Integrating clinical and behavioral studies in primary care

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Topics to be discussed

- Clinical trial definition
- The drug development process, clinical trial statistics
- Documents in clinical trials: a brief review
- Challenges in clinical trials - feasibility, site selection and patient enrollment
- Recruitment strategies in Primary Care – findings from literature

Topics to be discussed

- Feasibility of clinical trials in Primary Care – What about Greece
- Where to focus and what kind of clinical trials could be conducted in PHC
- Behavioral health in PHC
- Cost-effectiveness of behavioral interventions in PHC: findings from literature
- Some conclusions

Clinical Trial – what is it?

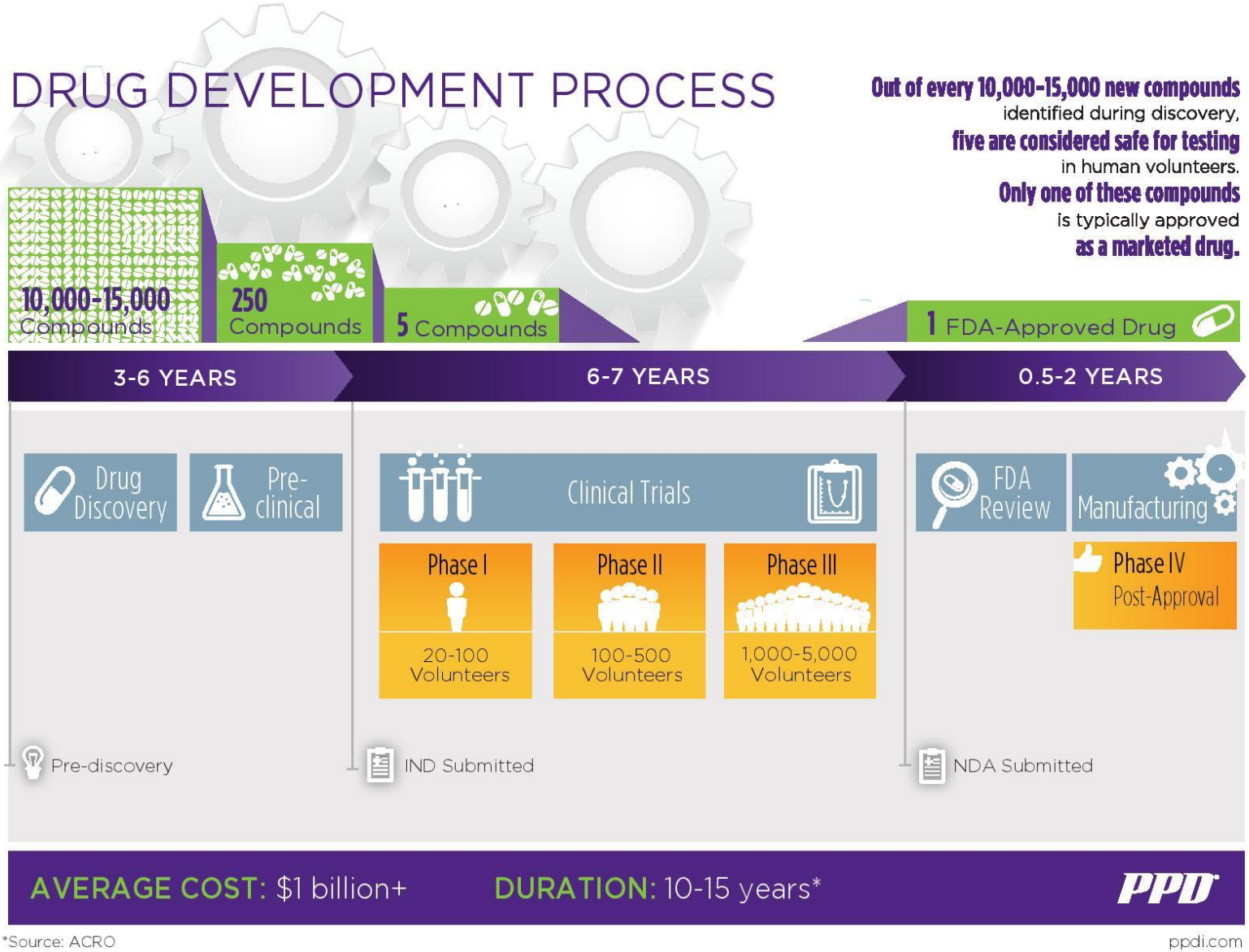
- Clinical trials, also known as clinical studies, test potential treatments in human volunteers to see whether they should be approved for wider use in the general population

- A treatment could be a drug, medical device, or biologic, such as a vaccine, blood product, or gene therapy

- This is the way to innovative and life-changing therapies

Source: The Food and Drug Administration (FDA)

