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Evaluation of effectiveness of complex interventions – proposal of an approval process

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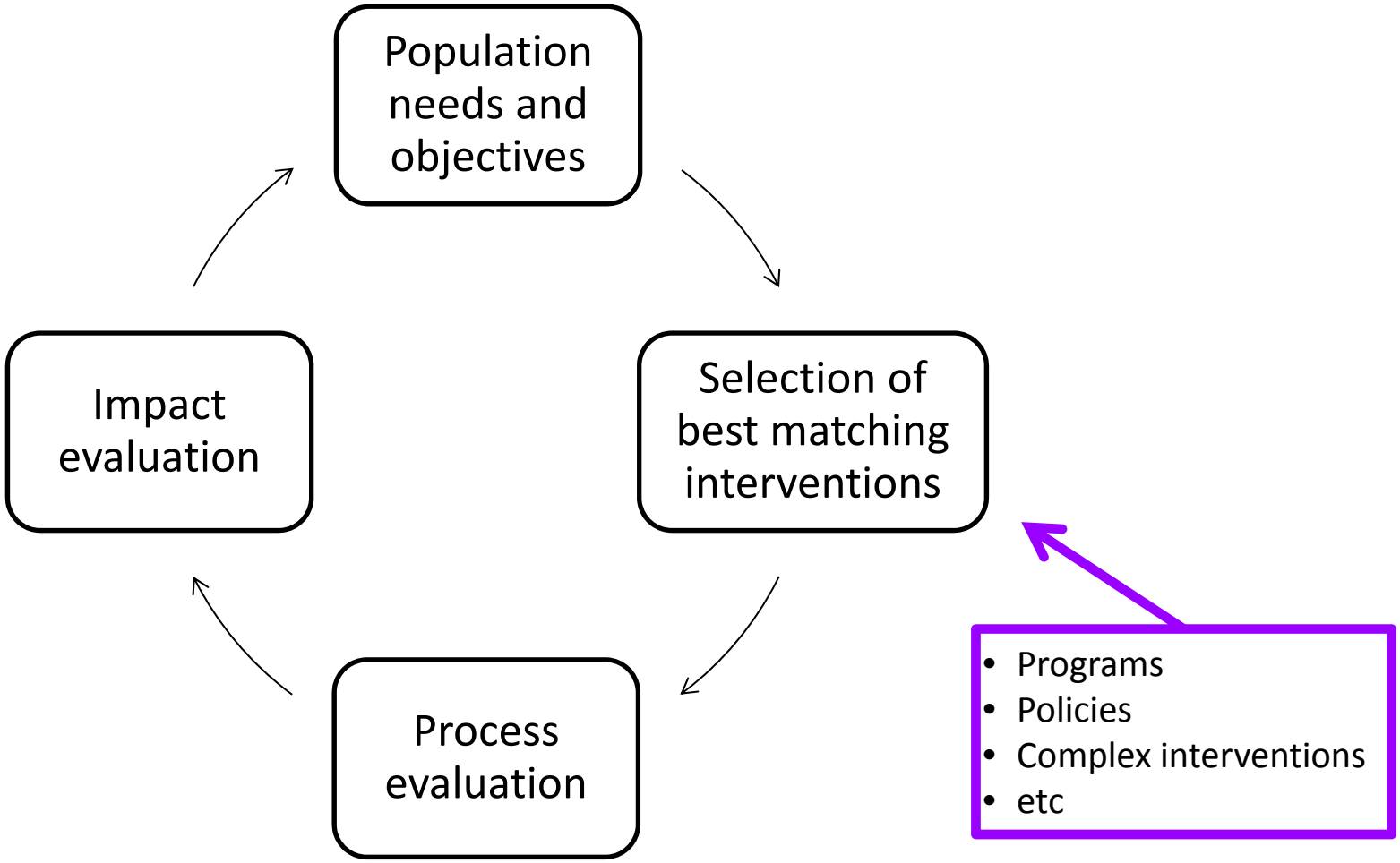
Objectives

1. To argue that the current procedures of selection of prevention interventions are mostly
   - inefficient
   - ineffective
   - unequal
   - and potentially harmful
2. To propose an international process of approval of prevention interventions

Prevention intervention cycle



Matching interventions to needs

- How this matching is done in Europe?
  - Mostly trough an informal process of selection of existing interventions
  - and by “creative prevention”
    - development of new interventions based on theories, variation of existing interventions, or on “new ideas”
  - Virtually everybody can develop a prevention program and apply it on the target population
    - Public health professionals
    - Teachers
    - Public officers
    - Private sector

An example from Italy

- A survey of prevention interventions carried out during 2008 showed
  - 1501 different interventions carried out against the 4 risk factors of ***Gaining Health*** (Tobacco, alcohol, diet and physical activity)
  - Around 14 were evaluated by observational studies,
  - 1 was evaluated by a RCT
  - 1476 didn't have any evaluation!

