can post non-anonymous feedback to Lilly and colleagues and engage in chats/debates about patients and treatments</td>
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<td>• Preceptorships</td>
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<td>Let them tinker</td>
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<td></td>
<td>• Experience trials / Clinical trial involvement / Research Grants</td>
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<td>• Symposia, CME with “new” content, Telesessions, Audio Conference</td>
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**Thought Leaders**
Cross Brand Key Players: Thought Leaders
The Zyprexa Guild and Executive level Thought Leaders are well respected and acknowledged by their peers, other experts and key audiences as leaders and influence the thinking and the treatment practices of their peers at a national, regional or local level. The Zyprexa Guild and Executive Thought Leaders are experts in the disease and the diagnosis of the disease. They are typically in the academic setting (professors/researchers) and treat a minimal number of patients, if any. The Guild and the Executive Thought Leaders usually serve on the academic advisory boards, providing feedback to the Zyprexa Product and Brand Team.

The Consultants currently have greater clinical experience and are primarily responsible for continuing to shape and to define Zyprexa as extraordinary in moving lives forward in the bipolar and the schizophrenia marketplace. The Consultant Thought Leaders are the core advocates between the Guild and those at the regional and local levels, and are on our demand realization advisory boards. These clinicians are a critical component of successful DTP interventions and stimulate the physicians at both the regional and the local level.
Opening the ‘black box’ …… further

Zy100504593 Handling hyperglycemia/diabetes Nov 2001

Action:

- Zyprexa causes weight gain
  - First probe then
    - Weight change sell sheet and simple lifestyle changes

- Zyprexa causes weight change that leads to hyperglycemia
  - First probe then
    - Diabetes sell sheet: pie charts from second page then, top graph front page.

- Zyprexa causes Diabetes
  - First probe then
    - Diabetes sell sheet: top graph first page, bottom graph first page pie charts

Get back to selling!
Opening the ‘black box’ ….. further ….. still

And just to show that it is not just Eli-Lilly…
…. The AstraZeneca and Quetiapine [Seroquel] story

The data don’t look good. In fact, I don’t know how we can get a paper out of this.

Subject: RE: US/Canada Investigator meeting and Study 15

I am not 100% comfortable with this data being made publically available at the present time….however I understand that we have little choice….Lisa has done a great ‘smoke-and-mirrors’ job!

Adopting the approach Don has outlined should minimise (and dare I venture to suggest) could put a positive spin (in terms of safety) on this cursed study

AstraZeneca went on in 2010 to be fined $520M for promoting off-label use of Seroquel
Medical research …..

- Review of the references in the Hickie controversy revealed the complexity of the ‘entanglement’ of research and the PI:
  - Funding of research – including multi-centre [donations drugs]
  - Collection and analysis of data ['ownership'] & ‘data checking’
  - Funding for review and development of manuscripts ['ghost writing’]
  - Inclusion of company employees in research team [greatest bias]
  - Compounded by honoraria, advisory board, speakers [KOL]

- Over the last 30 years, the PI has “gained unprecedented control over the evaluation of its own products [and] this threatens the independence and impartiality essential to medical research.” [Agnell]
  - Unequivocal evidence that show clear association between PI funding of clinical trials and pro-industry bias
  - Researchers express confidence in capacity to remain impervious – at odds with evidence
  - Financial interests not only or most powerful influence
An influential Harvard child psychiatrist told the drug giant Johnson & Johnson that planned studies of its medicines in children would yield results benefiting the company.

The psychiatrist, Dr. Joseph Biederman, outlined plans to test Johnson & Johnson’s drugs in presentations to company executives. One slide referred to a proposed trial in preschool children of risperidone, an antipsychotic drug made by the drug company. The trial, the slide stated, “will support the safety and effectiveness of risperidone in this age group.”

Dr. Biederman was the lead author of a trial published last year concluding that treatment with risperidone improved symptoms of attention deficit and hyperactivity disorder in bipolar children.
Clinical Practice Guidelines and DSM 1V & V …..

- Working Group members for APA CPG development - Schizophrenia, Bipolar and Major Depressive Disorder [Cosgrove 2009]
  - 90% had at least 1 financial interest with PI
  - All involved companies whose products were specifically considered
  - 78% research funding, 72% consultancies, 44% corporate boards
  - None of financial associations disclosed

- DSM 1V – 170 panel members:
  - 56% had 1 or more financial interests with PI
  - 100% panels Mood Disorders, Schizophrenia and other psychotic disorders

- DSM V Task Force Members:
  - Early 2011 – 72%
  - Currently 69%
Prescribing behaviour …

- PI has become adept at influencing physician prescribing behaviour
  - Directly - through drug reps, samples, gifts, CME, journal adverts
  - Indirectly – through ‘control’ of research and use of Key Opinion Leaders

Source: Orkowsk and Wateska
*There’s no such thing as a free lunch.*
Chest July 1992
Medical research is the foundation of ‘evidence-based medicine’
- Underpins training, CME & clinical practice

Clinical Opinion Leaders play a critical role in the PI strategies for marketing – and in training and professional development of peers

Medical Journals also play a critical role in marketing – and in informing and educating the profession [−ve studies, reprints]
“To many critics of the concept of conflict of interest, it seems arbitrary to assume the worst and to attach blame without proof of wrongdoing. These critics, however, neglect the significance of the basic concept – trust is a social role. Trust is a delicate matter that often depends as much on appearance as reality.”

Brody 2010

We need to uphold the public’s trust in our position

Just as importantly

We need to uphold our own trust in our profession
Redefining the relationship ……

- Proposals for redefining the relationship – 2 broad categories:
  - Management strategies – clear rules to deal with & limit any ‘ill effect’
  - Divestment strategies - “weaning ourselves off” [Moynihan]

- Separating or putting at arms-length clinical research and PI funding
What are your views on disentangling the relationship between medicine & the Pharmaceutical Industry?