Regulation and Access to Medicines

CapeTown IPHU-2019
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What is regulation

In the field of public policy, *regulation* refers to the usage of targeted rules, typically accompanied by some mechanism for monitoring and enforcing compliance of standards.

Ideally governments should undertake the work of regulation to see that there is no undue influence (of the pharma sector).

Why is regulation necessary for medicines

Pharmaceutical regulations across the world play an important role in ensuring the safety and efficacy of the approved drugs. They not only regulate the pricing of drugs but the quality as well. The regulations are required both for new innovations and already existing products, in order to improve health status.

The optimal regulation of medicines will increase the accessibility, correct usage and confidence for their usage. However, it is necessary to remember that at times excessive regulation has been used as a tool to suppress competition of generic medicines.

National Medicines Regulatory authority

Most of the countries/regions in the world have regulatory authority for medicines and also some autonomous organisations. However, in addition, they may also look into areas such as -national drug policy, essential medicines, regulates poisons, regulate food, medical devices, cosmetics and herbal drugs.

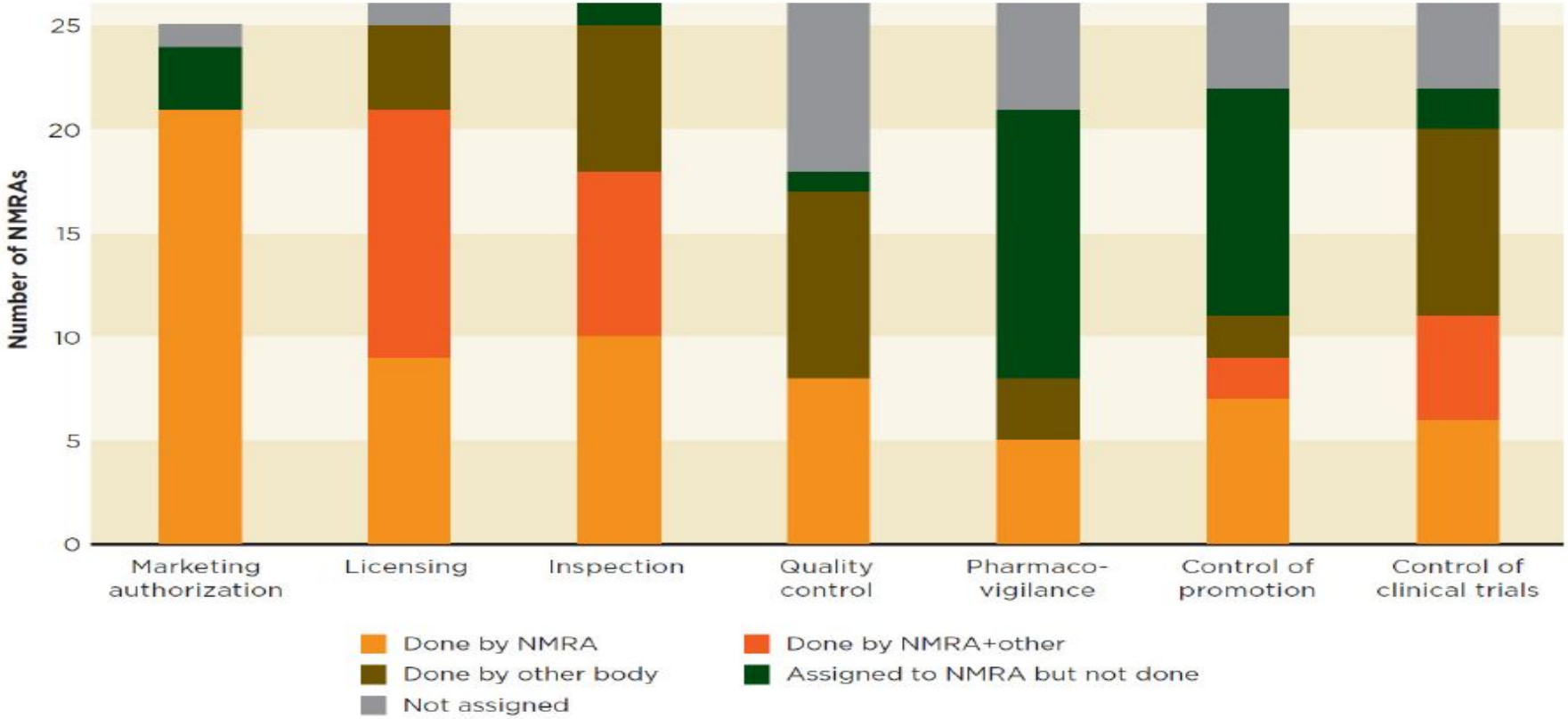


FIGURE 4–4 Number of sub-Saharan African countries out of 26 surveyed meeting the main functions of a regulatory authority.

