Pharmacoeconomics and Management in Pharmacy IV

[John Vella B.Pharm.(Hons.) M.Sc.(Pharmacoeconomics)]

Pharmacoeconomic news review

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PE in the news (i)

Pharma representatives call for reimbursement

by Vanessa Macdonald - editorial@di-ve.com
Current Affairs -- 12 December 2010 -- 16:35CEST

Representatives of pharmaceutical companies are calling on the government and the Opposition to review the current system whereby a limited range of medicines are dispensed free to Yellow Card holders, saying that this was denying patients access to innovative medicines.

"What is happening is that the government is saying that 'everything' will remain free of charge for ever whereas the reality is that not 'everything' is available," one representative told www.di-ve.com.

The problem is mainly innovative drugs, which offer the latest treatment but which are most expensive in the first years that they are available – often dropping to 1/10th their cost once the patent runs out and generics flood the market.

The pharmaceutical companies clearly have an interest in recouping their heavy research investment during these years – but while abroad innovative medicines make in onto the approved list of medicines within a few months, there is a considerable backlog here in Malta and since the Government Formulary List Advisory Committee was set up in January 2010, only 16 new drugs have been approved (meaning that they can be prescribed by government doctors).

In fact, they said, of the €3 million allocated for innovative drugs in the budget for 2010, hardly anything has been spent (although allocated to particular drugs).

Reimbursement (i)

- Various actors in the pharmaceutical field are calling for a reimbursement system
- In such a scenario, patients would pay the full price for their medicines and get the whole amount refunded(full reimbursement),pay part of the cost(co-pay), or pay a fixed prescription fee
- Elderly citizens might get vouchers to defray the social implications of such a system

Reimbursement (ii)

- The act of having to sustain out-of-pocket expenses might deter resource wastage
- A highly contentious move that, in all probability would not be possible without all round political consensus
- The article quoted is stimulated by the need of the ‘big pharma’ companies to further penetrate the state formulary

PE in the news (ii)

Saturday, 4th December 2010

EU mounts new generic pharma probe

AFP

The European Commission announced new surprise inspections in the pharmaceutical sector yesterday amid suspicions companies are colluding to block the development of cheaper generic drugs.

A spokeswoman for AstraZeneca, Britain's second biggest drugmaker by sales after market leader GlaxoSmithKline, said that it had been inspected in checks relating to heartburn drugs.

"Commission officials carried out unannounced inspections at the premises of a limited number of companies active in the pharma-ceutical sector in several member states," the commission said of the spot checks held on Tuesday.

"The Commission has reason to believe that the companies concerned may have acted individually or jointly, notably to delay generic entry for a particular medicine.

"If confirmed, this could be a potential violation of EU antitrust rules that prohibit restrictive business practices and/or the abuse of a dominant market position."

The AstraZeneca spokeswoman said visits "relate to alleged practices regarding esomeprazole (Nexium) in Europe and we're cooperating with the authorities".

European citizens spend hundreds of euros on medicine each year, with the market worth hundreds of billions of euros at retail prices, according to commission data.

The relationship between companies that patent their products as brand-named medicine, as well as their ties with generic drug prod-ucers, has been a focus for commission inspectors over recent years.

Generic drugs are cheaper and save patients and insurance firms money without compromising on effectiveness. But some companies have in the past been accused of using patent filings to stop generic medicines hitting the market, or tying up potential competitors for years in legal disputes.

In the worst example uncovered, 1,300 separate patent filings were made for a single medicine across the 27-nation EU.

Generic medicines (i)

- The article addresses the concerns of the EU regarding anti-competitive measures employed by branded originator companies to delay the entry of generic versions to the market
- Originator companies file ‘patent clusters’ in abuse of the spirit of the patent system
- Incremental patents are also filed

Generic medicines (ii)

- E.g. Coversyl 4mg and the newly available Coversyl 5mg.
- The manufacturers claim improved stability and therapeutic effect, but realistically it is all part of the extension of the lifecycle of a product range, or patent ‘evergreening’

PE in the news (iii)

Thursday, 14th September 2006

Proposal to ban prescription of brand medicines turned down

Massimo Farrugia

The government has turned down a suggestion to amend the Medicines Act so that doctors would no longer be allowed to prescribe branded medicines.

