NBP – net benefit prediction:
A method to introduce quantitative information into therapeutic medical decision making

François GUEYFFIER

Lyon University Hospitals Pharmacology & Toxicology Department

Biometry & Evolutionnary Biology Lab

Open seminar on Thursday August 31 afternoon

Presentations related to primary care classifications

Introduction : population and individual therapeutic decisions

- The demonstration that the *net benefit*, i.e. the difference between benefit(s) and harm(s) is favorable, stems from the population of participants in clinical trials.
- For public health decision such as marketing authorization, therapeutic arsenal, reimbursement issues, the *average net benefit* is considered.
- For individual decision, the application of the results of clinical trial(s) requires a *translation* from an information collected at the population level in a more or less recent past period, to the evolution forecast of one single individual.

The NBP project: a solution to apply population results to individual situations

- It is unethical to prescribe a drug when its benefits do not outweigh its harms.
- Therapeutic problem solving relies on the unbiased results of randomized clinical trials (RCT), their syntheses through meta-analyses, their application from RCTs participants population to the individual patient, patient's values and expectations.
- The net benefit project (NBP) project applies this approach.

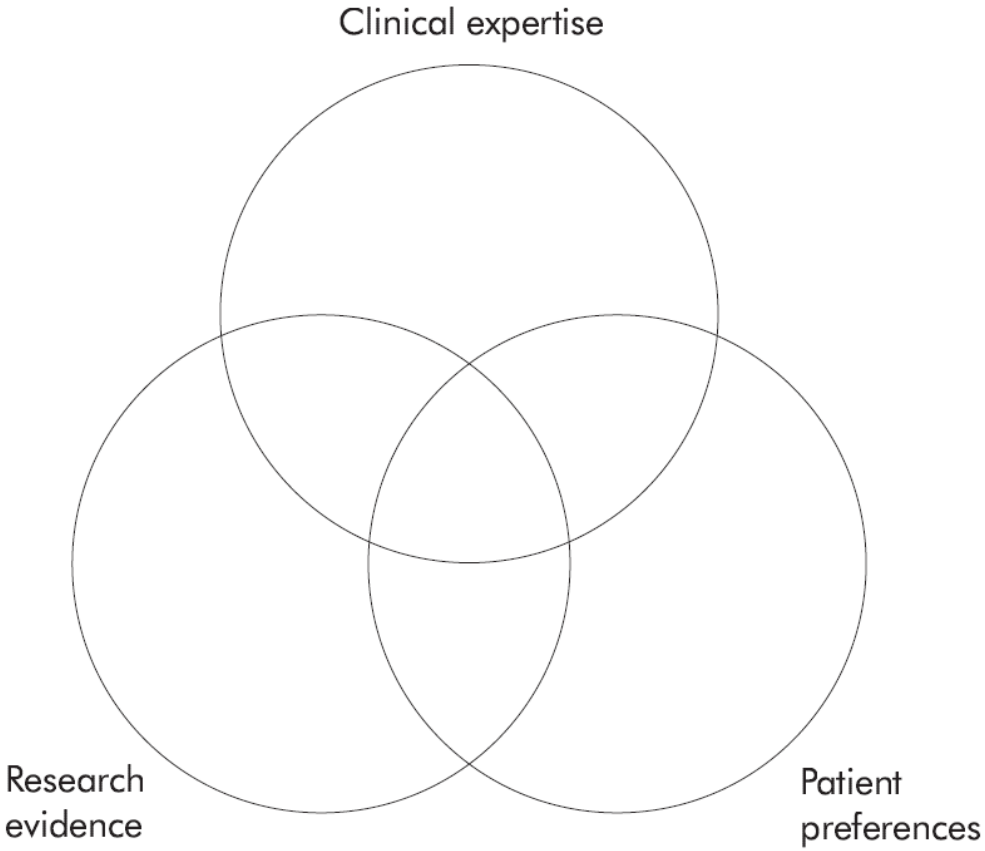

Figure 1 Early model of the key elements for evidence-based clinical decisions

Clinical expertise in the era of evidence-based medicine and patient choice

R Brian Haynes, P J Devereaux and Gordon H Guyatt

Evid. Based Med. 2002;7;36-38
doi:10.1136/ebm.7.2.36

We suggest that this translation be done using simple tools integrated in the prescriber computer environment, and following these few steps:

1. Identification of the situation
2. Determination of the therapeutic objective(s) to be addressed with the drug(s)
3. Prediction of the spontaneous risk (Rc)

regarding this therapeutic objective

1. Estimation of the treatment effects;
    1. E.g. Relative risk (RR)
    2. RR * Rc ➔ ARR : absolute risk reduction
    3. 1/ARR ➔ NNT : number needed to treat
    4. Same algorithm for harms
2. Presentation of information to the patient

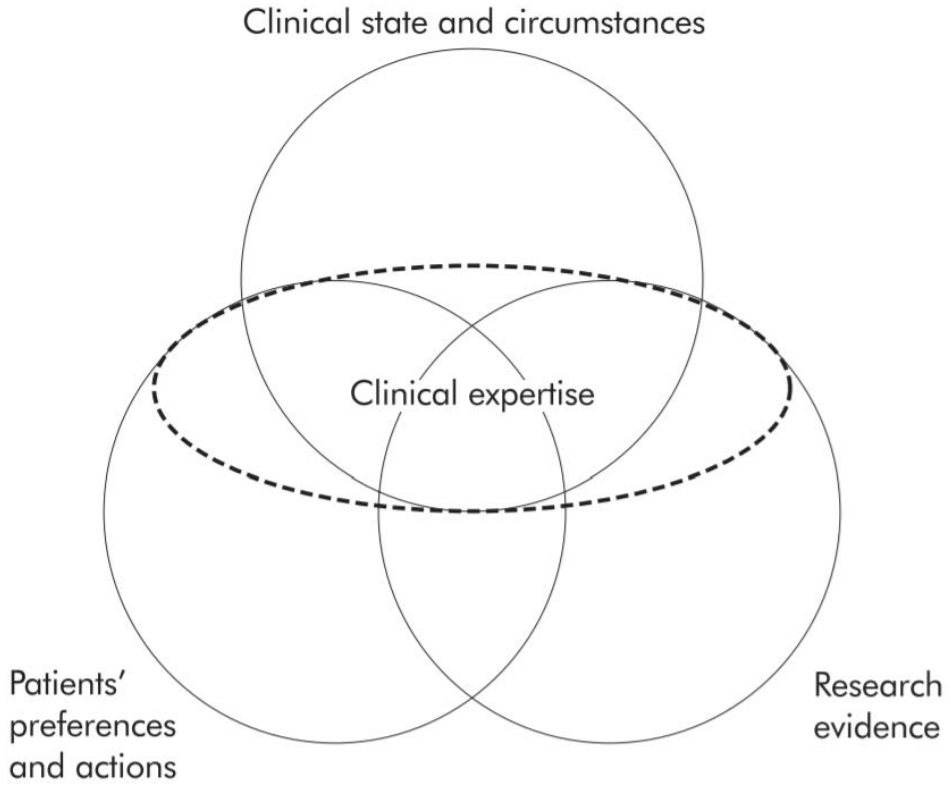

Figure 2 An updated model for evidence-based clinical decisions.

An approach readily available, with a minimum of funding

- All items required for the approach are accessible
  - Publications related to risk scores,
  - Meta-analyses for relative risk, and
  - Available statistical models.
- Integrated platform presenting these various elements within the office or hospital-based patient management software.
- ANSM (Agence Nationale de Sécurité du Médicament) funded the project to test its acceptability 5 years ago, in partnership with department of General Practice of university of Lyon.

Example

- Mrs MB, 65 years of age, T2DM (metformin + sitagliptin), non smoker ever, treated for hypertension (valsartan + HCTZ) with high BP variability
- Her GP requested advice about her BP, apparently uncontrolled
- ECG was normal, as CV exam, noting some overweight
- High BP variability is common in diabetes and she received already two BP lowering drugs
- Renal function was normal, as optic fundus, neurological exam; proteinuria was 20mg/L, total cholesterol 2g/L, HDL 0.7g/L

