The Need for a Common Language in Non-Pharmacological Interventions (NPIs)

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CEPS Platform, Methodology Platform for NPIs

www.CEPSplatform.eu
Our work

One example among many

“These findings are open to criticism because of the notable heterogeneity across the included studies and the shortcomings of the included studies.”

Jassim et al. (2015, Cochrane Database Syst Rev)
I am a trialist

ETP-BPCO RCT (disease management education / COPD / cost-efficacy): 2002-11 10 years
   Ninot et al. (2011, Respiratory Medicine)
APAC RCT (exercise / tobacco dependence / smoking cessation): 2009-14 5 years
   Bernard et al. (2015, Journal of Dual Diagnosis)
Actimarche RCT (exercise / elderly / fall): 2010-15 6 years
   Bernard et al. (2016, Aging Clinical and Experimental Research)
APAD RCT (exercise / breast cancer / fatigue): 2010-16 7 years
   Carayol et al. (2013, Contemporary Clinical Trials)
Challenge international RCT (exercise / breast / disease free survival at 10 years): 2014-30 17 years
   Courneya et al. (2014, Current Colorectal Cancer Reports)

I am a meta-analyst and reviewer

Review (post-rehab interventions / COPD / health and HRQL): <10% trials included: 2006-07 2 years
   Mouleec et al. (2007, Revue des Maladies Respiratoires)
Meta-analysis (exercise / breast cancer / fatigue and anx-dep): <1% trials included: 2012-13 2 years
   Carayol et al. (2013, Annals of Oncology)
Meta-analysis (theory based interventions / adults / exercise): <10% trials included: 2013-16 4 years
   Gourlan et al. (2016, Health Psychology Review)
Review (exercise / chronic disease / health and HRQL): <5% trials included: 2015-16 2 years
   Collective Expertise INSERM (2016, INSERM)
As well as so many researchers in the world

Since 2000, an exponential growth of publications citing clinical trial and a NPI categories
Nevertheles, Health Authorities are still waiting for Evidence of NPI Efficacy.

« In light of the standards usually applied to evaluate the efficacy of medical treatments, most studies assessing the efficacy of non-pharmacological therapies [hygiene and dietary practices, psychological treatments, physical therapies] suffer from methodological weaknesses.»

French Health Authority – HAS (April 2011, p.40)
Thus, as a clinical researcher, I am frustrated

But, as a citizen and patient...
Context: Unprecedented NPI growth since 2010

Pharmacies

1986

2016

(e.g., supplementary food, e-health device)
Context: Unprecedented NPI growth since 2010

Diets

1986

2016
Context: Unprecedented NPI growth since 2010

Health devices

1986

2016
Psychotherapies

Context: Unprecedented NPI growth since 2010
Exercise programs

1986

2016
An Explosion of Self-help Health Best-sellers

Propagated Extensively by the Media and the Internet

Making patients more less naïve...

... but paradoxically, more vulnerable to:
- abuse (e.g., sects, dangerous practices, etc.),
- misinformation (e.g., Marketing vs. Science).
Refusing to act for one’s own health ("laisser faire")

Acting for one’s own health by putting it into the hands of others (God, gurus, etc.)

Oldest School of Medicine in Europe
Montpellier
France

Saint-Roch Church
Montpellier
France
Context: Unprecedented NPI growth since 2010

Acting for one’s own health with Non-Pharmacological Interventions (NPIs)

<table>
<thead>
<tr>
<th>Nutritional interventions</th>
<th>Body Interventions</th>
<th>Psychological Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Nutritional icons" /></td>
<td><img src="image2" alt="Body icons" /></td>
<td><img src="image3" alt="Psychological icons" /></td>
</tr>
</tbody>
</table>

Complementary or alternative to conventional treatments?
(e.g., drug, gene/cell therapy, surgery, implantable devices, radiotherapy)

In which goal? CURE, CARE or PREVENT
Defining NPIs

- primary prevention actions
- secondary prevention actions
- tertiary prevention actions
- technical and technological aids
- health claims
- medical devices
- non-pharmacological interventions
- alternative medicine
- Chinese medicine
- complementary medicine
- behavioral medicine
- natural medicine
- traditional medicine

- Internet of Things (IoT, mHealth)
- health products
- health services
- adjuvant therapy
- supportive care
- eHealth
- non-conventional therapy
- non-pharmacological therapy
- complementary therapy
- complementary treatments
- non-pharmacological treatments
“NPIs are non-invasive methods of care (programs, products or services) whose efficacy in improving the health and quality of life of human beings has been proven. Their effects on health and quality of life markers are observable (with measured risks and benefits beyond mere user opinions) and can be linked to identified biological and/or psychosocial processes. They can also have a positive impact on health behaviours and socio-economic indicators.”