Is there any problem?

What's prevention?

- Prevention is the reduction of incidence of a health problem ***by reducing or eliminating risk factors***
- But, which are main ***risk factors*** of ***risky behaviours***?

1. Individual factors

- Character traits
  - impulsivity, sensation seeking, hopelessness, anxiety sensitivity
- Knowledge about risks

2. Environmental factors

- Mass media (advertisements, films, TV)
- Peer and family influence
- Other models (teachers, health professionals, politicians)
- Availability and accessibility….

Formal theories

- ***Reasoned action attitude*** (Fishbein and Ajzen in 1980) / ***Health belief model*** (Rosenstock 1950) – *human behaviour is rational, and persons acts on the bases of their perception of utility, or of risks, associated to a behaviour.* ***Perceived risks and benefits for health are the key factors in motivating the action***
- ***Problem behaviour theory*** (Jessor and Jessor, 1977) – ***problem behaviour is*** *that* ***socially defined*** *as source of concern, or as undesirable by the social and/or legal norms of society.*

Formal theories

- ***Social learning theory*** (Bandura 1977) / ***Social norms theory*** (Campbell, 1964; Durkheim, 1951, Perkins 1986) – ***People tend to adopt the attitudes of the group*** *and act in accordance with group expectations . With a particular emphasis on the importance of observing emotional reaction of others*
- ***Gateway Drugs Hypothesis*** (Kandel, Science, 1975) - *It assumes a* ***causal chain*** *sequence in which (a) tobacco is used prior to the onset of (b) cannabis and the use of cannabis increases the likelihood of using (c) other illicit drugs*
- ***Psychological vulnerability*** (Sher, 2000) - *Personality factors (hopelessness, anxiety sensitivity,* ***impulsivity, and sensation seeking) are a predictive risk factors for substance misuse*** in adolescence

Everything is complex and nothing is simple in healthcare

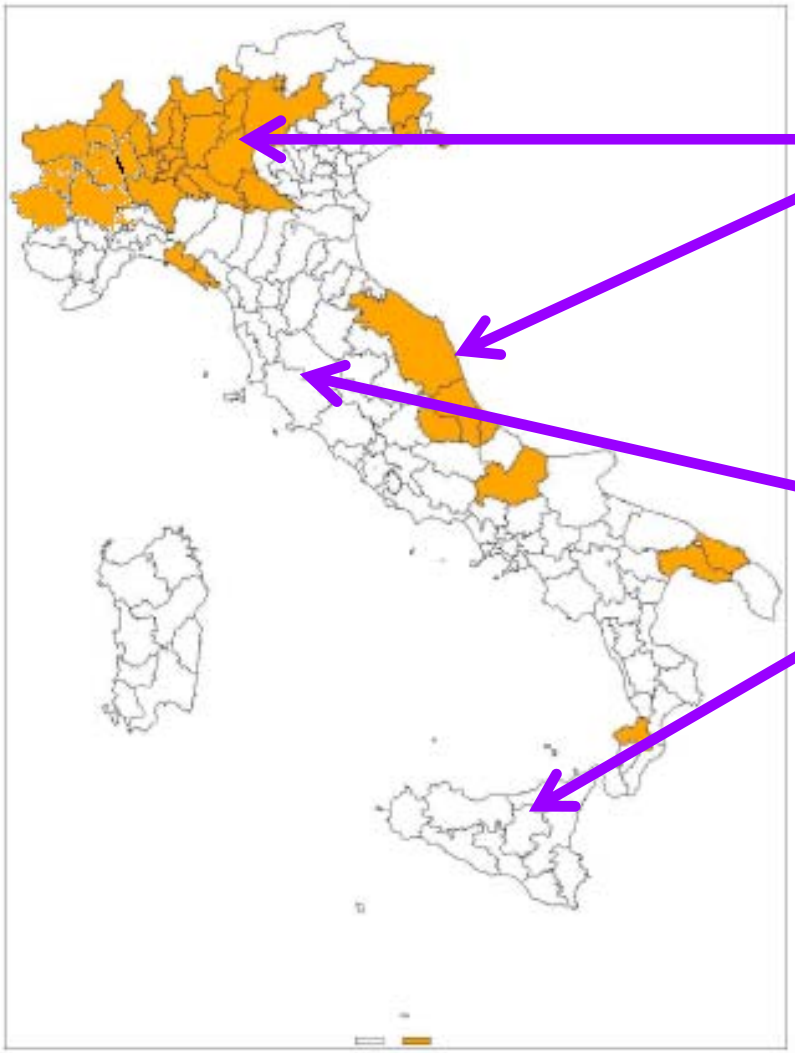
- These THEORIES explain factors involved in adopting a behavior, and can suggest intervention strategies