The drug development process



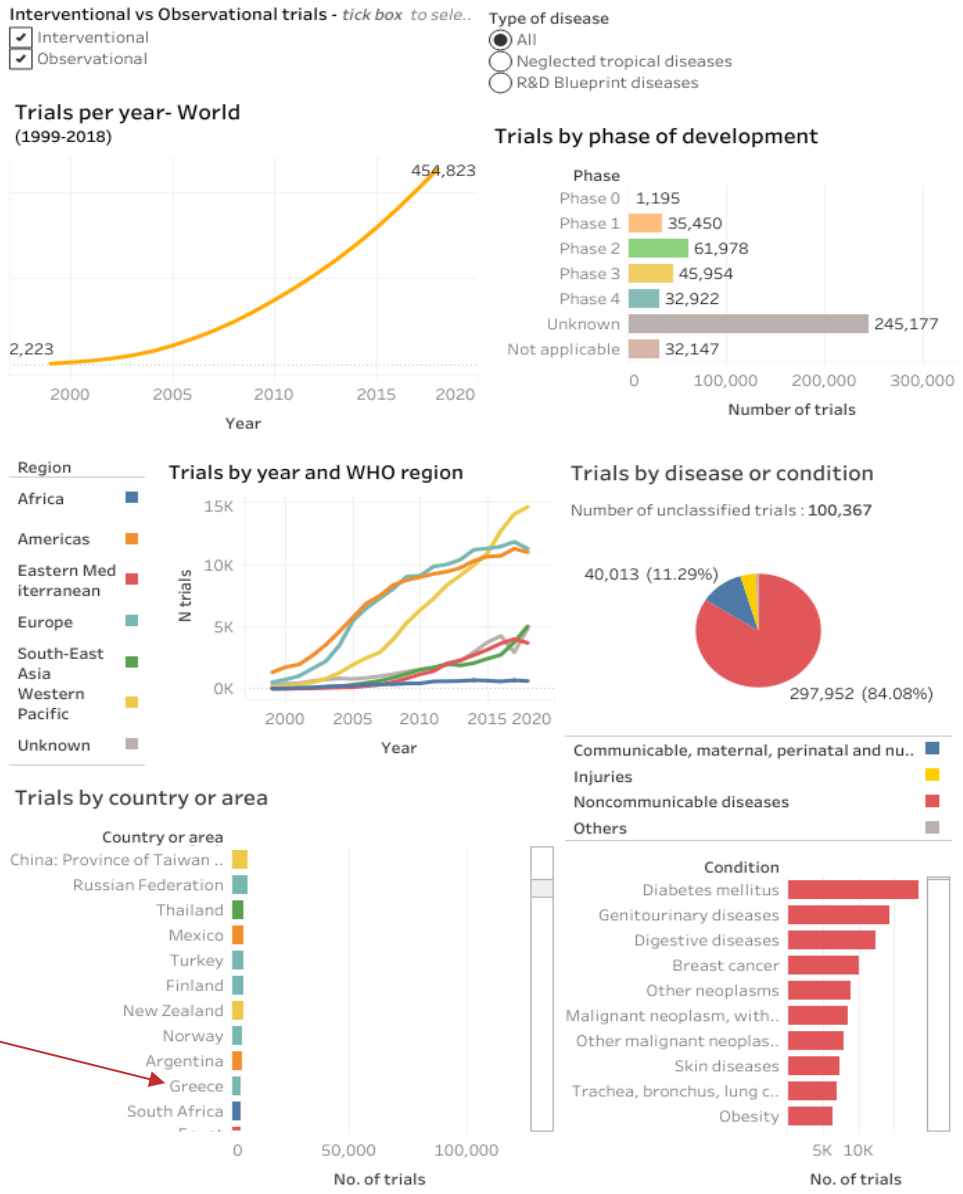
Source: Pharmaceutical Product Development (PPD) and ACRO

Clinical trial statistics

The total number of clinical trials is extremely growing

Expecting NCDs breakthroughs next years

Greece should be a powerful player



Source: Global Observatory on Health R&D, WHO, 15 Sep 2019

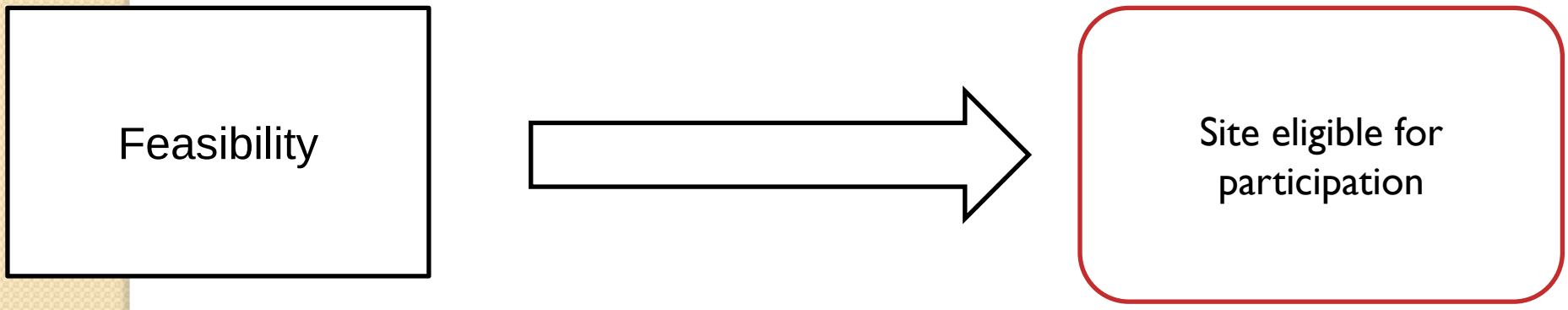
Some documents in clinical trials – country and site level