CEPS Platform, April 2016
UNPRECEDENTED NPI GROWTH SINCE 2010:

MAIN REASONS
1. Epigenetics research has evidenced the impact of the environment on human biology.

Context: Unprecedented NPI growth since 2010

Carey (2013)
2. The results of the first human cohorts over a 60-year period have shown the impact of behaviors on the advent of diseases and their related complications.

Smoking and Food Behaviors

Minus 7 years of life expectancy

Sedentary Behaviors

3-5 km per day in 2016 vs. 21-35 in 1900

Steptoe et al. (2015, Lancet)
3. Global population aging and therapeutic advances have led to the exponential growth of chronic diseases.

**Context:** Unprecedented NPI growth since 2010

**A life course approach to chronic diseases**

- **Infancy and childhood**
- **Adolescence**
- **Adult life**

**Accumulation of chronic disease risk**

WHO (2006)
4. Patients and relatives increasingly demand that patients’ quality of life be improved – and not just genetic/cell/organ treatment performance.

Context: Unprecedented NPI growth since 2010

Expert opinion


Patient opinion
5. Resilience for healthy aging and better life with a chronic disease.

Robert Marchand, 102 years young, pedaled his bike around a velodrome a distance of 26.9 kilometers (16.7 miles) in one hour, establishing a centenarian record.

Bolte Taylor (2008)
6. Clinical studies have highlighted direct and indirect savings linked to the use of NPIs.

RCT assessing COPD case manager:

Improvement of health markers and quality of life

Cost savings

<table>
<thead>
<tr>
<th>Table 3—Health-Care Resources, Mean Costs per Patient*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Items</td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Physician visits</td>
</tr>
<tr>
<td>Family physician</td>
</tr>
<tr>
<td>Specialist</td>
</tr>
<tr>
<td>Emergency department visits</td>
</tr>
<tr>
<td>For acute exacerbation</td>
</tr>
<tr>
<td>For other health problems</td>
</tr>
<tr>
<td>Hospitalizations</td>
</tr>
<tr>
<td>For acute exacerbation</td>
</tr>
<tr>
<td>For other health problems</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

*Data are presented as mean ± SD unless otherwise indicated.
†Index of hospital health resources utilization.18
7. The advent of e-health facilitates NPI use and the monitoring of health behaviors.
8. The advent of *Evidence-Based Medicine/Prevention/Psychology* lays the foundations for best professional care practices.

David L. Sackett
American and Canadian

OC, FRSC, BA (Lawrence), MD (Illinois & Basel), MSc (Harvard), FRCP (Ottawa, London, Edinburgh)

(November 17, 1934 – May 13, 2015)
9. The culture of prevention is gaining traction.

La Culture de prévention en santé : des questions fondamentales

Introduction

1. La prévention en médecine est un humanisme (J.-F. Mattei)
2. Définition de la culture de prévention (C. Dreux)
3. Pourquoi et comment développer une culture de prévention en santé publique ? (A. Vacheron)

French Academy of Medicine (Dreux, 2013)  European Union (2014)
10. Paradigm shift from single for-pay medical service to overall care path management.

**Pasteur Model**: 1 problem => 1 mechanism => 1 therapeutic solution

**Chronic Disease Model**: 1(n) problem(s) => complex mechanism(s) => n solutions (complementary and coordinated treatment solutions), overall care and life path management

Pr. Jacques Bringer, Dean of Montpellier’s Faculty of Medicine,
iCEPS Conference 2015
NPIs ARE USED EVERY DAY

AND YET

RCT EVIDENCE IS LACKING

MOST ARE NOT REIMBURSED
Coming out of the dark, just like they did 50 years ago for pharmaceutical drugs

“Until the 60’s, many therapeutic interventions only relied, we might say, on the strength of habit (routine), a naive belief in traditions, or on generalizations made on the basis of anecdotal and sporadic instances **abusively labeled as professional experience.**”

Bouvenot (2006, p. XIII)

4 phases for any Drug

- **Phase 1**: Checking for Safety
  - 20-100 volunteers
  - **1st state of testing in humans**

- **Phase 2**: Checking for Efficacy
  - 100 - 500 patients
  - How well does the drug work?