… but THEORIES ALONE cannot predict the success of prevention programs

Everything is complex and nothing is simple in healthcare

- This is because these theories involve ***complex systems*** which are very sensitive (*psychological, and social systems*).
- As for medicines, an active prevention component intervening at a psychological level, can act in the expected direction (***doing good***), but also in an unexpected one (***doing harm***)
- the absence of common quality standards make the dissemination of effective intervention very ***unequal***!

Unplugged in Italy



areas implementing effective programs

areas implementing any other program

All bad art is the result of good intentions

- Several programs
  - based on reference theories
  - planned by very experienced *expert groups* from multidisciplinary fields
  - well funded
- … have shown ***iatrogenic effect*** once evaluated (harms instead of beneficial effects)

Any iatrogenic effect of prevention interventions is NOT ACCEPTABLE from an ETHICAL POINT OF VIEW

The case of Life Education

- Life Education is a school-based program based on Moskowitz Model (knowledge + positive life)
- Developed in Australia during 1988-1992
- In a first evaluation, it resulted in a good ***increase in knowledge*** of drug effects and in a fair ***decrease of intentions to use*** drugs
- It has been disseminated across all Australia (and in many other countries) by law

The case of Life Education

- After its dissemination a study had been conducted to evaluate the ***effects on behavior***:
- The evaluation study involved 1800 **intervention** students and 1800 **controls**

- Main results:
- ***Cigarettes:*** ***RR=1.6***
- ***Alcohol:*** ***RR=1.4***
- ***Other substances:*** ***RR=1.4***

The case of Life Education

When the data are extrapolated to the state-wide smoking and drinking estimates …

…of all smoking among year 6 schollchildren, 25% of girls' and 19% of boys' smoking could be attributed to participation in Life Education, as could 22% of all boys' recent drinking.

- The program was extended to all Australia, UK, USA, … India, China, … South Africa….
- The findings suggest that ***intervention programmes should be thoroughly evaluated prior to widespread implementation***

Hawthorne, Addiction, 1995

American National Youth Anti-drug Media Campaign

- planned by the National Drug Control Policy (ONDCP)
- funded in 1997 by the United States Congress with **$1.5 billion dollars**
- main objective: “to educate and enable America’s youth to reject illegal drugs as well as alcohol and tobacco”
- televised antidrug public service announcements (PSAs) broadcasted 1998-2004

American National Youth Anti-drug Media Campaign

- Evaluation provides ***no evidence of positive effect in relation to teen drug use***, and shows some indications of a negative impact.
- the ***past month use of marijuana appeared significantly increased by 2.5% among 14-18 years*** (Orwin, GAO, 2006).

- RR of marijuana use in past year: ***1.21 (1.19-1.65)***
- Antimarijuana Social Norms Scale: ***-6.3 (-10.4,-2.2)***

Hornik, AAAPSS, 2009

Other examples

- ***Spark RCT study*** findings: an intervention for the ***promotion of physical activity*** carried out in elementary schools significantly ***increased Body Mass Index (BMI)*** of students of intervention group at the 18 months follow-up (Sallis 1993)

- Il ***Postponing Sexual Involvement curriculum*** RCT findings: actually ***increased frequency*** of sexual intercourses, number of partners, STD, (ns) and ***pregnancies ($p<0.05$),*** both in the peer-leaded and in the adult-leaded arm (Kirby 1997)

Why theories alone didn't work?

- These interventions are very well designed and based on theories
- But the ***complexity of the biologic world*** (and in interaction with social and psychologic)
- and the ***inadequacy of life sciences*** (biology, psychology, sociology etc) to explain this complexity
- do not allow for prediction of results

- In the ***real world***, theories are always ***temporary*** e ***unreliable*** until some ***experimental evidence*** can sustain them (Popper-like)

Extensive overview over prevention interventions

Issue	N.°	(%) col	N.°	(%) row	N.°	(%) row	N.°	(%) row	
ALC	124	24,7	48	38,7	4	3,2	72	58,1	
CVD	7	1,4	2	28,6	0	0,0	5	71,4	
HPR	0	0,0	0	0,0	0	0,0	0	0,0	
IDU	90	17,9	32	35,6	5	5,6	53	58,9	
NPS	62	12,3	19	30,7	0	0,0	43	69,4	
OBE	30	6,0	8	26,7	0	0,0	22	73,3	
PRE	35	7,0	5	14,3	0	0,0	30	85,7	
TOB	155	30,8	57	36,8	7	4,5	91	58,7	
Tot	**503**	**100,0**	**171**	**34,0**	**16**	**3,2**	**316**	**62,8**	**100,0**