NOTE: NMRA = National Medicines Regulatory Authority.

SOURCE: WHO, 2010a.

Can you name a few Medical Regulatory Authority

Examples are

- United States Food and Drug Administration
- European Medicines Evaluation Agency
- Can you tell us who regulates medicines in your region/country?

Various avenues for regulation

- Control of clinical trials
- Marketing Authorisation
- Licensing of activities and premises
- Inspection- Compliance with good manufacturing practice (GMP)
- Quality control
- Pharmacovigilance
- Control of promotion
- Pricing control agency

Regulation of the pharmacy profession (usually done by assocations/councils)

Clinical Trials

- Approval process for clinical trials.

- As a condition for registration of medicines to establish their safety, efficacy or bioequivalence

- Registration, following of ethics, trial monitoring and reporting.

Marketing Authorisation

- After the completion of the clinical trials phase 3, medicines can be authorised by the regulatory authority for the commercial sale of medicines.

- A new medicine must pass three hurdles before its approval by the national drug regulatory authority. Sufficient evidence is required to show the new drug to be • of good quality, • effective, and • safe for the purpose or purposes for which it is proposed

- Quality data
  - composition of the drug substance and the drug product
  - batch consistency
  - stability data
  - sterility data (if applicable)
  - the impurity content
- Nonclinical data
  - pharmacology data
  - toxicology data
- Clinical data
  - results of clinical trials
  - results of post-approval surveillance

Pharmacovigilance

Pharmacovigilance (PV) is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.

It can be said that Pharmacovigilance is the follow up of the Clinical Trials phase 4- which is post-marketing studies gather information on the health technology's efficacy in various populations and a side-effect associated with long-term use.

Risk management plan

- analysis (and review) of safety profile of drug
- initial drug evaluation data for marketing approval
- Risk monitoring activities
  - routine
  - additional
- Risk minimisation activities
  - routine
  - additional

Risk monitoring

- Routine
  - evaluation for approval
  - adverse event reporting
  - periodic update safety reports
  - identification and analysis of safety signals (eg WHO product alerts)
- Additional
  - clinical trials
  - post-authorisation safety studies
  - drug utilisation studies
  - patient registries
  - physician surveys
  - prescription event monitoring

Risk minimisation

- Routine
  - product information
  - consumer medicine information
  - directions for use document
  - labelling, pack size and design
  - legal (prescription) status
- Additional
  - education programs
  - prescriber checklists
  - controlled access programs
  - medical software alerts

Example – lumiracoxib cancellation

- Lumiracoxib:
  - registered July 2004
  - COX-2 inhibitor, not the first in class
  - PBS subsidy August 2006
  - 60,000 users.
- Eight reports of serious hepatotoxicity, with two deaths and two transplants.
- Registration cancelled August 2007.
- Liver death (fatality or transplant) 1 in 15,000:
  - rule of 3: would need 45,000 in a trial
  - therefore, impossible to detect premarket
  - but a significant risk considering underlying disease, efficacy and availability of alternatives.

Quality control

Usually countries maintain quality control laboratories which on a regular basis test the quality of medicines. They see if there are any medicines which are substandard or falsified.

In the name of quality control, pharma companies have persuaded WHO to refer to substandard and falsified medicines as counterfeit. In order to conflate the problem of Substandard and Falsified medicine with their problem of generic competition . Under the slogan of counterfeit, which technically refers to copyright infringement and not patent infringement. In 2016, WHO resolved to no longer use the word counterfeit in regards to quality/safety/efficacy.