During talks between medicine agents and the government, as a result of which Maltese patients should soon have access to more medicines at lower prices, the Chamber of Small and Medium Enterprise (GRTU) claimed patients should not be forced to buy a branded product when they could get generic medicines. These medicines imitate branded drugs but are cheaper because they are patent free.

Since the medicine purchased by patients is determined to a great extent by doctors' prescription, the GRTU argued, reducing registration fees to encourage the importation of generics should be backed by a change in the law forcing doctors to prescribe the international non-propriety name (INN) for a product's active ingredient and not a particular brand.

"Generics certified in the European Union, which are those imported to Malta, are of high quality despite the fact that some still view them with disdain locally," GRTU's Mario Debono, a pharmacist and medicine importer, said yesterday.

But during the talks, government representatives claimed that such a judgement should lie with doctors, whose professional discretion should not be overruled by legislation.

The government's side, led by Parliamentary Secretary Tonio Fenech, argued that as the law stands, pharmacists may offer an alternative brand or cheaper generic equivalents, "unless the prescriber specifically requests a particular branded product by writing 'branded' or '®' on the prescription".

Reginald Fava, of the Malta Chamber of Commerce and Enterprise and a branded-medicine importer, was of a different view. During a press conference on Tuesday afternoon, Mr Fava said pharmacists had no right to change what the doctor prescribed.

"If dispensers were to have the right to change what the doctor prescribes, they would sell the products on which they profit most," he said, standing his ground when reporters pointed out that a pharmacist may, by law, offer generics unless the doctor specifically notes that no substitution is allowed.

Though it is often rumoured that doctors' and pharmacists' behaviour is influenced by drug companies, especially when it comes to prescribing and dispensing medicine, Medical Association of Malta general secretary Martin Balzan had told The Times in an interview that prescribing was in no way influenced by drug companies, saying that it was not ethical for doctors to promote one company's product over another.

INN prescribing

- In addition in 2008, savings through increased prescribing efficiency were calculated at £364M in England alone
- This was enhanced by high International non-proprietary name (INN) prescribing currently at over 83% of overall prescriptions, rising to over 99% for certain generics

INN prescribing

- Efforts were made locally, but opposed by the MAM
- Ideally the practice would start from medical school and onto the state run hospitals and healthcentres, from where a large percentage of prescriptions originate

INN prescribing

(extracted *from Sustaining generic medicines markets in Europe, Simoens & De Coster*)

prescribe brand-name medicines.

INN prescribing does not necessarily lead to generic medicines' use. The success of INN prescribing policies in stimulating generic medicines' use depends on regulation governing which medicine the pharmacist needs to dispense. The decision of which medicine to dispense is also influenced by the financial remuneration of pharmacists. If INN dispensing regulation and remuneration of pharmacists favour generic medicines, then INN prescribing can be expected to raise generic medicines' use.

PE in healthcare policy

The following are some examples of initiatives that have been undertaken over the past year to improve health system performance and bring about long term sustainability:

- Commencement of work to draw up a defined health care package of services.
- Introduction of a new process for inclusion of medicines on the formulary which imposes maximum price capping at point of introduction.
- Use of health technology assessment methods to assess introduction of new technologies to ensure value for money, affordability and sustainability.
- Costings exercise to update the legal notice on fees for foreigners not entitled to health care in Malta thereby envisaged to provide increased revenue to hospitals.
- Work on the introduction of data reporting according to the EUROSTAT "System of Health Accounts" to enable better monitoring and benchmarking.
- The first wave of financial controllers have been recruited and are being assigned specific tasks within the Ministry for Social Policy;
- Mechanisms to ensure more efficient procurement of medicines with reduction of idle stock are being implemented.