NPS: Neuro-psychiatric; **HPR:** Health Promotion; **TOB**: Tobacco; **CVD**: Cardiovascular Disease; **IDU**: Illicit Drugs Use; **ALC**: Alcohol; **PRE**: Pregnancy; **OBE**: Obesity

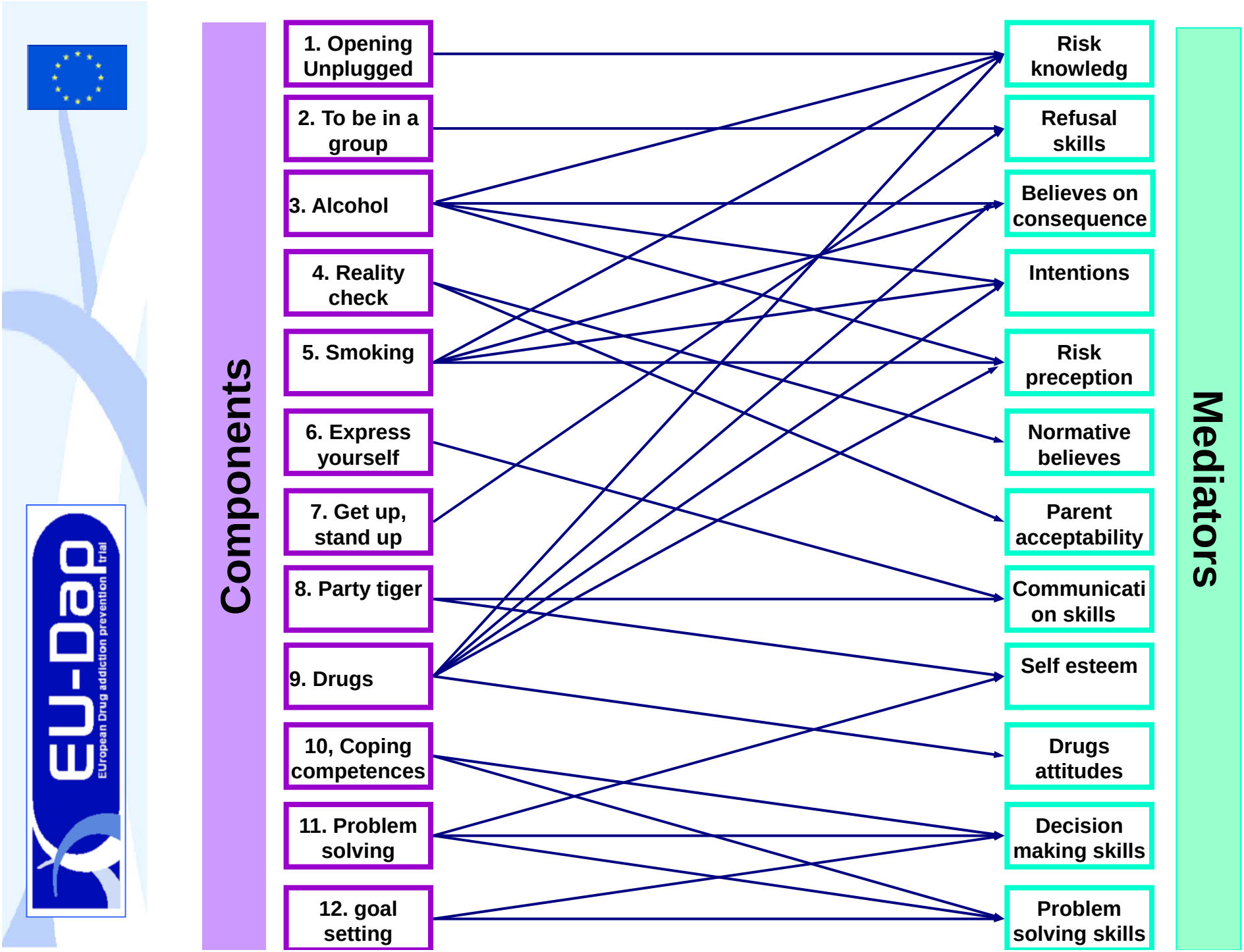
Concina, EUSPR, 2012

The problem

1 *"High quality scientific evidence is needed when professionals intervene in the lives of other people"*

(Ian Chalmers)

What are we actually evaluating?