Inappropriate use

- Impact
  - over use
  - wrong treatment
  - inadequate treatment
- Causes
  - doctors' lack of information
  - doctors' lack of commitment to evidence based practice
  - aggressive marketing
  - weak regulation
  - consumer pressure
- Necessary background
  - medicines promotion; principles, precedents and politics
  - professional education
  - struggles over medicines regulation
  - community attitudes and expectations

WHO (2002)

- Worldwide more than 50% of all medicines are prescribed, dispensed, or sold inappropriately, while 50% of patients fail to take them correctly.

- Common types of irrational medicine use are:
  - the use of too many medicines per patient (polypharmacy);
  - inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections;
  - over-use of injections when oral formulations would be more appropriate;
  - failure to prescribe in accordance with clinical guidelines;
  - inappropriate self-medication, often of prescription only medicines.

WHO (2002). Promoting Rational Use of Medicines: Core Components. WHO Policy Perspectives on Medicines. Geneva, World Health Organization

Inappropriate prescribing for the elderly

- Brazil (60+ years, discharged from tertiary hospital)
  - 13.9% potentially inappropriate medications
  - 39.1% potential prescribing omissions

- Los Angeles (400 elderly African Americans)
  - 70% potentially inappropriate medications
  - 27% taking at least one medication classified as “Avoid”

- US Veterans Health Administration (older adults receiving OP care)
  - 12.3% potentially inappropriate prescriptions

Inappropriate antibiotic use (WHO, 2005)

- In industrialized countries, around 80-90% of antibiotic use for humans occurs in the community
  - at least half of this is based on incorrect indications, mostly viral infections
  - contributing to widening threat of resistance
- Extensive use of antibiotics in livestock production contribute to spread of resistance
- Antimicrobial resistance plus reduced R&D threatens a ‘post-antibiotic era’

Medicines promotion

- Aggressive marketing of under-patent drugs standard practice
  - maximise revenues before patent expires
  - embed brand name familiarity to maintain price premium after patent expires
- Includes
  - public relations
  - advertising
  - direct marketing (‘medical representatives’)
- Spending 50-100% more than on R&D
- Benefits and risks
  - rapid translation of therapeutic advances into practice
  - encourages over-servicing and inappropriate prescribing
  - drives cost escalation
  - builds community expectations: ‘a pill for every ill’
- WHO ‘Ethical criteria’
- National regulatory norms
  - principles and precedents
- Politics and debates

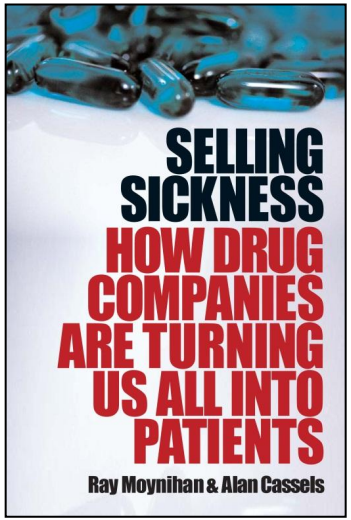
WHO: ethical criteria for drug promotion

- … claims concerning medicinal drugs should be reliable, accurate, truthful, informative, balanced, up-to-date, capable of substantiation and in good taste
- [promotional material] should not contain misleading or unverifiable statements or omissions likely to induce medically unjustifiable drug use or to give rise to undue risks
- The word "safe" should only be used if properly qualified. Comparison of products should be factual, fair and capable of substantiation.
- Promotional material should not be designed so as to disguise its real nature.
- Scientific and educational activities should not be deliberately used for promotional purposes.
- Advertisements to the general public … should not generally be permitted for prescription drugs or to promote drugs for certain serious conditions that can be treated only by qualified health practitioners.

Common practices

- Advertising
- Public relations
- Medical detailing
- Advertisements within prescribing software
- Gifts (equipment, travel, accommodation, etc)
- Sponsored dinners, recreational events
- Conference sponsorship
- Journal support through advertising
- Sponsored research
- Sponsored clinical guidelines
- Consultancies and advisory boards
- Ghostwriting
- Support for patient associations
- Disease mongering (meetings, media, reports)

Disease mongering



PLoS Medicine. A collection of articles on disease mongering: how drug companies sell sickness. Presented at the Inaugural Conference on Disease Mongering, Newcastle, Australia, April 11-13, 2006. http://collections.plos.org/diseasemongering-2006.php

Drug Promotion: Why the concern?