2011 Budget Estimates (i)

MINISTRY FOR HEALTH, THE ELDERLY AND COMMUNITY CARE

Ministry for Health, the Elderly and Community Care (continued) — Vote 42 Recurrent

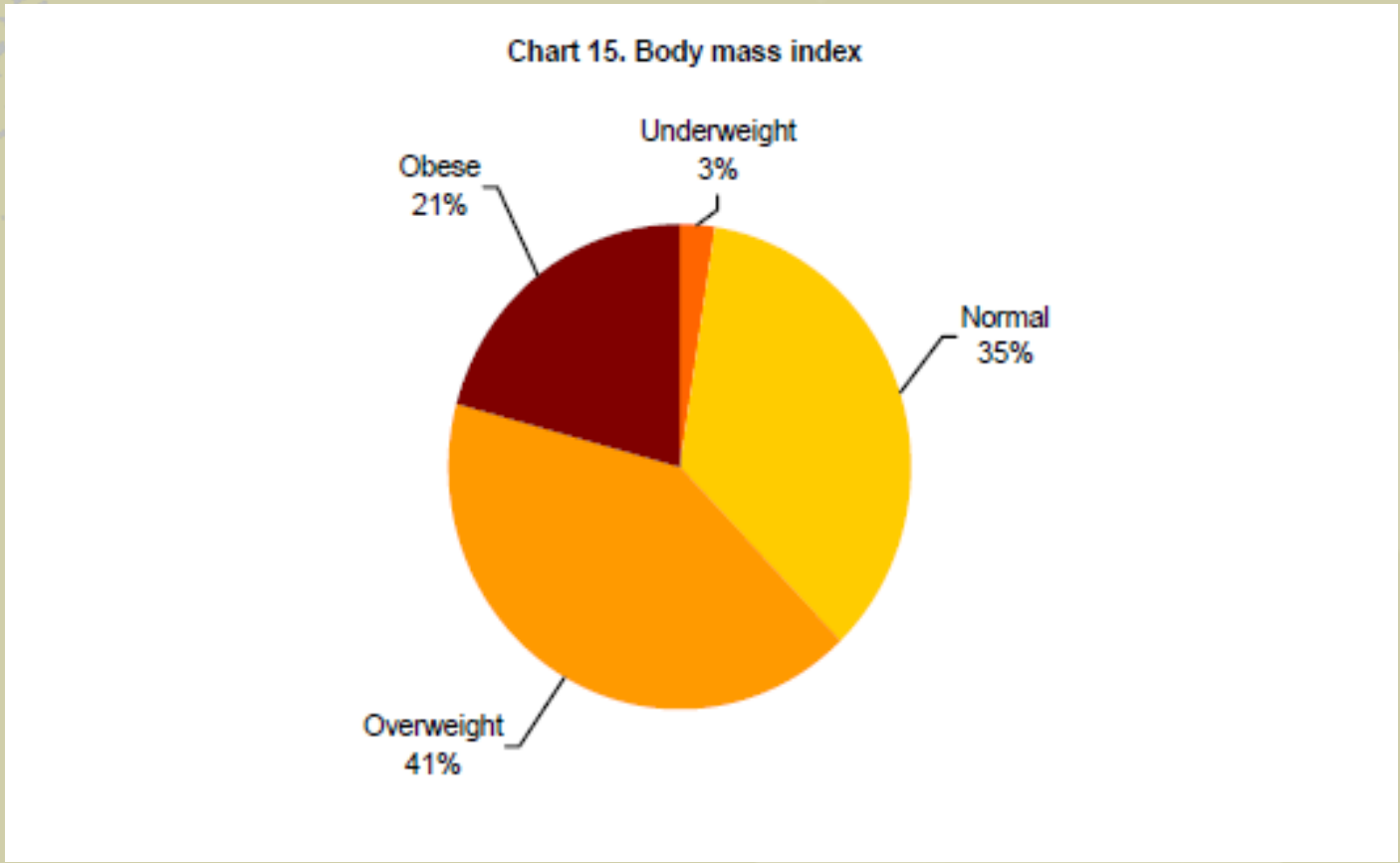
	Expenditure by Standard Item	Actual Expenditure 2009 €	Approved Estimate 2010 €	Estimate 2011 €
	Programmes and Initiatives			
5029	Residential Care in Private Homes (a)	[2,118,512]	[2,250,000]	**3,682,000**
5043	National Bioethics Consultative Commission	59	5,000	**3,000**
5055	Specialised Treatment by Foreign Experts of Patients Locally and Abroad	1,140,968	1,500,000	**1,500,000**
5057	Health Education and Nutrition Unit	158,042	100,000	**120,000**
5060	Specialised Prosthetic/Orthotic Service	658,587	636,000	**500,000**
5062	Pest Control	22,336	28,000	**28,000**
5196	Ex-Gratia Compensation to Haemophiliacs	52,411	58,000	**58,000**
5242	National Commission Mental Health Reform	2,201	10,000	**4,000**
5244	Homes for the Elderly (a)	[4,121,375]	[3,200,000]	**4,000,000**
5321	Primary Health Care	61,479	30,000	**25,000**
5382	Quality Service Initiative	0	5,000	**1,000**
5388	Anzjan tas-Sena	7,367	5,000	**5,000**
5400	Medicines and Surgical Materials	76,377,999	64,000,000	**64,000,000**
5485	Pharmacy of Your Choice	657,823	1,500,000	**2,300,000**
5486	Mellieha Home for the Elderly (a)	[2,999,180]	[3,145,000]	**3,145,000**
5504	Post-Graduate Training	125,374	800,000	**1,000,000**
5505	Breast Screening	640,264	1,640,000	**1,400,000**
5506	Mater Dei Hospital Non-medical Equipment Facilities Management	5,478,382	7,500,000	**5,800,000**
5507	Congress for Nurses	89,999	50,000	**150,000**
5508	Maintenance of Medical Equipment	2,136,293	2,500,000	**2,300,000**
5509	Mount Carmel Hospital - Sectorisation Project	275,000	570,000	**450,000**
5542	Mount Carmel Hospital - Crisis Intervention Team	---	200,000	**100,000**
5543	Specialist Training	---	420,000	**400,000**
5544	New Technology Services	---	500,000	**300,000**
5559	Waiting Lists for Medical Services (Outsourcing)	---	4,000,000	**2,300,000**
5560	Radiography Course	---	122,000	**267,000**
5561	Strategy on Obesity	---	150,000	**220,000**
5608	Sexual Health Policy	---	---	**200,000**
5609	National Cancer Plan	---	---	**900,000**
5610	Care Services - NGOs	---	---	**1,000,000**
5611	Union of the Mediterranean Ministers of Health Summit	---	---	**35,000**