- Study protocol and protocol synopsis, insurance certificate
- ICF (Informed Consent Form) – main, pregnant, genetic
- IB (Investigational Brochure)
- PSP (Protocol Signature Page)
- CV, GCP, ML, CTA, Submissions to SC, Annex I, Annex II
- Medical laboratory tests and many other docs…

Challenges in clinical trials

Feasibility in clinical trial

- Feasibility is the evaluation of the possibility of conducting a particular clinical trial in a particular geographical region with the overall objective of optimum project completion in terms of timelines, targets and cost
- Many types of feasibilities, such as in study level and site level
- Feasibility is performed under specific criteria



Site selection process

- One of the greatest challenges in clinical trial execution
- A considerable number of clinical studies experience delays
- This contributes to increased duration and costs
- Terms, such as eligible for participation, eligible for activation, potential for activation etc.

Factors influencing clinical trial site selection in Europe

- The Survey of Attitudes towards Trial sites in Europe (SAT-EU Study)

- Investigator factors, Hospital/unit factors, Environmental factors, Cost factors (as a result costs appear less important)

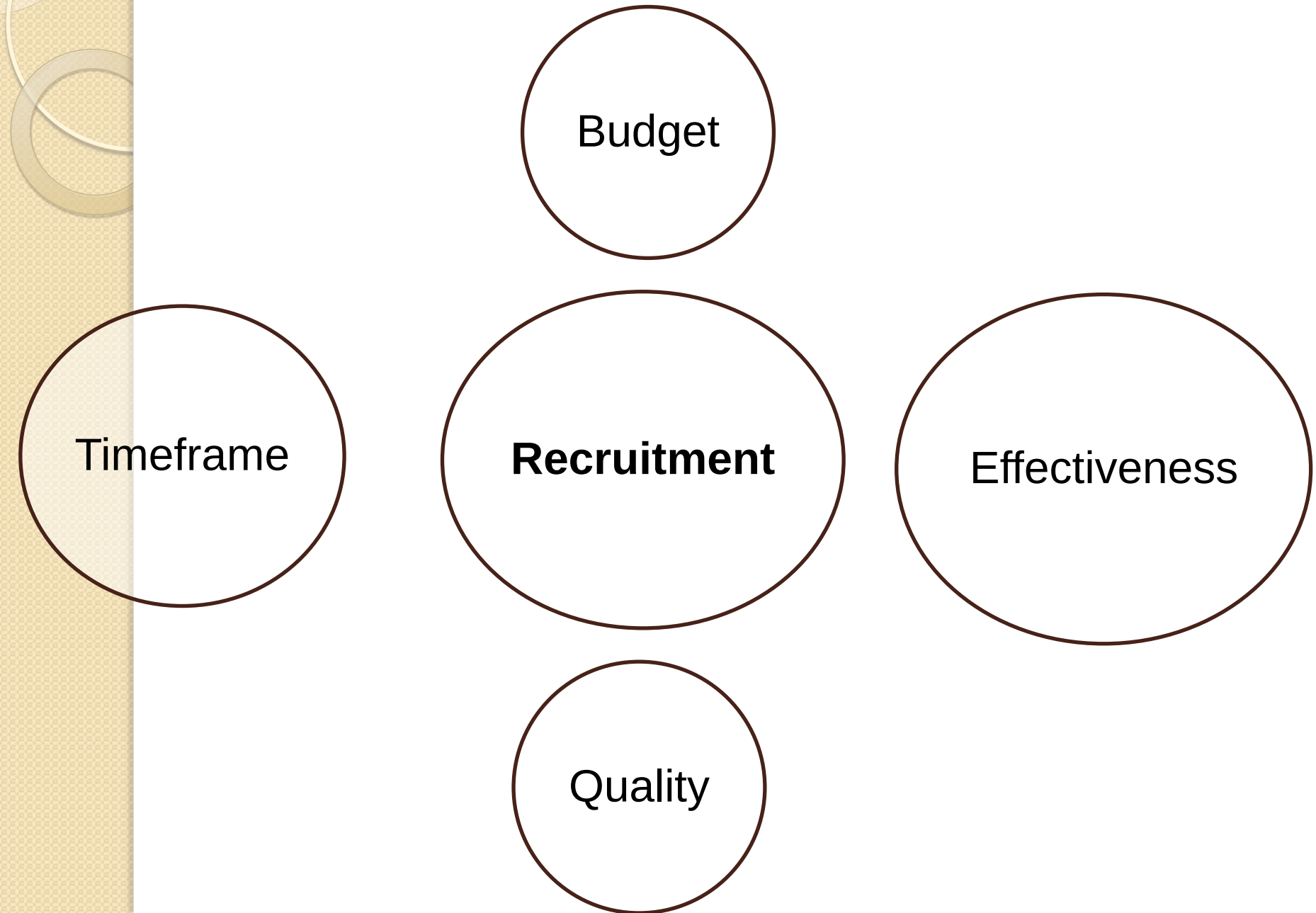
Investigator factors	Environment-driven criteria	Hospital-driven criteria
Investigator recruitment/retention track record	Size of market/eligible patients in a region	Site personnel experience and training
Investigator experience in previous trials	Speed of MoH/ethics committees approval	Previous experience with site
Investigator interest	Disease management system/networks	Facilities/equipment required by trial