EU-Dap
EUropean Drug addiction prevention trial
Components
1. Opening Unplugged
2. To be in a group
3. Alcohol
4. Reality check
5. Smoking
6. Express yourself
7. Get up, stand up
8. Party tiger
9. Drugs
10, Coping competences
11. Problem solving
12. goal setting
Risk knowledg
Refusal skills
Believes on consequence
Intentions
Risk preception
Normative believes
Parent acceptability
Communicati on skills
Self esteem
Drugs attitudes
Decision making skills
Problem solving skills
Mediators

Ingredients of Unplugged

- 12 units
- Parental added component
- Peer added component
- Dose (units per time)
- Way of delivery
  - trained teacher as unique deliverer
  - interaction as main modality
- Materials
- Tools to promote compliance and fidelity implementation
- …

The process of prevention research

- All the ingredients of *Unplugged* have been ***evaluated together*** (trial results are ***an average*** of the ingredients' effect)
- and it is ***virtually impossible to disentangle*** the effect of a specific component
- This is ***highly inefficient***, because:
  - what have to be changed (*to improve the program*)?
  - single effective ingredient cannot be identified (*to develop novel interventions*)
  - effective components are often in common across behavioral domains (Peters, BMC Public Health, 2009)

The process of prevention research

- In his brilliant review of 48 effective programs on substance use prevention (*Health education research 2007; 22:* 351-60), Hansen showed that:
  - in average ***programs addressed 8.5 content areas each*** (he identified at least 23 content areas!)
  - programs are not truly theory driven and they do not adhere usually to a theory's tenets
- The ***effectiveness*** of any single prevention intervention ***is the result of the specific combination of ingredients*** (the recipe)

The problem (2)

1 *"High quality scientific evidence is needed when professionals intervene in the lives of other people"*

(Ian Chalmers)

2 *"Current evaluation …is not able to measure more than the average effect of … amalgams of … content areas that are independent of formal theories"*

(Bill Hansen)

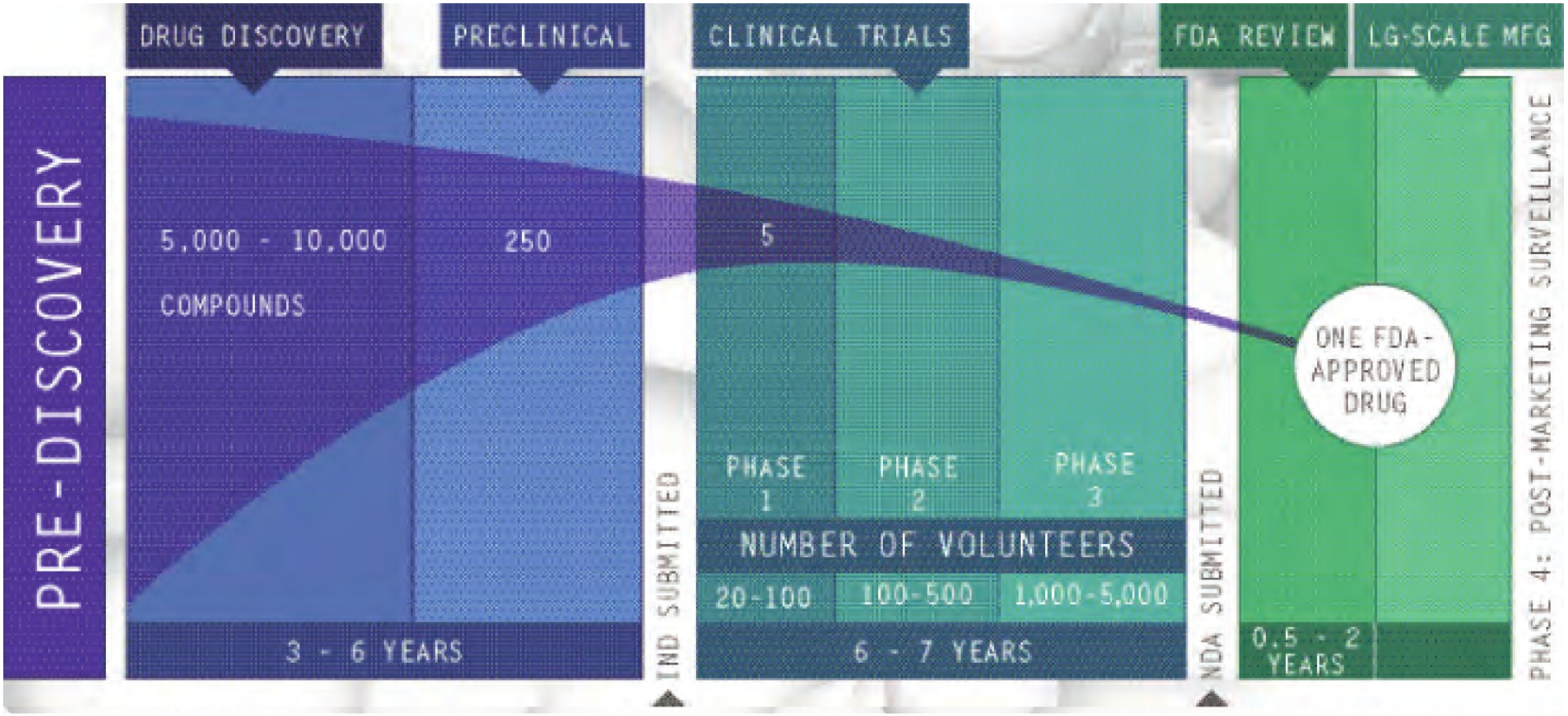
Is this inevitable?