2011 Budget Estimates (ii)

- € 64 million voted for *Medicines and surgical materials*
- This equates to € 160 per Maltese citizen
- € 220,000 voted for a national *Strategy on Obesity*, an infinitely small amount when one considers the results of the latest NSO lifestyle survey

2011 Budget Estimates (iii)

(Extracted from *the Lifestyle Survey 2007, NSO Malta*)



Vaccination benefits (i)

Varicella-Related Hospital Stays Down With Vaccine

By Michael Smith, North American Correspondent, MedPage Today
January 03, 2011

MedPage Today Action Points

- Note that the beneficial effects of vaccination were seen in all age groups, allaying fears that vaccinating children would shift the burden of disease to older adults.

- Point out that patients with a diagnosis of herpes zoster were excluded from the study.

Review

The yearly number of varicella-related inpatient stays in the U.S. fell by at least 65% after the introduction of the one-dose vaccination program, researchers reported.

The decline -- based on analysis of two large national surveys -- was seen in all age groups, including adults, according to Adriana Lopez, MHS, and colleagues at the CDC.

The analysis suggests vaccination prevented about 50,000 inpatient stays related to varicella over a seven-year period, Lopez and colleagues reported online in *Pediatrics*.

The findings appear to alleviate fears that vaccinating children would simply shift the burden of disease to an older population, the researchers argued.

Vaccination benefits (ii)

- Varicella vaccine has a high initial cost, RRP of around € 70
- The investment in the vaccination programme raised costs immediately, but provided the required savings in the future, when hospitilisation due to Varicella dropped significantly
- Not outwardly a popular or easy administrative move

Critique of a PE journal article

Background facts (i)

- “only 1% of the articles in medical journals are scientifically sound”[1]
- There are perhaps 30,000 biomedical journals in the world, and they have grown steadily by 7% a year since the seventeenth century[2]

- [1] Professor David Eddy, Duke University
- [2]Dr. Richard Smith, BMJ editor

Background facts (ii)

- Critical reviews of papers in medical journals have consistently found that about 50% of published articles used incorrect statistical methods
- can lead to invalid results and inappropriate conclusions. A conservative estimate is that about 25% of medical research is flawed because of incorrect conclusions drawn from confounded experimental designs and the misuse of statistical methods[1]

