



# Communicating Risk Effectively

the CORE  project

Sigrid Piening,<sup>1</sup> Flora M. Haaijer-Ruskamp,<sup>1</sup> Pieter A. de Graeff,<sup>1,2</sup>

Sabine M.J.M. Straus,<sup>2,3</sup> and Peter G.M. Mol<sup>1,2</sup>

<sup>1</sup>Dept. Clinical Pharmacology, University Medical Center Groningen,

<sup>2</sup>Medicines Evaluation Board (CBG-MEB), Utrecht,

<sup>3</sup>Medical Informatics, Erasmus Medical Center, Rotterdam, The Netherlands.



# The CORE project

Unconditional grant of the Dutch Medicines  
Evaluation Board (CBG-MEB)

Aim: To improve risk communication of safety  
issues of drugs (post approval).





# Content

- Introduction (DHPCs & effectiveness)
- Determinants of impact of warnings
- Survey; opinion of healthcare providers
- Intervention study (*ongoing*)
- Conclusion



# The DHPC

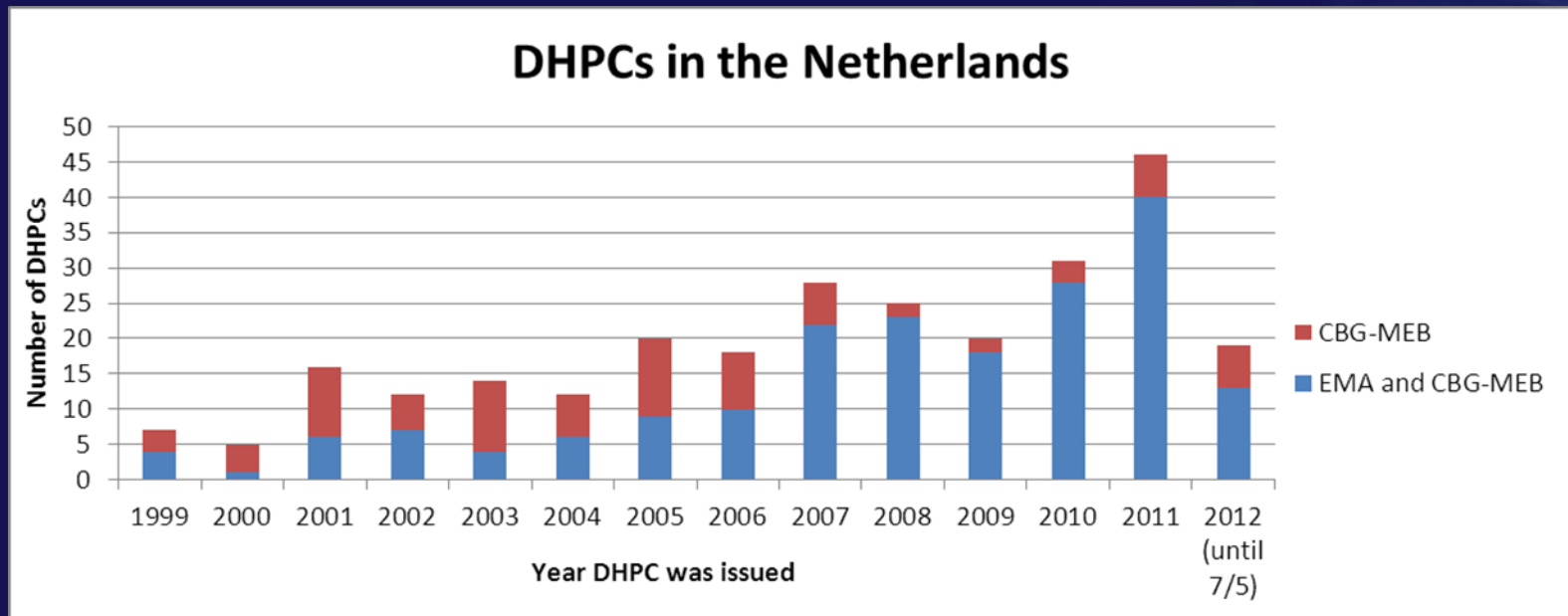
## Direct Healthcare Professional Communication Or 'Dear Doctor Letter'