There are some formal processes of selection already in place

1. US National Registry of Evidence-based Programs and Practices (NREPP), http://nrepp.samhsa.gov/.
2. EMCDDA Best Practice Portal www.emcdda.europa.eu
3. Dutch Recognition System www.nji.nl

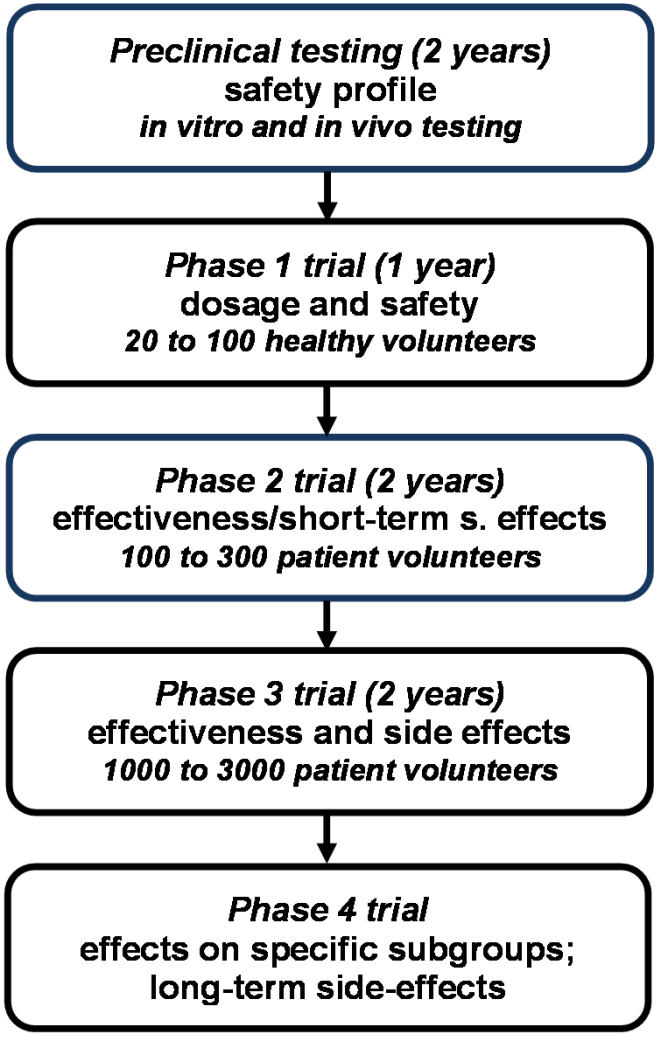
But no one reflects all the aspects of the need for a rigorous evaluation

FDA/EMA Registration process



Pharmaceutical Research and Manufacturers of America. Drug Discovery and Development: understanding the R&D process [Internet]. 2007 [cited 2011 Jul 21]. Available from: http://www.phrma.org/sites/default/files/159/rd_brochure_022307.pdf

Medicine registration process



Food & drugs Administration (FDA)

European Medicine Agency (EMA)

This is the process that ensures the effectiveness medicines in pharmacies

DRUG REGISTRATION

A registration process for prevention?

- A similar process applied to prevention interventions could ensure
  - a ***list of E-b interventions available*** for the practice
  - transparent and rigorous evaluation standards
  - But this may also encourage the evaluation of innovative and promising interventions

Previous proposals: evaluation of complex interventions

After a *'Pre-Clinical' or theoretical phase,* selecting potentially active ingredients :

- *Phase I or modelling:* intervention's components and interrelationships (qualitative testing, small observational studies)
- *Phase II or exploratory trial:* varying different components to see effects on the intervention
- *Phase III or main trial:* RCT to evaluate the intervention's main effect
- *Phase IV or long term surveillance:* long-term and real-life effectiveness of the intervention.