Drug giant forks out $65,000 on posh nosh for doctors

The Australian, July 21, 2006

- Pharmaceutical promotion selectively promotes the benefits of the latest and most expensive drugs.
- It provides minimal information about drug side-effects, contra-indications and opportunity costs.
- Cost-effective generic drugs and non-drug solutions are rarely promoted.

“Pigs and reptiles”

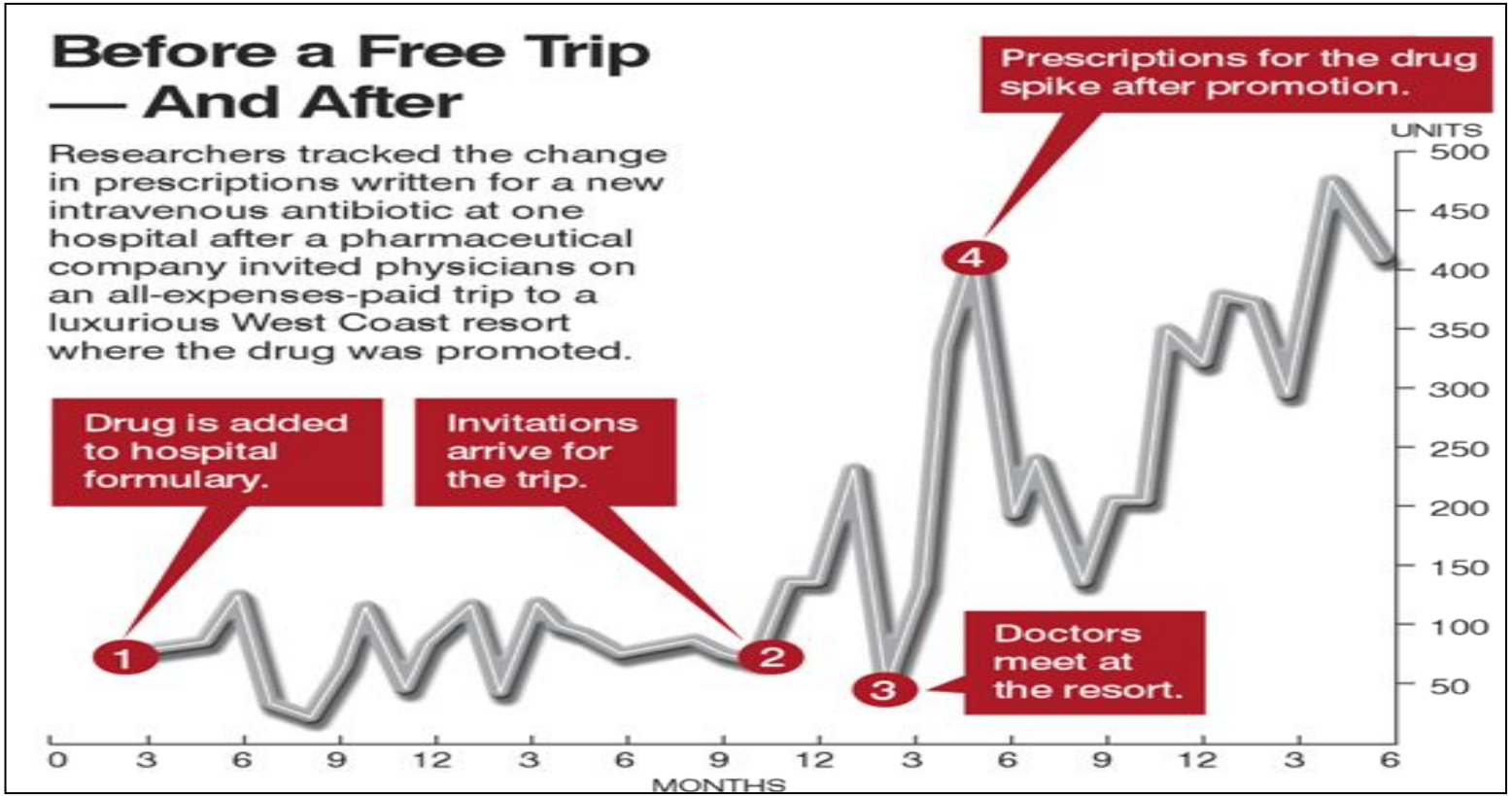
BMJ 2003;326 (31 May)

- Some 80-95% of doctors regularly see drug reps despite evidence that their information is overly positive and prescribing habits are less appropriate as a result.
- Many doctors receive multiple gifts from drug companies every year, yet most doctors deny their influence despite considerable evidence to the contrary.