Source: Gehring M. et al (2013)

Patient recruitment in clinical trials

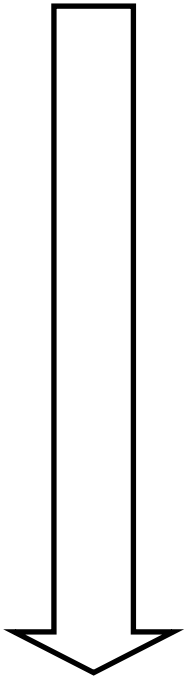
- Many factors contribute to effective, high-quality clinical trials
- One of the most important sections is the enrollment, recruitment and retention of patients - identifying and recruiting patients who meet protocol criteria is challenging
- The process of enrolling patient volunteers into early phase studies
- This process affects the effectiveness of clinical trial

Recruitment – how can affect the trial



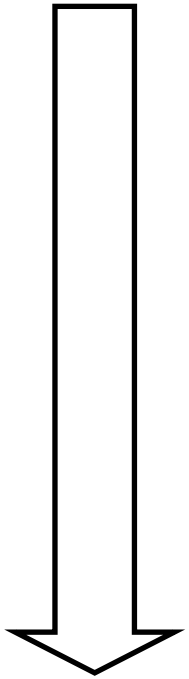
Recruitment strategies in primary care – patient level

Using practitioner database



242 patients (in 6 months) and
at a cost of £27.66 per patient

Using a local newspaper



66 patients (in 1 month) and
at a cost of £2.72 per patient

Source: Ngune I. et al (2012)

Recruitment strategies in primary care – patient level

Patient incentives

$2 incentive for joining the study, $15 pending survey completion or the chance to win a $200 prize

The $15 incentive pending survey completion yielded the greatest effect

Comparing waiting room patient screening and a practice mail-out

More patients have been involved in study through mails

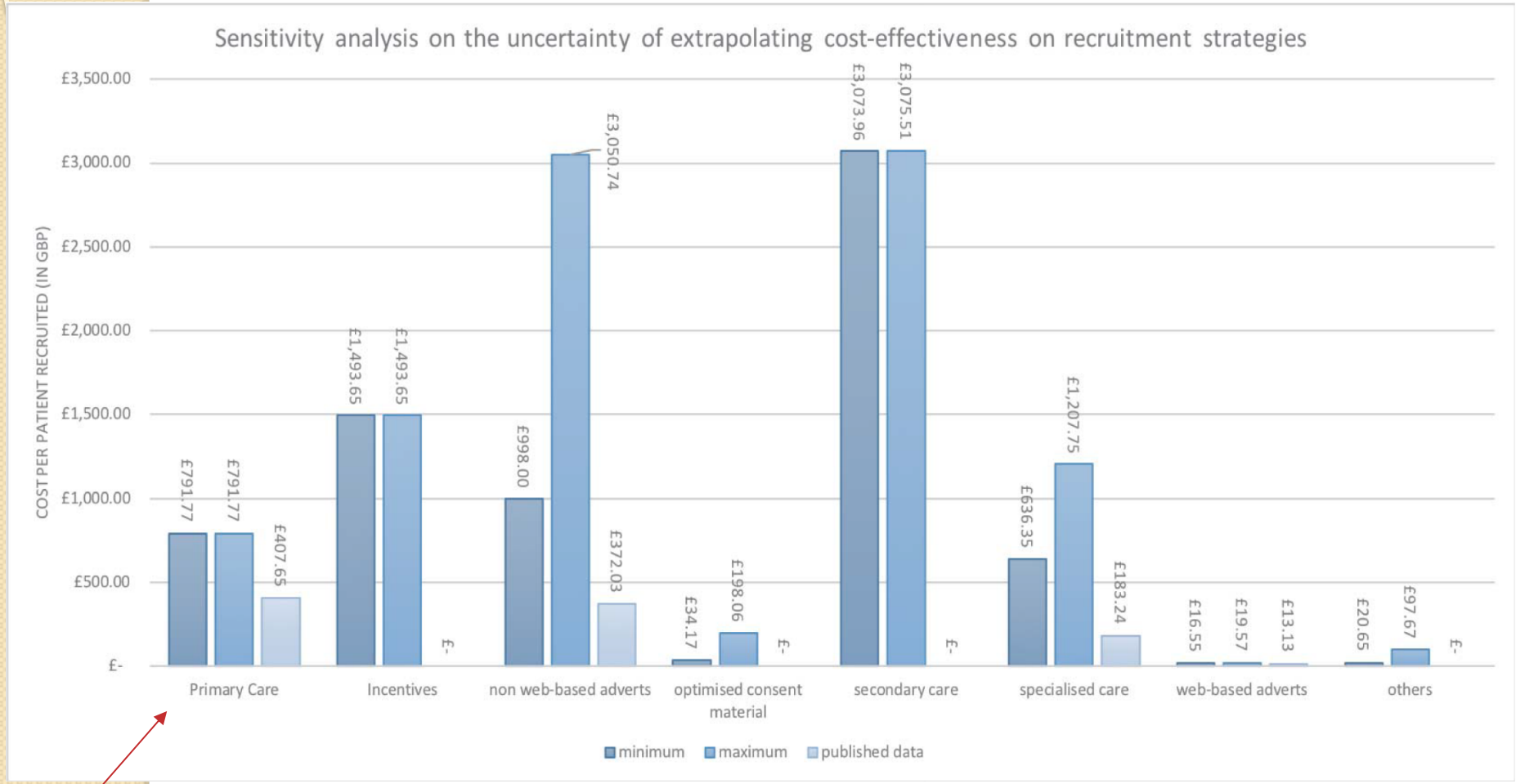
Source: Ngune I. et al (2012)