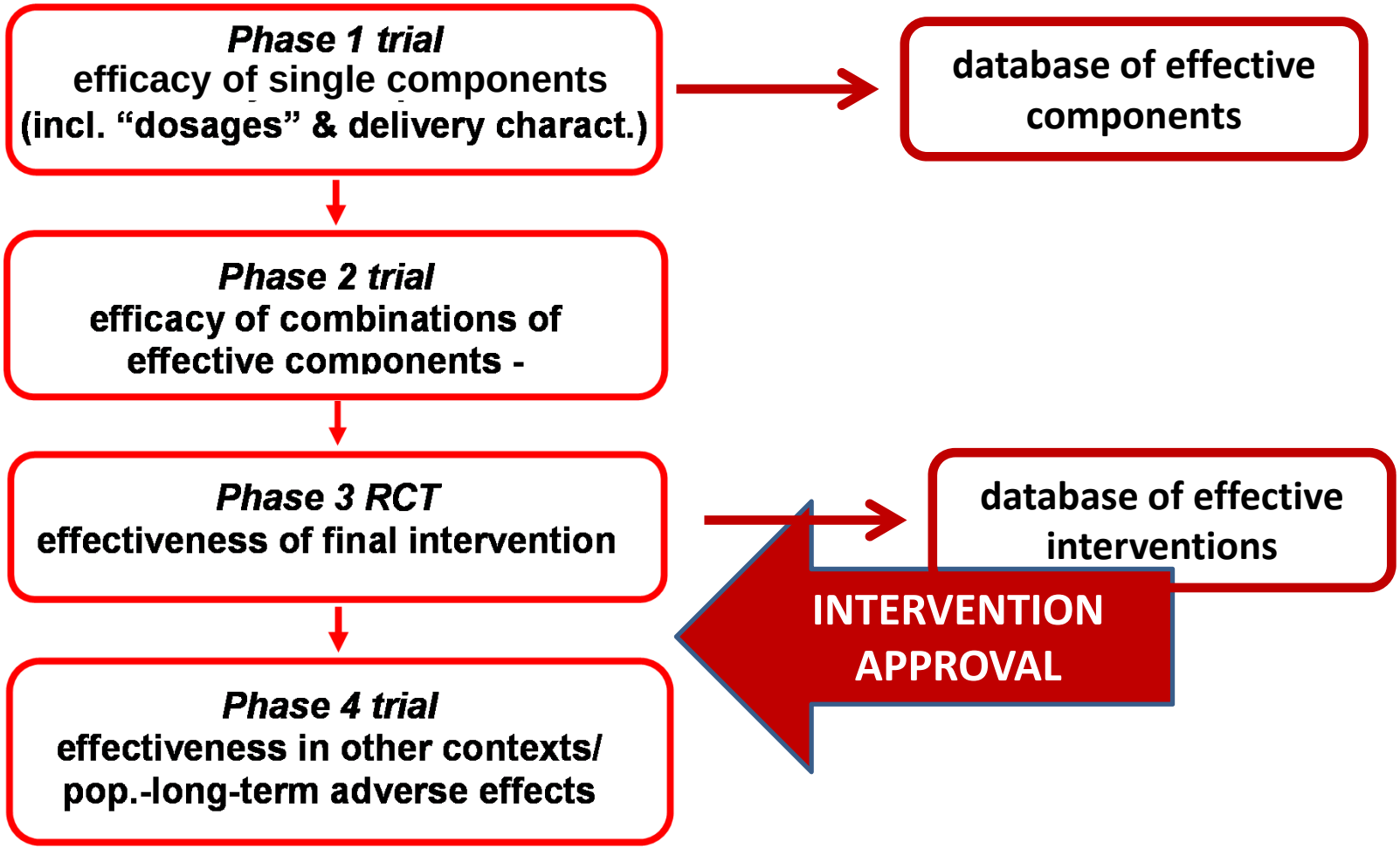
Campbell, BMJ, 2000

Previous proposals: evaluation of complex interventions

- 1 step - phased experimental approach, based on ***factorial randomised trial*** has been proposed to test separately each active component and their interaction
  - 2 components: A vs B vs AB vs Control
  - 3 components: A vs B vs C vs AB vs AC vs BC vs ABC vs Control
  - …
  - 8 components: > 40.000 arms!
- Project JUMBO…