However

Industry-doctor interaction correlates with:

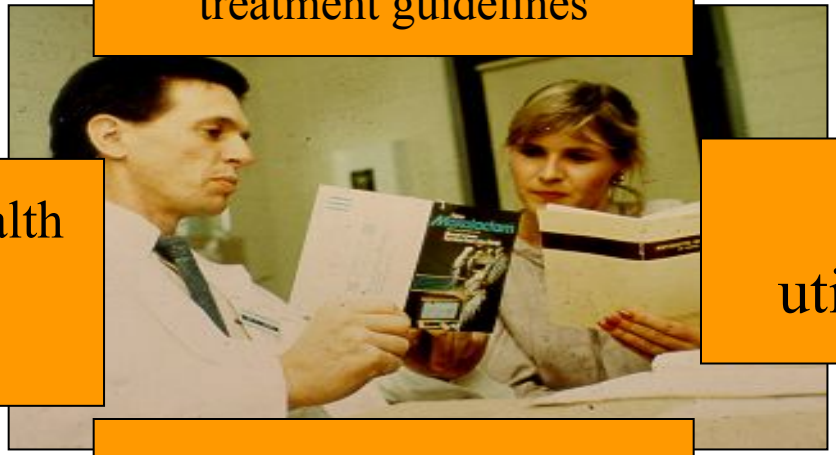
- doctors' preferences for new products that hold no demonstrated advantage over existing ones.
- decreased prescribing of generic drugs.
- a rise in both and irrational and incautious prescribing.
- rising prescription expenditures.


Before a Free Trip — And After
Researchers tracked the change in prescriptions written for a new intravenous antibiotic at one hospital after a pharmaceutical company invited physicians on an all-expenses-paid trip to a luxurious West Coast resort where the drug was promoted.
Drug is added to hospital formulary.
Invitations arrive for the trip.
Doctors meet at the resort.
Prescriptions for the drug spike after promotion.
1
2
3
4
UNITS
500
450
400
350
300
250
200
150
100
50
0 3 6 9 12 3 6 9 12 3 6 9 12 3 6
MONTHS

Independent information

Quality Assurance Cycle

Continually updated standards of practice: treatment guidelines



Drug audit / utilisation review

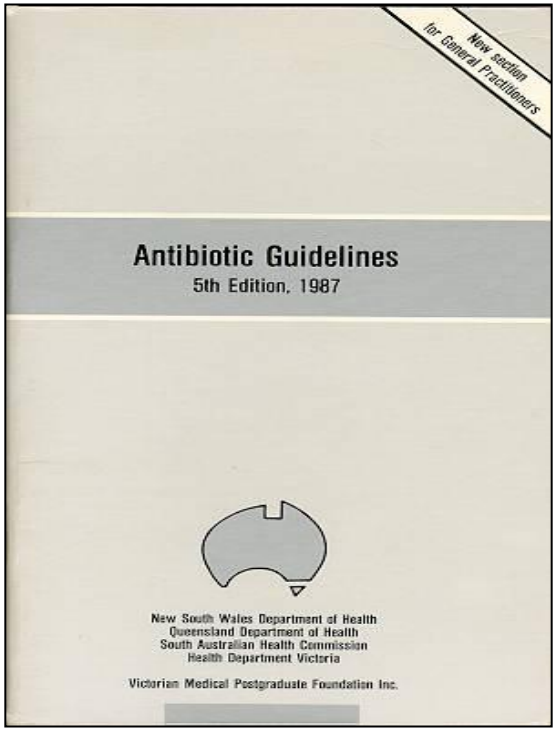
Practitioner reflection / targeted education

Feedback results to health administrators and guideline authors

Independent advice

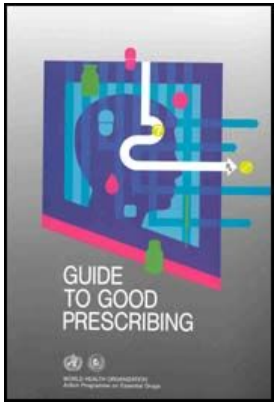
- Invest in provision of independent advice;
  - professionals (including clinical guidelines, academic detailing);
  - consumers (including social marketing) (inappropriate use)

Antibiotic Guidelines



- Best practice recommendations concerning the treatment of choice for common clinical problems.
- Written by teams of national experts.
- Evidence based where possible.
- Regularly updated.
- Endorsed by Medical Associations, Colleges, etc.
- Used for medical education, problem look-up, drug audit and targeted educational campaigns.