Example

1. Situation : primary cardiovascular prevention…
2. Therapeutic objective(s) to be addressed : MI, stroke & CHF; CV mortality
3. Prediction of risk at 10 year horizon
4. Estimation of the treatment effects;
    1. Relative risk / benefit from clinical trials / meta-analyses for the candidate drug(s);
    2. Application of this relative benefit to the risk level, obtaining the absolute risk reduction;
    3. Computation of the number of individuals needed to treat (NNT) to prevent one myocardial infarction;
    4. Application of the same algorithm to the harms associated to the drug(s);
5. Presentation of the summarized information to the concerned patient

Quantitated results

	MI	Stroke	CV death	CHF	CV disease
10 years risk	6,30%	8,80%	10,20%	7%	36%

Quantitated results

	MI	Stroke	**CV death**	CHF	CV disease
10 years risk	6,30%	8,80%	**10,20%**	7%	36%
Ideal profile	1,60%	1,40%	**1,30%**	2,50%	9,40%
Absolute risk excess	4,70%	7,40%	**8,90%**	4,50%	26,60%

Quantitated results

	MI	Stroke	**CV death**	CHF	CV disease
10 years risk	6,30%	8,80%	**10,20%**	7%	36%
Ideal profile	1,60%	1,40%	**1,30%**	2,50%	9,40%
Absolute risk excess	4,70%	7,40%	**8,90%**	4,50%	26,60%
relative risk with BPLD	-15%	-30%	**-15%**	-45%	-30%
relative risk with statin	-25%	-25%	**-15%**	0%	-25%
relative risk with aspirin	-20%	-20%	**-15%**	0%	-20%

Quantitated results

	MI	Stroke	**CV death**	CHF	CV disease
10 years risk	6,30%	8,80%	**10,20%**	7%	36%
Ideal profile	1,60%	1,40%	**1,30%**	2,50%	9,40%
Absolute risk excess	4,70%	7,40%	**8,90%**	4,50%	26,60%
relative risk with BPLD	-15%	-30%	**-15%**	-45%	-30%
relative risk with statin	-25%	-25%	**-15%**	0%	-25%
relative risk with aspirin	-20%	-20%	**-15%**	0%	-20%
ARR with BPLD	-0,95%	-2,64%	**-1,53%**	-3,15%	-10,80%
ARR with statin	-1,58%	-2,20%	**-1,53%**	0,00%	-9,00%
ARR with aspirin	-1,26%	-1,76%	**-1,53%**	0,00%	-7,20%
ARR with 2 drugs	-2,28%	-4,18%	**-2,83%**	-3,15%	-17,10%
ARR with 3 drugs	-3,09%	-5,10%	**-3,94%**	-3,15%	-20,88%

Quantitated results

	MI	Stroke	**CV death**	CHF	CV disease
10 years risk	6,30%	8,80%	**10,20%**	7%	36%
Ideal profile	1,60%	1,40%	**1,30%**	2,50%	9,40%
Absolute risk excess	4,70%	7,40%	**8,90%**	4,50%	26,60%
relative risk with BPLD	-15%	-30%	**-15%**	-45%	-30%
relative risk with statin	-25%	-25%	**-15%**	0%	-25%
relative risk with aspirin	-20%	-20%	**-15%**	0%	-20%
NNT with BPLD	106	38	**65**	32	9
NNT with statin	63	45	**65**	NA	11
NNT with aspirin	79	57	**65**	NA	14
NNT with 2 drugs	44	24	**35**	32	6
NNT with 3 drugs	32	20	**25**	32	5

NBP versus traditional approach, *in this case*

- The request was oriented on the risk factor control, a classical biomedical issue
- The NBP approach
  - focuses on CV risk prevention, i.e. the appropriate therapeutic objective
  - opens discussions on other pharmacological risk prevention tools than those involved in the apparent risk factor disorder
  - requires that physicians understands risk prevention issues
  - involves relevant management of patients preferences
- The NBP approach will help separating real patient care (NNT relevant for an individual) and public health decisions (NNT relevant for population perpective)

Perspectives

- All concepts and required information are available
- Funding required to
  - Set up the organisation required in a systematic way
  - Elaborate a demonstrator
  - Test the feasibility of the approach
  - Fine tune the demonstrator in order to address the end-users needs
- Various backgrounds are possible
  - Private company producing the software
  - Development of the system within academic world
    - Hospital
    - Scientific organisation, professional network, integration to file management soft ?