Recruitment strategies in primary care – Practitioner and health system level

- Peer recruitment
- Enlisting opinion leaders
- Minimising the research responsibilities of practitioners
- Recruiting practitioners who are interested in the research topic
- Professional bodies can support effectively

Source: Ngune I. et al (2012)

Recruitment and retention of patients



Source: Yifeng Liu, Emma Pencheon, Rachael Maree Hunter, et al. 2018

Why patients decline clinical trials?

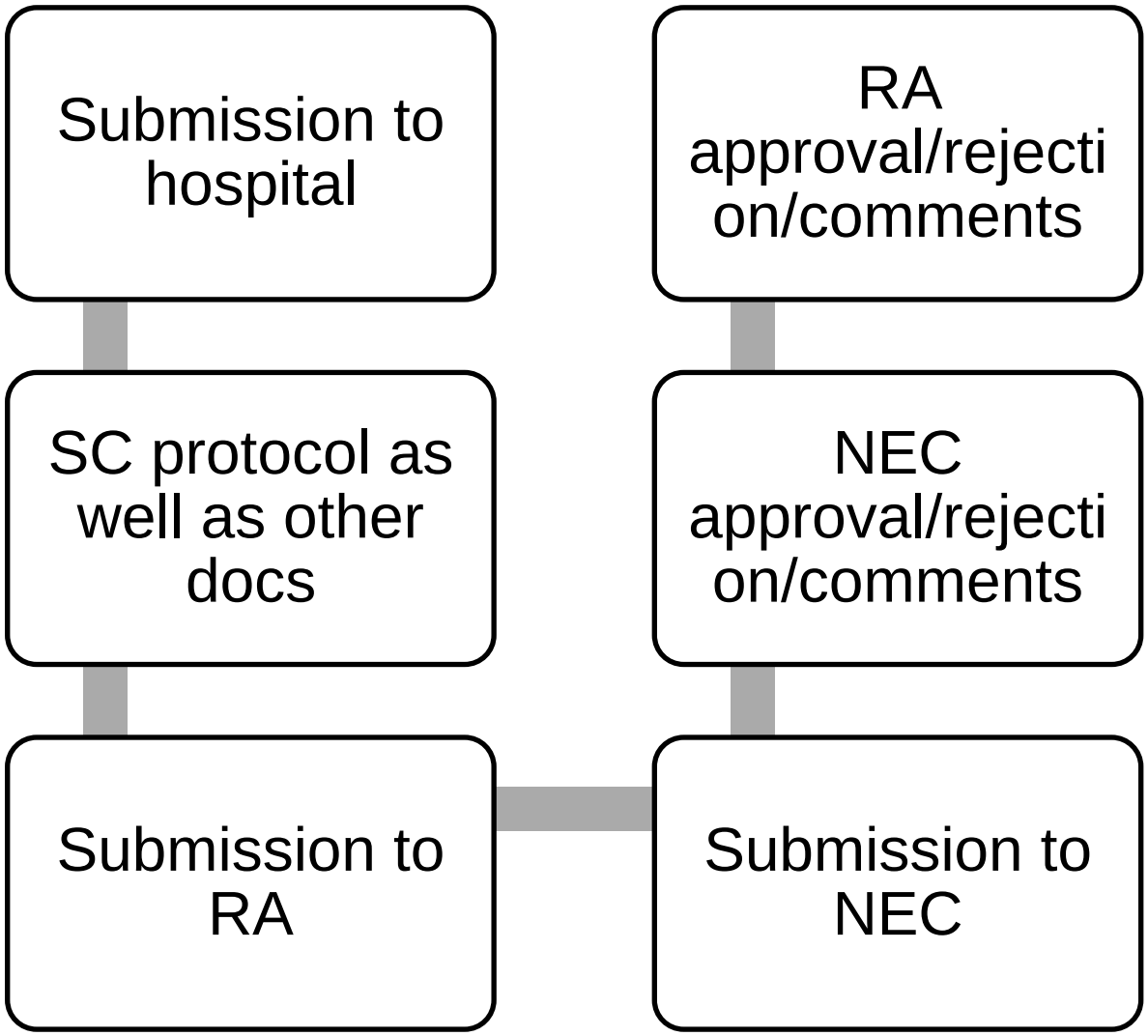
1. Fear of side effects
2. Randomization
3. Concern about costs