- [1] Zolman, 1993

Background facts (iii)

- Also, the bias generally favors the treatment over the control
- “Why are errors so common? Put simply, much poor research arises because researchers feel compelled for career reasons to carry out research that they are ill equipped to perform, and nobody stops them.”[1]

- [1] Altman, 1994

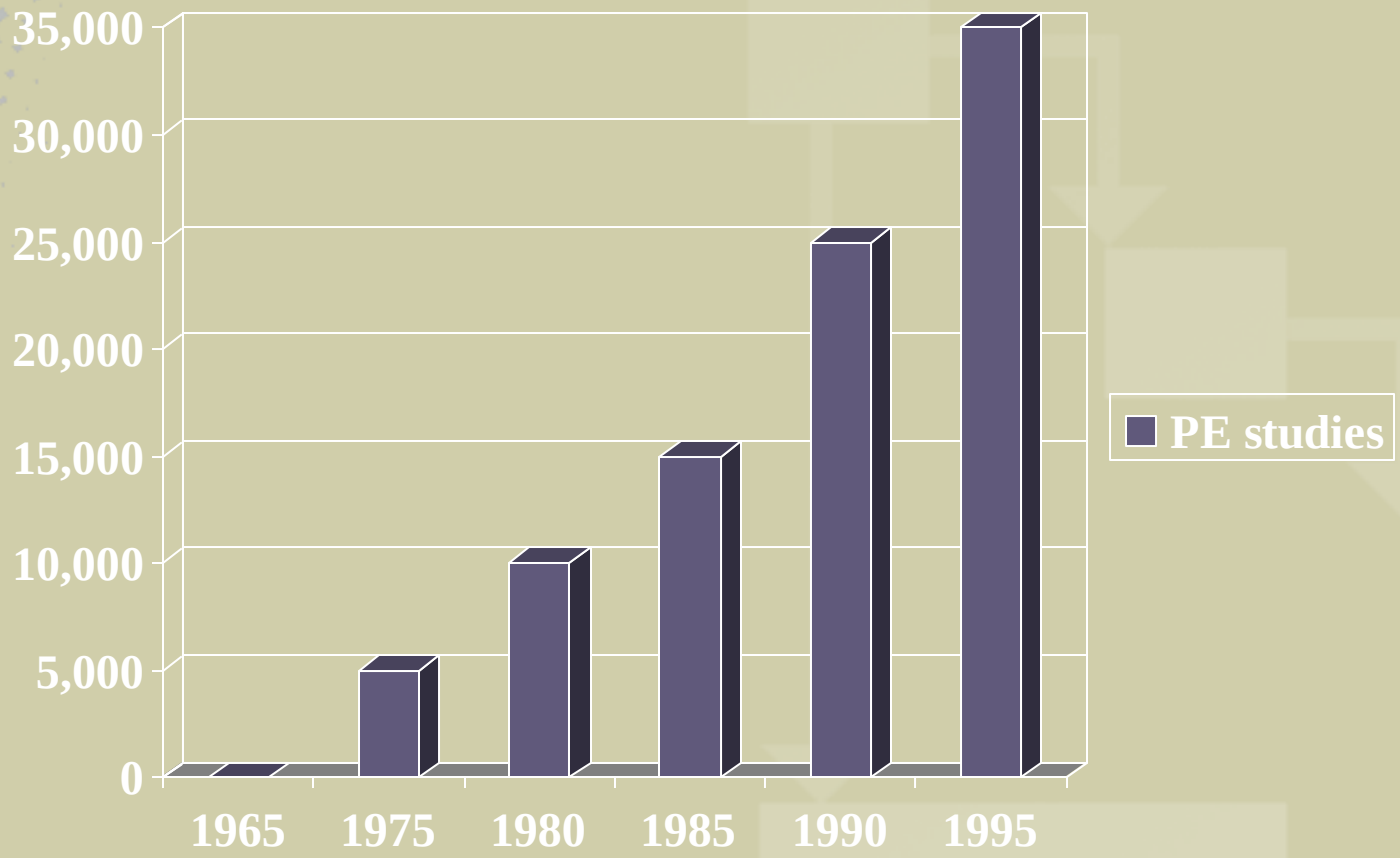
Background facts (iv)