# Introduction

- Serious safety issues leading to Direct Healthcare Professional Communications (DHPCs):
  - 9% - 10% of drugs (Mol et al. 2010; Lasser et al. 2002)
  - Issued throughout drugs' lifecycle
  - Increasing by 2.1 DHPCs/year (95%CI:1.2-3.1)





# Introduction

- Effectiveness of DHPC is questioned
  - Limited knowledge due to heterogenous study designs, few drug (groups) studied, various outcomes used  
*Piening et al. Drug Safety 2012 {systematic review}*
  - Impact often delayed, after repeated warnings, more impact on incident than prevalent use  
*Dusetzina et al. Med Care 2012 {systematic review}*
- New European legislation creates need for more information about impact of risk minimization measures like DHPCs.
- However: overview is lacking and point of reference is needed



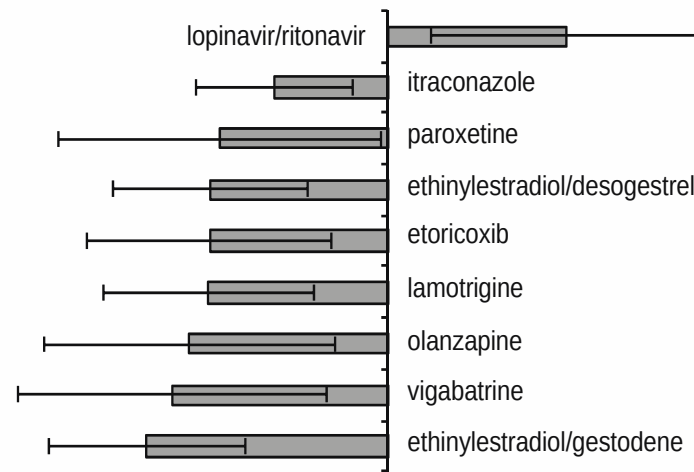
# Impact of DHPC

- Impact of DHPCs on new drug use
  - Dispensing data of 58 DHPCs/46 drugs (2001-2007)
  - Ambulatory care
- Short term effects
  - 48% of DHPCs lower drug use
- Long term effects
  - 34% Of DHPCs lower drug use.
  - Mean reduction in use: -27%

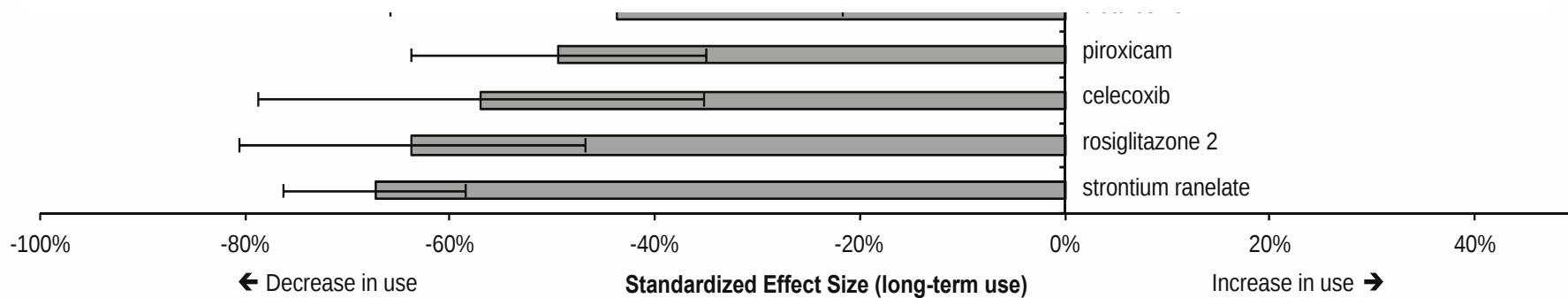


## Previous results CORE

Relative effect sizes (95% CI)  
of DHPCs with long term  
impact (N=20; 34%)



Conclusion: Limited impact of DHPCs,  
but decrease in drug use can be substantial.