Rank of Response				
STUDY	1ST	2ND	3RD	4TH
Cancer Patients				
Meropol, (2007) [72]	**Fear of side effects** "I fear side effects that might come with treatment on a clinical trial"	**Control** "I am uncomfortable with being randomly assigned (for example, a coin toss) to a treatment"	**Control** "I fear receiving a placebo (for example a sugar pill) on a clinical trial."	**Logistics** "I would be unable to fulfill trial requirements due to logistical barriers such as transportation."
Unger, (2013) [30]	**Control** "Random treatment, and protocol would determine care"	"Did not want treatment"	**Fear of side effects** "Treatment side effects"	"No personal benefit"
Lara, (2001) [139]	**Control** "Desire for other treatment"	**Logistics** "Distance from clinic"	"Unknown"	**Costs** "Insurance denial"
Klabunde, (1999) [111]	"Concerns about experimentation"	"Unspecified"	**Costs** "Concern about cost" and "Insurance refusal"	**Fear of side effects** "Concerns about toxicity"
Zaleta, (2017) [206] (Minorities)	**Control** "Feeling uncomfortable with being randomly assigned to a treatment"	**Control** "Fearing receiving a placebo"	**Fear of side effects** "Fearing side effects that may come with treatment."	**Costs** "Believing that health insurance would not cover a clinical trial."
Javid, (2012) [34]	**Control** "Did not like that protocol dictated treatment"	**Fear of side effects** "Concerned that offered treatment had too many side effects"	Lack of personal benefit "Did not want treatment offered on clinical trial"	**Logistics** "Test and procedures and getting to/from required too much effort"

Source: Cancer Action Network, American Cancer Society

Is it feasible for primary health care in Greece to be involved in clinical research? What about behavioral clinical trials?

Clinical trial approval process in Greece



RA: Regulatory Authority, NEC: National Ethics Committee, SC: Scientific Committee

What kind of clinical trials could be conducted in PHC?

- Obesity – Greece has high rates of obesity and seems to be a growing health concern. Studies on diet, exercise are growing globally

- Lifestyle and Physical inactivity – Only 14.1% of young people aged 11-17 years old meet the WHO recommended physical activity levels for health. This is strange if we consider that Physical education is mandatory in primary and secondary schools across Greece.

- Tobacco use – Although smoking rates are declining, they're still too high in Greece compared with other countries.

WHO, GREECE PHYSICAL ACTIVITY FACTSHEET, Eurostat

What kind of clinical trials could be conducted in PHC?

- Mental health disorders - Many behavioral interventions contributed to greater improvement in anxiety, depression, and quality of care (Bradford, et al., 2011; Roy-Byrne, et al., 2010; Lang, 2003)

- Diabetes – Results from interventions in Primary Care have shown treatment adherence for patients with comorbid diabetes (Lamers, Jonkers, Bosma, Knottnerus, & Van Eijk, 2011;). Interventions such as educational information, diet, exercise, social support

- Pediatrics – Integrating children's behavioral health

Behavioral health in Primary Care

- Primary care is the focal point of patients' health and wellbeing
- Behavioral health integration in Primary Care is clinically effective
- Are behavioral interventions in Primary Care cost-effective?

Cost-effectiveness of behavioral interventions in Primary Care: Findings from literature

Inclusion criteria → > 40 years or older having Type 1 or 2 Diabetes

Low cost and cost-effective intervention that contributes to long-term positive outcomes and patient satisfaction

ELSEVIER

Patient Education and Counseling 32 (1997) 175–184

PATIENT EDUCATION AND COUNSELING

Long term effects and costs of brief behavioural dietary intervention for patients with diabetes delivered from the medical office

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Abstract

Table 3
Economic dissemination model: cost **per patient** for various numbers of patients seen