- Researchers often use of the wrong techniques (either willfully or in ignorance)
- Use the right techniques wrongly
- Misinterpret their results
- Report their results selectively
- Cite the literature selectively
- Draw unjustified conclusions

Journal articles (i)

- Tens of thousands of articles are out there
- Electronic media has increased accessibility
- It is imperative that poor articles are discarded and good quality research appreciated and referenced
- No study is perfect; thoroughness is balanced with the practicality of the research

Quantity of available studies



Journal articles (ii)

- It is imperative to evaluate research findings in the light of their validity and general application
- That is, findings reported must be based on valid methodology and data and results can be extrapolated to general populations, without the need for protocol controlled environments

Journal Articles (iii)

- If a study is carefully reviewed to ensure that the author(s) included all meaningful components of an economic evaluation, the likelihood of finding credible and useful results is higher
- This lecture will highlight the basic rules to follow when evaluating an economic study[1-2]

- [1]Adapted from Rascati K, Essentials of Pharmacoeconomics
- [2]Adapted from Say L, Critical Appraisal of Research Reports

Journal Articles (iv)

- Review of more than 4200 published medical reports in about 30 journals(many of them prestigious e.g. BMJ, JAMA, NEJM, Lancet) in terms of scientific adequacy of study designs, data collection and statistical methods *(Williamson, 1986)*
- – only 20% of 4235 research reports met the validity
- criteria
- – ~80% of those inadequately designed and analysed
- had reported positive findings whereas ~ 25% of those
- with adequate designs reported positive results

Basic points

- Is the article relevant to current needs?
- Are the results valid?
- Can they be applied to general practice?

Title: Is the Title Appropriate?

Randomised controlled trial comparing cost effectiveness of general practitioners and nurse practitioners in primary care

P Venning, A Durie, M Roland, C Roberts, B Leese

Title: Is the Title Appropriate?

- Can we make out what type of PE study was carried out?
- Is it a CMA, CEA, CUA, or CBA?
- Is the author stating his biases in the manner in which the title is worded?
- Is the journal a respectable peer-reviewed and often quoted one?

Title: Is the Title Appropriate?

- In this case the study is clearly identified as an RCT, meaning that strict protocols were in place
- The type of PE approach is not specified
- However, the setting (primary care) is indicated
- No bias is present in the title statement
- The BMJ is one of the top medical journals in which to have a paper accepted

Is a Clear Objective Stated?

The aim of this study was to compare the process, outcome, and costs of care given by general practitioners and nurse practitioners for patients requesting a same day appointment in 20 general practices. This group of patients was chosen because a high proportion would be likely to agree to randomisation as they would not have a strong preference for one practitioner who was already involved in their ongoing care.

Is a Clear Objective Stated?

- Does the author(s) clearly state the aim and objectives at the beginning of the study?
- A well designed PE evaluations sets out its targets early on, revealing that the relevant groundwork has been diligently carried out
- Flawed research will tend to be vague in where it wants to get, and how it will get there

Is a Clear Objective Stated?

- The extract shown before was taken from the second paragraph of the article
- The manner in which the study will be carried out is clearly defined, as is the setting
- The rationale for adopting a particular approach is also argued

Is a Clear Objective Stated?

- E.g. of a weak study title:

- An analysis of the cost of anti-hypertensive treatment in the elderly

Is the study design appropriate?

The study took place in 20 geographically dispersed practices in England and Wales. Table 1 shows the location, list size, and number of general practitioner partners in the practices recruited. Ethical approval was obtained for the 20 practices from local research ethics committees. Each practice employed a nurse who had completed a one or two year nurse practitioner training programme at diploma, BSc, or MSc level. The median length of time the nurses had been qualified as nurse practitioners was 3 (range 1-5) years and the median time as registered nurses was 22 (9-35) years. Each nurse practitioner had been seeing patients as first point of contact for at least two years.

Is the study design appropriate?