Collins, Clinical trials, 2009

Possible approval process for prevention



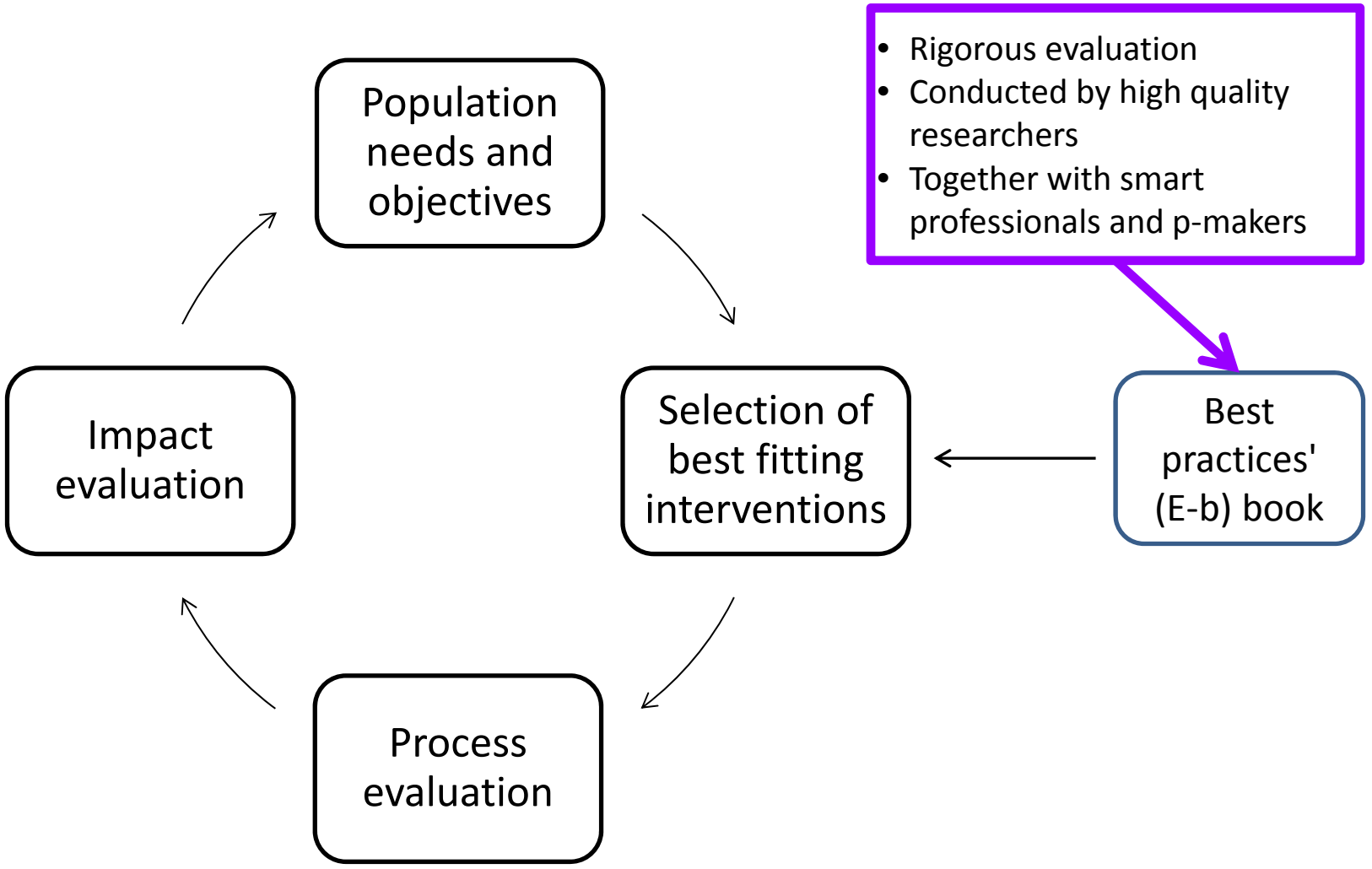
As for the component effects?

- Evaluation of short-term effects on the mediators theoretically targeted by components
  - (this would force an explicit identification of the causal chain)
- adopting randomized design
- relatively small sample sizes (to focus large effects)
- and qualitative analysis

Other suggested characteritics of the process

- access to the repository of findings and documentation on components and programs for practitionners and policy-makers
- availability of findings of all evaluation phases for researchers
- internationally conducted (possibly involving international agencies)

Prevention intervention cycle



Conclusions

- Many countries are working on the establishment of lists of E-b programs (Spain, UK…)
- An international approval system could ensure ***larger impact*** and ***standardized methods***, and
  - ***increase the number of E-b interventions*** available for the practice
  - increase the circulation of evidence useful for program developers
- EUSPR would have a role in this