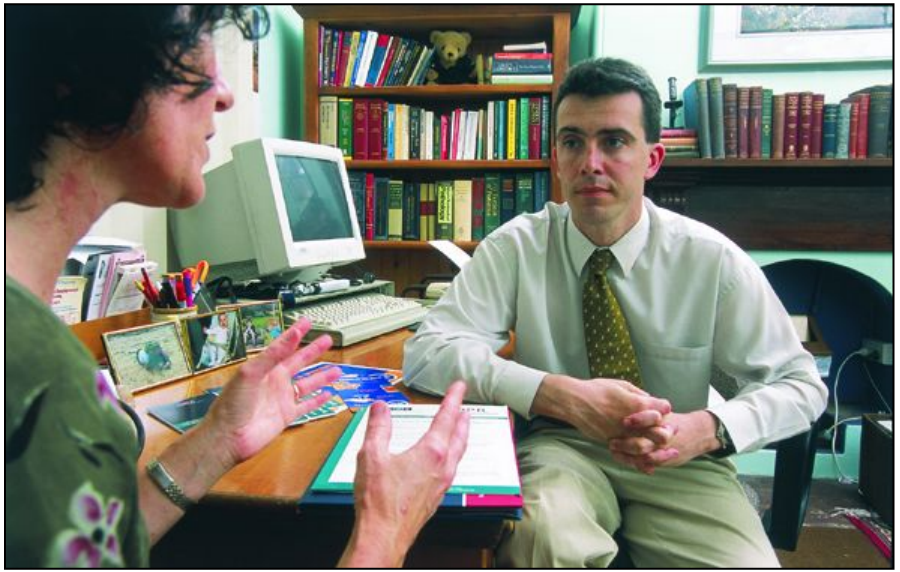
NPS: Core curriculum



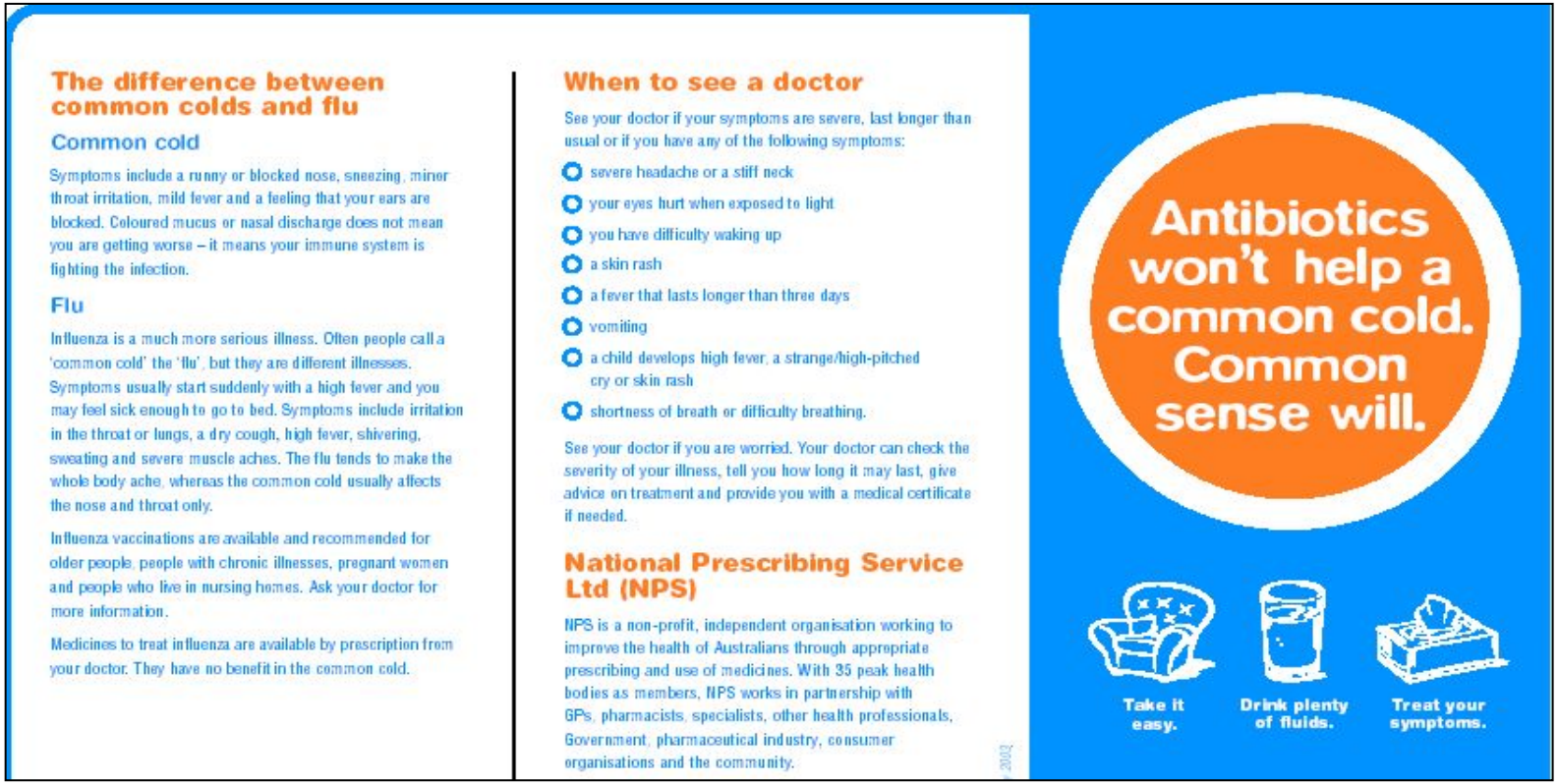
http://nps.unisa.edu.au/new/index.htm

NPS: Academic detailing

Also: home medication review by pharmacists



NPS: Consumer Campaigns



The difference between common colds and flu

Common cold

Symptoms include a runny or blocked nose, sneezing, minor throat irritation, mild fever and a feeling that your ears are blocked. Coloured mucus or nasal discharge does not mean you are getting worse – it means your immune system is fighting the infection.

Flu

Influenza is a much more serious illness. Often people call a 'common cold' the 'flu', but they are different illnesses. Symptoms usually start suddenly with a high fever and you may feel sick enough to go to bed. Symptoms include irritation in the throat or lungs, a dry cough, high fever, shivering, sweating and severe muscle aches. The flu tends to make the whole body ache, whereas the common cold usually affects the nose and throat only.

Influenza vaccinations are available and recommended for older people, people with chronic illnesses, pregnant women and people who live in nursing homes. Ask your doctor for more information.

Medicines to treat influenza are available by prescription from your doctor. They have no benefit in the common cold.

When to see a doctor

See your doctor if your symptoms are severe, last longer than usual or if you have any of the following symptoms:

- severe headache or a stiff neck
- your eyes hurt when exposed to light
- you have difficulty waking up
- a skin rash
- a fever that lasts longer than three days
- vomiting
- a child develops high fever, a strange/high-pitched cry or skin rash
- shortness of breath or difficulty breathing.

See your doctor if you are worried. Your doctor can check the severity of your illness, tell you how long it may last, give advice on treatment and provide you with a medical certificate if needed.

National Prescribing Service Ltd (NPS)

NPS is a non-profit, independent organisation working to improve the health of Australians through appropriate prescribing and use of medicines. With 35 peak health bodies as members, NPS works in partnership with GPs, pharmacists, specialists, other health professionals, Government, pharmaceutical industry, consumer organisations and the community.

2003

Antibiotics won't help a common cold. Common sense will.