- When comparing interventions or treatments, it is imperative to draw a comparison to the best alternative available
- Drawing parallels to *weaker* alternatives falsely strengthens results
- E.g. comparing a new cox-2 inhibitor to aspirin will inordinately favour the compound

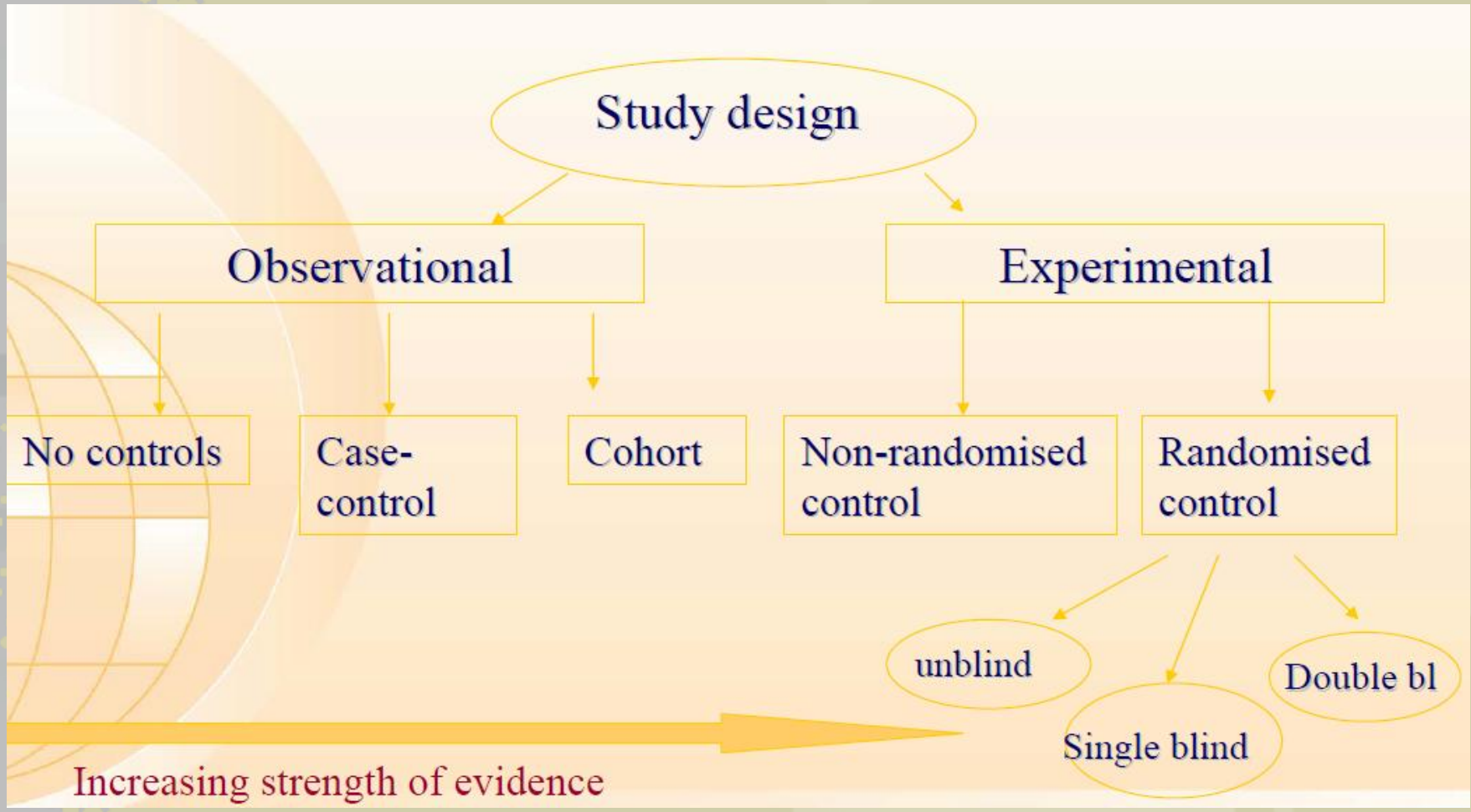
Is the study design appropriate?

- The same study compared the effectiveness of nurse practitioners to GPs
- This is an appropriate choice
- Small sample sizes, and short empirical time-frames are the sign of a weak study design

Is the study design appropriate?