# Determinants of impact of DHPCs

Which drug and DHPC characteristics explain  
impact of DHPCs on drug use?





# Determinants

- Drug characteristics:
  - Time to DHPC since registration
  - Trend in use before DHPC was issued
  - Innovativeness
  - Type of initial prescriber (GP vs. specialist)
- DHPC characteristics
  - First/repeated DHPC
  - Timing of DHPC in study period
  - Seriousness of safety issue





# Methods

- Study population
  - Same as previous study (58 DHPCs/46 drugs [2001-2007])
- Outcome measure
  - Relative change in new use
- Determinants
  - Drug related characteristics
  - DHPC related characteristics
- Analysis: multivariate regression



# Results - Drug Characteristics

| Drug characteristics                          | B [95% CI]                           | $\beta$       | P value      |
|-----------------------------------------------|--------------------------------------|---------------|--------------|
| Time to DHPC (month)                          | $2.23 \cdot 10^{-4}$ [-0.000; 0.001] | 0.109         | 0.369        |
| Trend in use (before DHPC)                    |                                      |               |              |
| Increasing                                    | ref                                  | ref           |              |
| No change                                     | 0.013 [-0.109; 0.135]                | 0.030         | 0.833        |
| Decreasing                                    | <b>-0.177 [-0.335; -0.019]</b>       | <b>-0.353</b> | <b>0.029</b> |
| Degree of therapeutic innovation <sup>b</sup> | -0.005 [-0.055; 0.046]               | -0.027        | 0.851        |
| Type of prescriber required                   |                                      |               |              |
| No medical specialist                         | ref                                  | ref           |              |
| Medical specialist                            | <b>0.168 [0.048; 0.288]</b>          | <b>0.396</b>  | <b>0.007</b> |



# Results – DHPC Characteristics

| DHPC characteristics                            | B [95% CI]                     | $\beta$       | P value      |
|-------------------------------------------------|--------------------------------|---------------|--------------|
| <b>First/repeated DHPC</b>                      |                                |               |              |
| First                                           | ref                            | ref           |              |
| Repeated                                        | -0.076 [-0.202; 0.051]         | -0.153        | 0.234        |
| <b>Timing of DHPC (study month)</b>             | -0.002 [-0.004; 0.000]         | -0.255        | 0.056        |
| <b>Type of serious safety issue</b>             |                                |               |              |
| Death                                           | <b>-0.278 [-0.437; -0.120]</b> | <b>-0.474</b> | <b>0.001</b> |
| Hospitalization                                 | -0.021 [-0.169; 0.126]         | -0.044        | 0.775        |
| <b>Disability / Incapacity / Teratogenicity</b> | <b>-0.141 [-0.280; -0.001]</b> | <b>-0.315</b> | <b>0.048</b> |
| Other                                           | ref                            | ref           |              |

Adjusted  $R^2 = 0.363$



# Conclusion

- Determinants affecting impact of DHPCs:
  - DHPC characteristics (decreased use)
    - Seriousness of safety issue (death & disability)
    - Newer DHPCs
  - Drug characteristic
    - Specialist initiates therapy (increased use)
      - *Experienced physician*
    - Already decreasing use (decreased use)



## Discussion

- These results should be considered when planning risk communication
- Future research: What is the impact of DHPCs on other, more specific outcome measures
  - New users – more sensitive than overall use
  - Decrease in use is not always desired impact of DHPC





# Survey

Evaluating the perception, knowledge and preferences  
of different Dutch healthcare professional groups  
regarding DHPCs



