Innovation for Better Health & Value

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Vancouver Feb 25, 2009

Health Innovation for Patients and Populations

Awash in Innovations

- 1147 newly patented drugs approved, 1990-2003 by Canadian Board
- But only 68 = substantial improvement
  - The rest = small or no advantage
- Since 1960s, consistent pattern of 2-3% breakthroughs, 11-14% substantial clinical advantage.
  - **6 in 7 little or no advantage**

Why so little innovation for health gain?

1) Benchmark for approval and use is not *clinically* better than existing treatments, but better than placebo.
   - **-or non-inferior "a mockery of medical advance"**

   - Better than placebo against surrogates has led to new "risks" and "problems" that prove clinically secondary.
     - Eg lowering high cholesterol in healthy people
     - Eg serotonin model of depression
     - Eg restoring "bone loss" to prevent breaks

Why so little innovation for health gain?

2) Testing for public and safety is left to sponsoring company.

- Naturally, design to maximize evidence of benefits & minimize evidence of harms.
  - **Trials with strong doses too short to pick up toxic effects. Double risk to patients.**
  - **Rule out subjects with co-morbidities common among users.**
  - **Do not count side effects of those who quit.**
  - **Measure only selected side effects. Split into sub-groups so no statistical significance.**
  - **Screen out subjects w/ strong placebo effect.**

Why so little innovation for health gain?

3) Pay much more for new drugs of little advantage.

- **Reward little or no advance**
- **The opposite of free mkt competition and rewarding good value**

4) Allow extensive commercial promotion to shape prescribing

- **Off-label syndrome, commercializes medical leaders and practicing physicians**

Thus Innovators do what we reward them to do

- **Turn out hundreds of seemingly better drugs**
  - -Spend billions on Drs to prescribe them.
- **Commercialize science**
  - Goal of science has become to discover patentable new products that buyers will pay much more for, regardless of benefit to patients or populations. **(See Angell, Relman)**
  - **Ingenuity & Billions Misdirected**

Epidemic of toxic, costly side-effects

- FDA: 4th leading cause of death
- 45 million ADRs per year in USA
- 1.5 million hospitalizations
- Reports to FDA tripled 1995-2006.
  - Rising at +15% a year.
- "Off-label" means unapproved uses. 73% have no evidence. Spreading rapidly.

Epidemic of toxic, costly side effects

- New drugs higher risk, with few offsetting benefits.
- Faster approvals result in more serious warnings and withdrawals.
- New biologicals not safer and takes 5 years to discover 70% of toxic effects.

Epidemic of toxic , costly side effects

- **US Drs cannot be trusted to protect patients.**
  - **See sales reps for main advice**
  - **Billions in favors, free samples**
  - **Usually prescribed advertised drugs when asked**
  - **Ignore warnings & keep prescribing**
  - **Keen to prescribe for untested and unapproved uses. 73% have no evidence of efficacy.**
  - **The perfect defense: expert intermediary**

Epidemic of toxic , costly side effects

- **Many leading specialists on the take.**
  - **Develop "evidence" for unapproved uses**
  - **Featured speakers for large fees**
  - **Key members of the sales force**
  - **Key sources of CME**
- **Angell - Medical Schools, Faculty complicit:**
  - **"…no longer possible to believe much of the clinical research that is published, or to rely on…authoritative guidelines."** **NYRB 15Jan09**

The Risk Proliferation Syndrome

1. **Efficacy against placebo and surrogate end points minimizes new benefits**
2. **Conflict of interest testing minimizes evidence of toxic side effects**
3. **1st & 2nd tier medical journals depend on pharmaceutical revenues. Avoidable.**
4. **Massive launches maximize patients exposed, despite greater risks.**

The Risk Proliferation Syndrome

5. Billions spent marketing to Drs neutralizes their fiduciary role and maximizes patients exposed. Risks sidelined or not mentioned.

6. Proliferation of unapproved uses led by paid clinical researchers.

7. Minimal and biased reported of side effects.

8. DTCA maximizes grey-area uses of unclear benefits. (Mintzes et al 2003)

New Rules Encourage Greater Risks to Patients

- FDA now allows reps to pass out articles on unapproved uses.
- This turns safety & efficacy review into a hollow ritual.
- FDA – faster reviews with slow sponsor responses results in up-against-the-clock approvals and greater toxic side effects.

New Rules Encourage Greater Risks to Patients

- **Medicare (US) expands, loosens payment for unapproved uses of cancer drugs.**
- **Need to require a consent form and utilization study of unapproved uses.**
- **Very high prices encourage cash to Drs to use them more. Few clinical advantages.**

Drug Safety and Health Canada

Going, Going … Gone? Lexchin

- **Unlike auto & airline safety, data not public but secret to protect companies and their sales. *Why? Indefensible.***

- **Health Canada cannot add warnings to labels without company consent.**
  - **Methods of warnings, cautions ineffective.**
  - **Do not affect prescribing.**

- **Public and Patient safety not protected.**

From “Smart” to Superior Regulation
Rewarding Better, Safer Medicines

- **Approve only drugs better than existing ones.**
- **Relieve companies of risk and cost of phase-3 trials. Public funding, independent researchers.**
  - **Cost much less than widely believed, and much less than commercial charges for trials.**
  - **Well designed to identify toxic effects. Measure all. Report all.**
  - **$2 evaluation fee per script**

From “Smart” to Superior Regulation Rewarding Better, Safer Medicines

- **Relieve companies of rollercoaster boom/bust revenues & profits. Reliable profits on fewer, better new products.**
- **Relieve companies of costs/risks of costly marketing, by developing first-class Medicare detailing.**
  - ***No free samples***

From “Smart” to Superior Regulation Rewarding Better, Safer Medicines

- **Price according to value added**
  - **End 5000%-9000% mark-ups for end of life drugs.**
  - **Huge mark-ups fund kickbacks, pay-offs, and massive marketing, not value.**
  - **Require controlled entry for approved uses with utilization studies.**

From “Smart” to Superior Regulation Rewarding Better, Safer Medicines

- **Price according to value added.**
  - **Net *median* R&D corporate cost much less than claimed, about $100 million per new drug.**
  - **Even less if public funding of III trials.**
  - **Risk much lower than claimed. Risk plummets as costs increase. (Risk is 1 in 1.8 when costs large)**
  - **Net median corporate costs of cancer drugs low. Most paid by govt, foundations. Smaller, shorter trials. Quicker development & review times.**

From “Smart” to Superior Regulation Rewarding Better, Safer Medicines

- **In sum, reward beneficial innovations, not any patentable “innovation”**
- **Fund a Medicare R&D Fund, like NHS R&D Fund, for post-market trials addressing clinical questions of efficacy & safety.**
  - **Drug Safety & Effectiveness Network is good but needs to be ramped up to capacities for the job.**

From “Smart” to Superior Regulation Rewarding Better, Safer Medicines

- **Use Swiss Dr-pharmacist “quality prescribing circles” to improve quality, save money.**
  - **Mobilize, change physician culture**
- **Have patient direct call-in Adverse Event Hotline.**
  - **Better than relying on Drs or companies**
  - **See forms, evidence that quality as good as Drs**