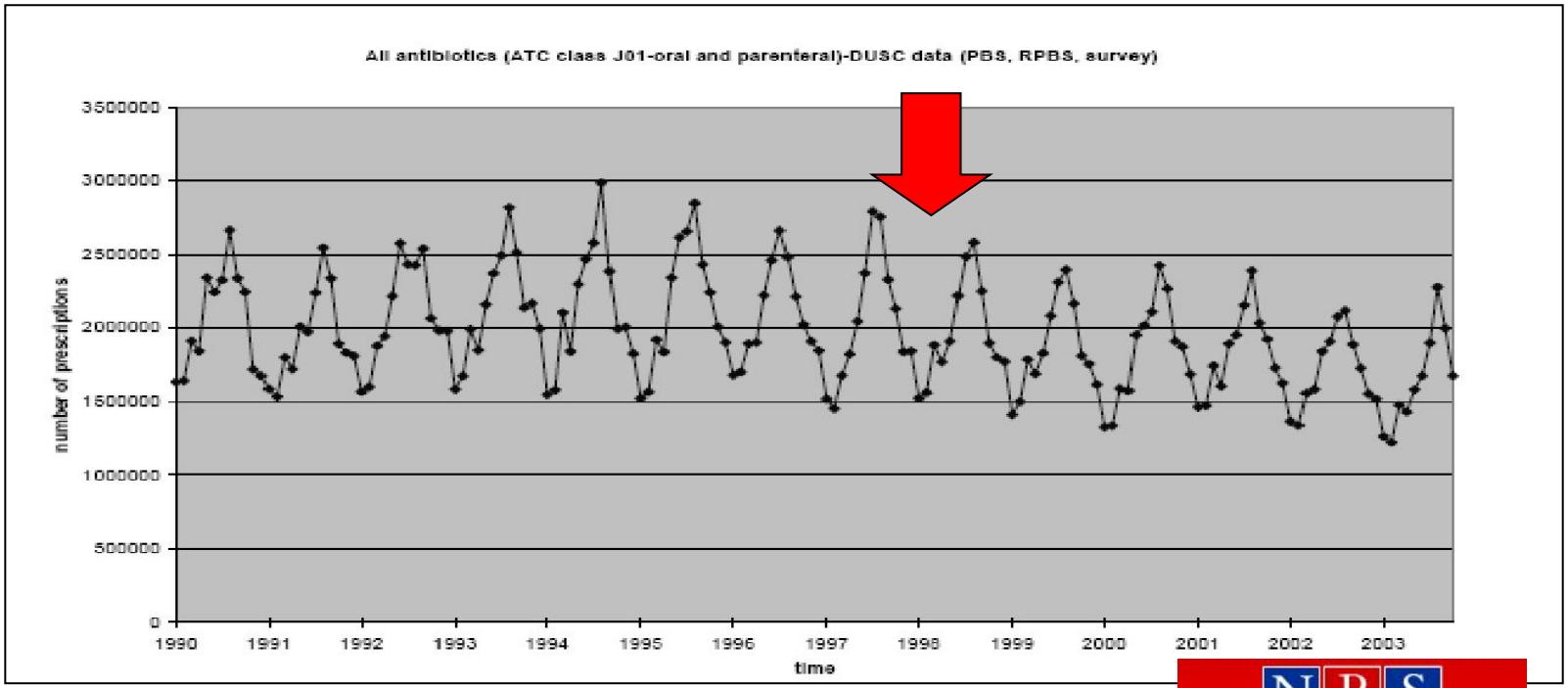
Take it easy.

Drink plenty of fluids.

Treat your symptoms.

http://www.gottacold.com/

Results: antibiotics scripts 1990-2004



National Prescribing Service Limited

- The NPS initially received about $5 million per annum (for four years) in 1997/98.
- A evaluation of their first three years of operations suggested their activities achieved PBS savings of over $15 million per annum for a cost of $5 million per annum.
- Their budget has subsequently been increased and a consumer education moiety has been added.
- Spending money on RDU activities saves money by reducing inappropriate drug use.

In hospitals: drug and therapeutics committees (DTCs)

- Select cost-effective drugs for the hospital formulary.
- Develop (or adapt) and implement standard treatment guidelines.
- Audit drug use to identify problems.
- Conduct interventions to improve drug use.
- Manage adverse drug reactions and medication errors

There is also a growing alliance between academia and the pharmaceutical and biotechnology industries. This has given rise to serious and widespread concern over ethical and scientific issues such as

- the potential for conflict of interest
- unethical patient recruitment practices
- inadequacy of informed consent
- lack of capacity to ensure on-going monitoring of clinical trials and adherence to principles of sound and ethical clinical practice
- poor reporting and management of adverse events.

Thank You