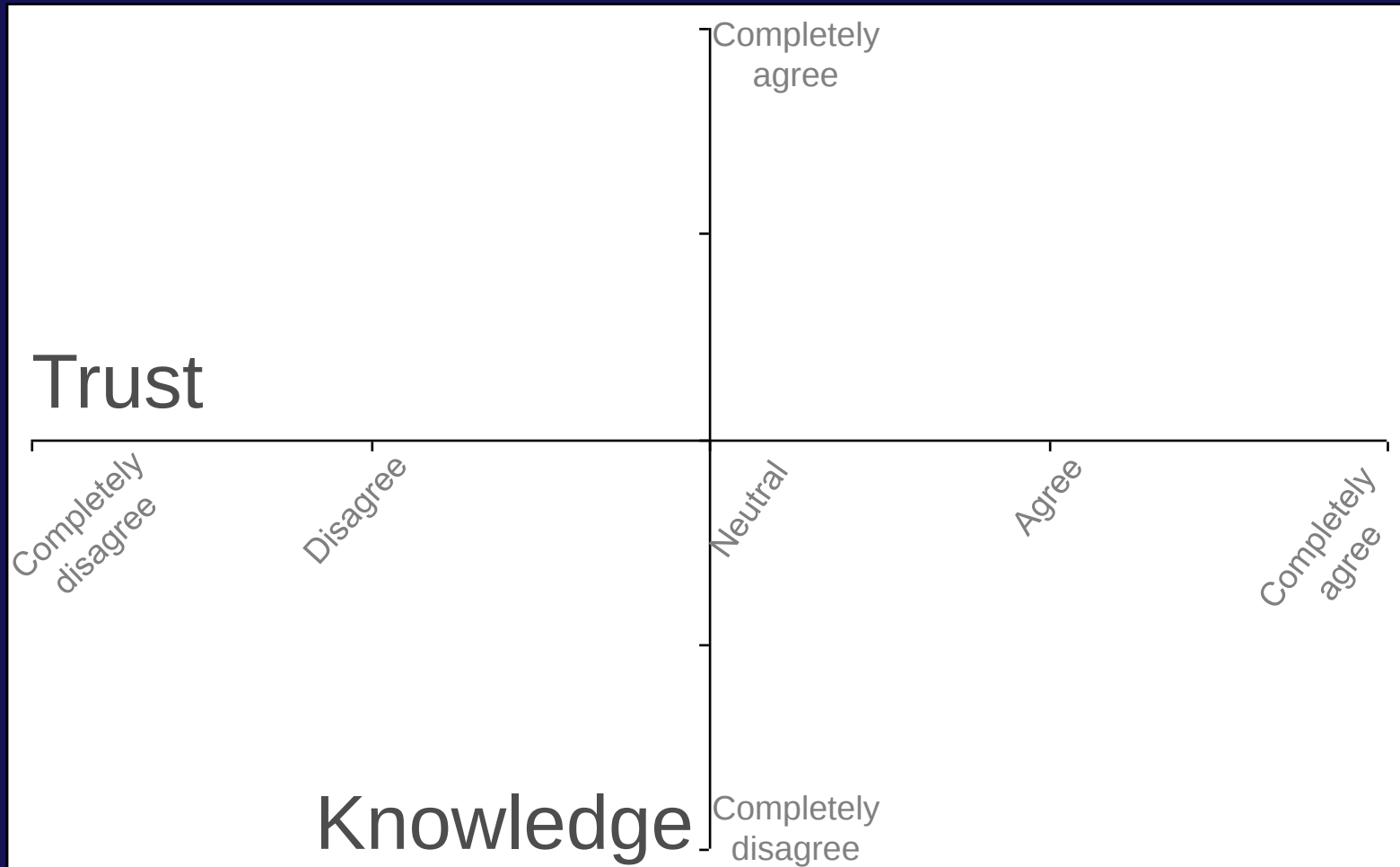
## Methods

- Design: Cross sectional survey
- Population: Dutch healthcare professionals (HCPs)
  - General practitioners (GPs), Internists, Community pharmacists, Hospital pharmacists.
- Paper-based questionnaire was sent to 3488 HCPs

|                 | GPs<br>(700) | Internists<br>(1696) | Community<br>Pharmacists<br>(700) | Hospital<br>Pharmacists<br>(392) | Total<br>(3488) |
|-----------------|--------------|----------------------|-----------------------------------|----------------------------------|-----------------|
| <b>Response</b> | 233 (33%)    | 410 (24%)            | 323 (46%)                         | 175 (45%)                        | 1141 (33%)      |