- **Phase 3**: Confirm results
  - 1,000 – 5,000 patients
  - Drug MUST be safe
  - Comparison with current 'gold standard' treatment

- **FDA Review / Phase 4 trials**: Safety surveillance in ‘Real-life’ patients
Pharmaceutical Drugs: a revolution with high quality of clinical trials began 50 years ago.

A unanimous definition

Official definition

A consensual paradigm of clinical investigation and surveillance evaluation (safety, efficacy, costs)

1 drug = 1 common procedure

A clear process for reimbursement, production and patient information channels

Continental and National authorities: agreement with Social Security and Private Insurance Coverage

Market players

World companies

Medium-sized companies and small businesses

Artisans
Medical devices: an attempt with high quality of clinical trials begun 10 years ago.

A definition in progress with some residual difficulties

Medical prescription or not
Implantable or not
Use only by patient or not (e.g., medical tool, family)

A nonconsensual paradigm of clinical investigation (except safety) and surveillance evaluation

1 medical device = 1 trials = 1 protocol

A challenging reimbursement, production and patient information procedures

National authorities discussions

Market players

World companies

Medium-sized companies and small businesses

Artisans
Behavioral interventions (included in NPIs): a dream of standardized high quality clinical trials

No clear definition of NPIs

   Prescription or not
   Supervised or not
   ...

No standardized paradigm of clinical investigation and surveillance more than safety at the moment

   Efficacy/effectiveness: between health and well-being
   Safety: few attention (e.g., interaction, sectarian abuses), few surveillance

Heterogeneous procedure for production and patient information, no option for reimbursement

   No demand

Market players

   World companies
   Medium-sized companies and small businesses

   Artisans
THE CHALLENGE:
A CRITICAL NEED TO CLARIFY
THE METHODOLOGICAL APPROACH
TO ASSESS THE EFFICACY AND THE SAFETY
OF NPIS
A need of high quality trials

How to Make More Published Research True

John P. A. Ioannidis

1 Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Stanford, California, United States of America, 2 Department of Medicine, Stanford Prevention Research Center, Stanford, California, United States of America, 3 Department of Health Research and Policy, Stanford University School of Medicine, Stanford, California, United States of America, 4 Department of Statistics, Stanford University School of Humanities and Sciences, Stanford, California, United States of America

Adoption of more appropriate statistical methods [38], standardized definitions and analyses and more stringent thresholds for claiming discoveries or “successes” [39] may decrease false-positive rates in fields that have to-date been too lenient (like epidemiology [40], psychology [41,42], or economics [43]). It may lead them to higher credibility, more akin to that of fields that have traditionally been more rigorous in this regard, like the physical sciences [44].
The Behavior Change Technique Taxonomy (v1) of 93 Hierarchically Clustered Techniques: Building an International Consensus for the Reporting of Behavior Change Interventions

Susan Michie, DPhil, CPsychol · Michelle Richardson, PhD · Marie Johnston, PhD, CPsychol · Charles Abraham, DPhil, CPsychol · Jill Francis, PhD, CPsychol · Wendy Hardeman, PhD · Martin P. Eccles, MD · James Cane, PhD · Caroline E. Wood, PhD
An Necessary Bottom Up Strategy

Defining techniques

Defining process/mechanism/theory

Defining dose and burden

Choosing design (e.g., decision tree)

Anticipating analyses (e.g., ITT)

Declaring (e.g., Clinical Trials, PROPERO)

Publishing (e.g., EQUATOR, PRISMA)

Explaining (e.g., patients notice)

Training (e.g., professional guideline)

Characterize intervention
NPI = method = theory + techniques + material

Characterize design
Guideline for researchers and authorities

Characterize results
Recommendations for dissemination
A Top Down Strategy

An Complementary Top Down Strategy

Keep in mind that behavioral interventions are not drugs

Excessive influence of the pharmaceutical standard validation phase (e.g., French Health Authority)
NPIs less dangerous therapy than “artificial” therapy especially for care and prevention
Accelerate time to market of NPIs innovations, because engineers have a different way of thinking

Behavioral intervention are also skills
An Complementary Top Down Strategy

NPIs need to be compared and optimized, as well as targeted to the right health problem at the right time.