Intervention components	Number of patients per year		
	100	500	1000
Touch screen computer package	$26	$5	$3
Materials and supplies	$43	$43	$43
Labor (including benefits)	$59	$59	$59
Postage	$10	$10	$10
Long distance phone	< $1	< $1	< $1
Total cost per patient	$139	$117	$115
Cost per 1% recent reduction in fat intake	$63	$53	$52
Cost per unit reduction in cholesterol	$8.40	$7.11	$6.95

cant intervention effects: fat consumption, saturated fat consumption, and serum cholesterol. Since there were not significant effects on HbA, economic analyses were not conducted

practical to implement in a variety of outpatient settings. The touchscreen computer is mounted on a portable cart that can be moved from one exam room to another. The intervention requires

Cost-effectiveness of behavioral interventions in Primary Care: Findings from literature

Interventions compared

1) Group-based peer support
2) Standardized diabetes care

International Journal of Technology Assessment in Health Care, 28:1 (2012), 3–11.
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Assessments

COST EFFECTIVENESS OF PEER SUPPORT FOR TYPE 2 DIABETES

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Objectives: The aim of this study is to examine the cost-effectiveness of a group-based peer support intervention in general practice for patients with type 2 diabetes.
Methods: Incremental cost utility analysis combining within trial and beyond trial components to compare the lifetime costs and benefits of alternative strategies: *Control:* standardized diabetes care; *Intervention:* group-based peer support in addition to standardized diabetes care. Within trial analysis was based on a cluster randomized controlled trial of 395 patients with type 2 diabetes in the east of Ireland. Beyond trial analysis was conducted using the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model. Uncertainty was explored using a range of sensitivity analyses and cost-effectiveness acceptability curves were generated.
Results: Compared with the control strategy, the intervention was associated with an increase of 0.09 (95 percent confidence interval [CI], −0.05 to 0.25) in mean quality-adjusted life-years per patient and savings of €637.43 (95 percent CI, −2455.19 to 1125.45) in mean healthcare cost per patient and €623.39 (95 percent CI, −2507.98 to 1298.49) in mean total cost per patient respectively. The likelihood of the intervention being cost-effective was appreciably higher than 80 percent for a range of potential willingness-to-pay cost-effectiveness thresholds.
Conclusions: Our results suggest that while a group-based peer support intervention shows a trend toward improved risk factor management, we found no significant differences in final cost or effectiveness endpoints between intervention and control. The probabilistic results suggest that the intervention was more cost-effective, with probability values of higher than 80 percent across a range of potential cost-effectiveness threshold values.

Keywords: Type 2 diabetes, Peer support, General practice, Cost-effectiveness analysis

Table 4. Incremental Cost-Effectiveness Results

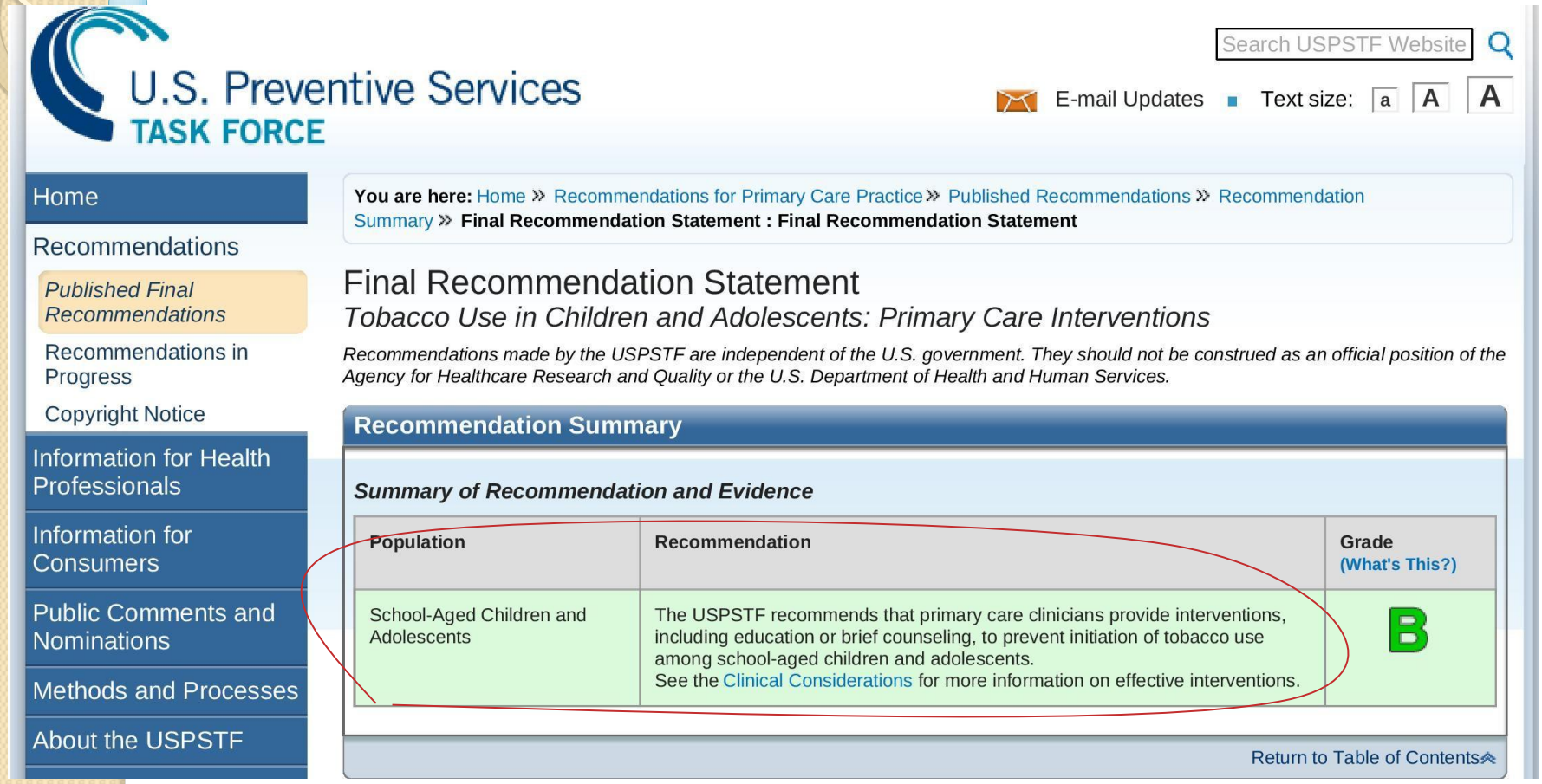
Variable/analysis	Incremental analysis (Intervention minus control) Mean (95% CIs)
Cost analysis	
Difference in trial based healthcare cost	−560.08 (−1738.89, 618.73)
Difference in trial based patient cost	4.01 (−53.63, 61.64)
Difference in trial based total cost	−527.83 (−1744.42, 688.75)
	Intervention / Control
Lifetime healthcare cost	17176.93 (16105.03, 18464.17) / 17814.36 (16667.18, 19309.25)
Difference in lifetime healthcare cost	−637.43 (−2445.19, 1125.45)
Lifetime total cost	17487.81 (16233.23, 18985.85) / 18111.21 (16844.09, 19570.46)
Difference in lifetime total cost	−623.39 (−2507.98, 1298.49)
Effectiveness analysis	Intervention / Control
Lifetime QALYs	6.76 (6.66,6.86) / 6.67 (6.55, 6.77)
Difference in QALYs	0.09 (−0.05, 0.25)