- E.g. Jupiter had 17,802 subjects over a median follow-up period of 1.9 years
- Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin
- One of the largest recent studies on statins

Evaluate the strength of the design



Study design

- The previous slide demonstrates that the ‘strongest’ evidence is provided by studies based on a double blind, randomised experimental study
- This is also known as an RCT, or Randomised Controlled Trial and is the gold standard for clinical trials

Types of RCTs (i)

- Classified by study design.
- Parallel-group – each participant is randomly assigned to a group, and all the participants in the group receive (or do not receive) an intervention
- Crossover – over time, each participant receives (or does not receive) an intervention in a random sequence

Types of RCTs (ii)

- Split-body – separate parts of the body of each participant (e.g., the left and right sides of the face) are randomised to receive (or not receive) an intervention
- Cluster – pre-existing groups of participants (e.g., villages, schools) are randomly selected to receive (or not receive) an intervention

Types of RCTs (iii)

- Factorial – each participant is randomly assigned to a group that receives a particular combination of interventions or non-interventions (e.g., group 1 receives vitamin X and vitamin Y, group 2 receives vitamin X and placebo Y, group 3 receives placebo X and vitamin Y, and group 4 receives placebo X and placebo Y)

Types of RCTs (iv)

- The advantages of proper randomisation in RCTs include:
- It eliminates bias in treatment assignment, specifically selection bias and confounding.
- It facilitates blinding (masking) of the identity of treatments from investigators, participants, and assessors.

Types of RCTs (v)

- It permits the use of probability theory to express the likelihood that any difference in outcome between treatment groups merely indicates chance.

Results (i)

- Are the statistics clear and relevant?
- Is the appropriate level of significance quoted?
- A p value of < 0.05 is considered to be the statistical level of acceptability for quoted results
- This means that the results will be replicated in 95% of the general population as compared to the sample studied

Results (ii)

- Has ethical approval been obtained for any patient involvement?
- This is vital, as the case with the MMR and autism controversy in the UK
- The children studied were included without the permission of their guardians or of the hospital administrators
- Chaos for a number of years in the immunisation schedules

Discussion (i)

- Should start off with a statement confirming or denying the initial hypothesis
- Focus should be on the inherent biases and limitations
- The results should be brought into the contextual perspective, that is their relevance to the body of knowledge on the subject matter should be emphasised

Discussion (ii)

- Comparisons to other studies are useful and can be utilised to increase the import of results
- Are the citations presented in a standard format?
- Is the list of contributors reasonable –twenty authors for a small study?

Discussion (iii)

- Conflict of interest –any financial / administrative relationships with institutions related to the outcome of interest
- Take as an example the recent admission by high ranking WHO administrators involved in the Avian/Swine Flu campaigns that they had vested interests in major multinational pharmaceutical companies

Skill summary (i)

- Describe what critical appraisal means and why it is needed
- Identify which information to seek in which sections of a research article
- Be familiar with the important characteristics of a study to be systematically searched in the article (think systematically when reading a research article)

Skill summary (ii)

- Be aware of the checklists and be able to use them to appraise different study designs
- Take on board the points raised and utilise them when producing original work
- Always keep in mind that the whole system of research and the advancement of knowledge is based on an interconnected web of published and referenced work

Skill summary (iii)

- Aware that being able to differentiate the mediocre from the good and outstanding increases the value and solidity of the whole academic knowledge base
- In the field of PE this is all the more important as certain researchers take advantage of the fact that the novelty of the specialty allows them to produce sub-standard and/or misleading work

Checklist (i)

- Use the internet: it is a free and limitless source
- Pick your sources well: only quote journals or peer-reviewed sites that are frequently mentioned within their field of expertise
- Download copies of all references utilised in research

Checklist (ii)

- Follow references around, that is, track down frequently quoted authors and look up more work by them
- File your saved work systematically, otherwise you will never find what you need when you need it
- Learn to scan articles before reading them: assimilate the main points and decide whether it is worth going further

Checklist (iii)

- Once you have identified the main authorities in a particular area you are researching, look up the people they reference and get hold of their work
- If you are not able to find a particular reference, contact the original author

Summary

- The fact that an article has made it to publication does not mean that it is worthwhile
- Critical appraisal of research is vital so as to decide on what to absorb and what to discard when carrying out further study in the field of interest

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