Smith and Pell (2003, Brit Med J)

What is the most secure?
An Complementary Top Down Strategy

A need for a dedicated and consensual paradigm of validation and surveillance

In context of entropy of methods without comparability

And also in context of New Industrial Players in the Health Field Advocating to an Engineering Model

See François Carbonnel IBTN 2016 poster
An Complementary Top Down Strategy is needed

A need to assess direct and indirect costs in effectiveness trials and to use qualitative methods.
Toward an Action Plan?

Create of an International Multilingual Glossary of NPI clinical trial concepts (with synonyms)

To decrease number of useless trials

www.blogensante.fr/en/

Oxford

McMaster

ibtn international behavioural trials network
Toward an Action Plan?

Build a collaborative NPI ontology

Category: Psychological intervention (synonyms)
Subcategory: Psychotherapy
Intervention: Mindfulness-Based Stress Reduction (MBSR)

See Loc Nguyen IBTN 2016 poster
Toward an Action Plan?

Create a consensual paradigm of NPI validation and surveillance

An International Perspective on Improving the Quality and Potential of Behavioral Clinical Trials

Simon L. Bacon · Kim L. Lavoie · Gregory Ninot · Susan Czajkowski · Kenneth E. Freedland · Susan Michie · Paul Montgomery · Lynda H. Powell · Bonnie Spring · for the International Behavioural Trials Network (IBTN)
Toward an Action Plan?

Create a Meta-Search Engine Dedicated to NPIs trials for 2018

Registered Trials

Published Protocols

Ethics Agreement

Published Results

ClinicalTrials.gov

PubMed

PubMed

Real-time Screening
Create an ID for each trial

Webcrawling and indexing NPI trials with an Internet bot

Search based on Methodological Criteria

New meta-analysis, interventional study, scientific publication

www.motrial.eu
Propositions

Toward an Action Plan?

An annual meeting alternating Montpellier and Montreal

1st Conference
March 2011
Montpellier, France

2nd Conference
April 2013
Montpellier, France

3rd Conference
March 2015
Montpellier, France

4th Conference
May 2016
Montreal, Canada

5th Conference
May 18-20, 2017
Montpellier, France

1-day event
320 participants
6 plenary lectures
6 professional workshops

1-day event
610 participants
11 plenary lectures
6 professional workshops

3-day event
1,030 participants
35 plenary lectures
11 professional workshops
68 scientific posters

3-day event
250 participants
8 plenary lectures
10 professional workshops
29 scientific posters

www.iceps.eu
To conclude

Conclusion

An International Multilingual Glossary of non-pharm clinical trial concepts is needed,

to decrease misunderstandings, biases, conflicts of interests and amalgams in NPIs clinical trials.

A rigorous and standardized methodological approach is needed,

to identify NPI uses, compare effects and deliver more evidence to Policymakers, Professionals and Patients.

A shorter validation (because of low risk) and a better surveillance procedures are needed,

to answer to Engineers of New industry in health and well-being.

Yes, we can with

www.ibtnetwork.org
Thank you for your attention

CEPS Platform
Methodology Platform for NPIs
Universities of Montpellier, France

www.CEPSPlatform.eu

www.blogensante.fr/en/

“preempt disease before it occurs, utilizing the participation of individuals, communities, and healthcare providers in a proactive fashion, as early as possible, and throughout the natural cycle of a disease process”

Elias Zerhouni (Director, NIH, 2008)
The CEPS Platform: An Academic Methodology Hub for NPI Research

www.CEPSplatform.eu

Founder & Executive Director: Pr. Gregory Ninot (University of Montpellier, France)
Associate Director: Raphael Trouillet (Paul Valery University, Montpellier, France)
Director of Technology & Data Analysis: Anne Laurent (University of Montpellier, France)
General Manager: Jerome Maitre (Paul Valery University, Montpellier, France)

The Center for the Evaluation of Health Prevention Programs and Non-Pharmacological Interventions (NPIs), known as the CEPS Platform, is an academic hub dedicated to the advancement of methodology expertise in clinical non-pharmacological research. This public platform aims to facilitate the work of European researchers who monitor, develop, carry out and publish clinical interventional studies on the efficacy of NPIs or of health prevention programs (safety, risks/benefits, impact on Quality of Life, costs/efficacy).

The CEPS Platform provides resources which help build and strengthen bridges between academic research and NPI innovations. These open-access resources include: scientific monitoring, methodology tools for non-pharmacological clinical trials, scientific events, information, and an interactive map of the field’s key players.