Note. Within Trial Analyses: Multilevel GEE regression model, with identity link function, Gamma variance function (Gaussian for Patient Cost), and exchangeable correlation structure. All models estimated controlling for *treatment group* and *baseline cost* for the 12 months before the trial.
Beyond Trial Analyses: Based on 10,000 Monte Carlo simulations in the UKPDS Outcomes model and 1,000 Monte Carlo simulations to combine within and beyond trial results

Cost savings of €637.43 per patient in healthcare costs

Increase in QALYs (0.09 per patient compared with control

Nowadays, organizations strongly recommend primary care interventions



The United States Preventive Services Task Force

Some conclusions

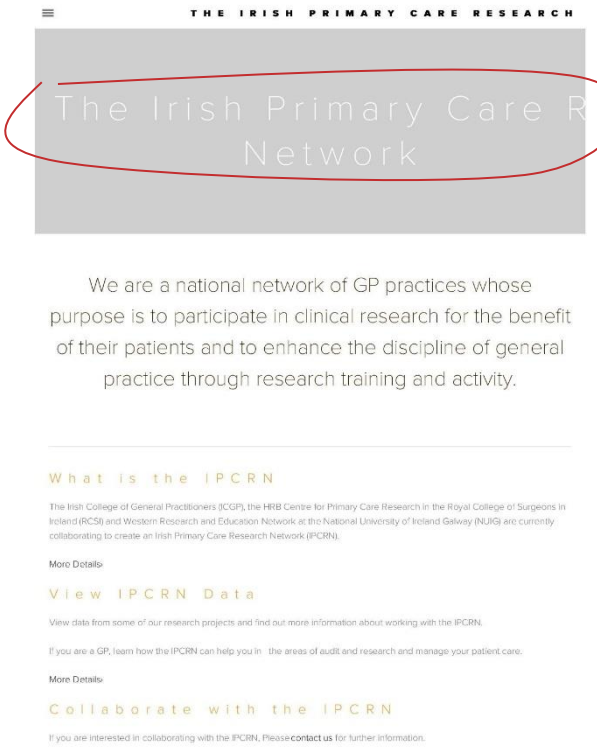
- Clinical trials are investments for public health
- Twenty-first century primary care is rapidly evolving. In Greece, we have to speed up
- Greece has to retain it’s high quality Family Physicians - Family physicians play a key role in healthcare delivery
- They could play a vital role in integrating behavioral studies in primary health system in Greece

Is this the answer to boost clinical research in Primary Care?

Scandinavian Journal of Primary Health Care, 2014; 32: 107–109

EDITORIAL

Research networks in primary care: An answer to the call for better clinical research



Thank you in advance!

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