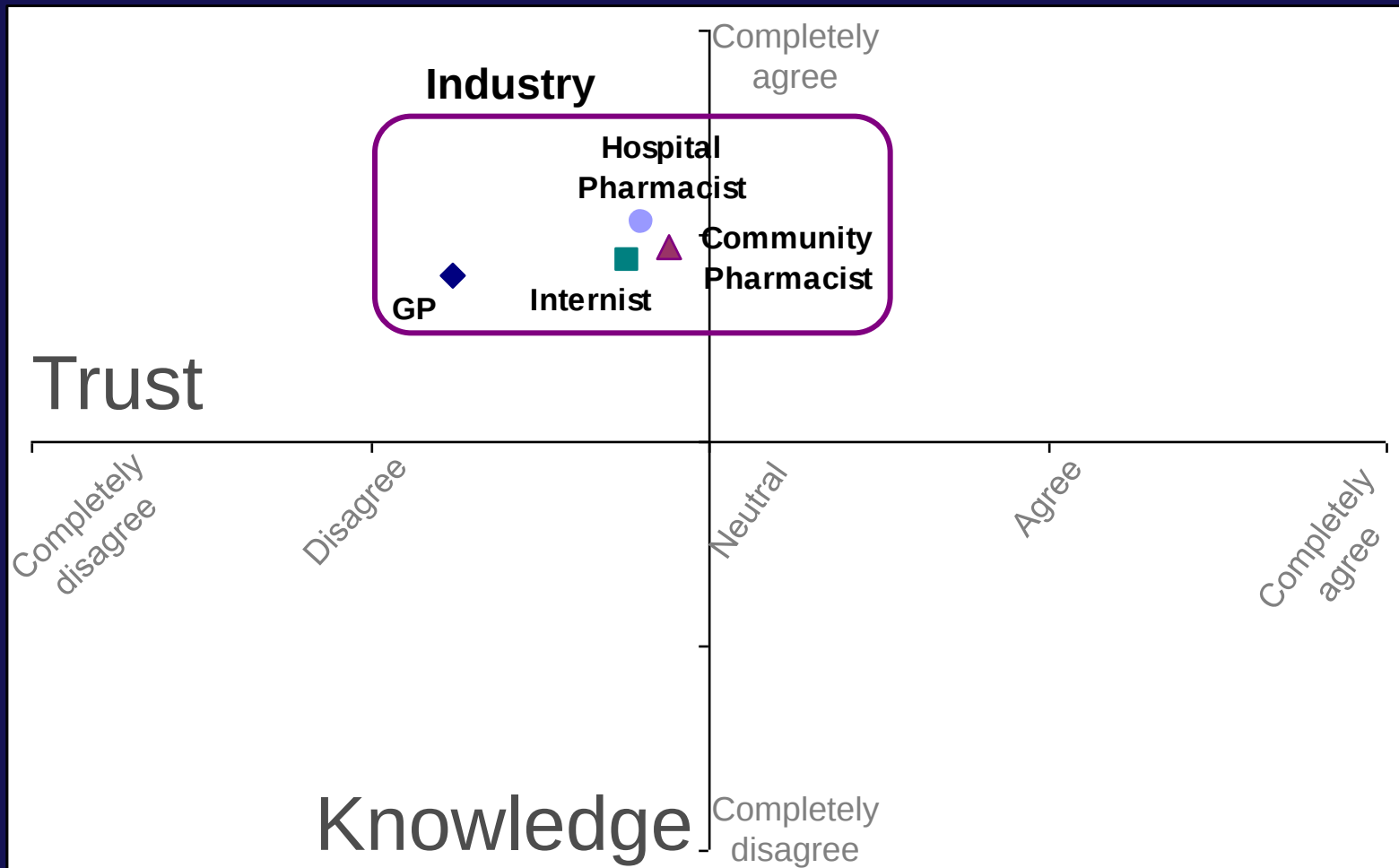


# Trust & Knowledge in Industry and MEB



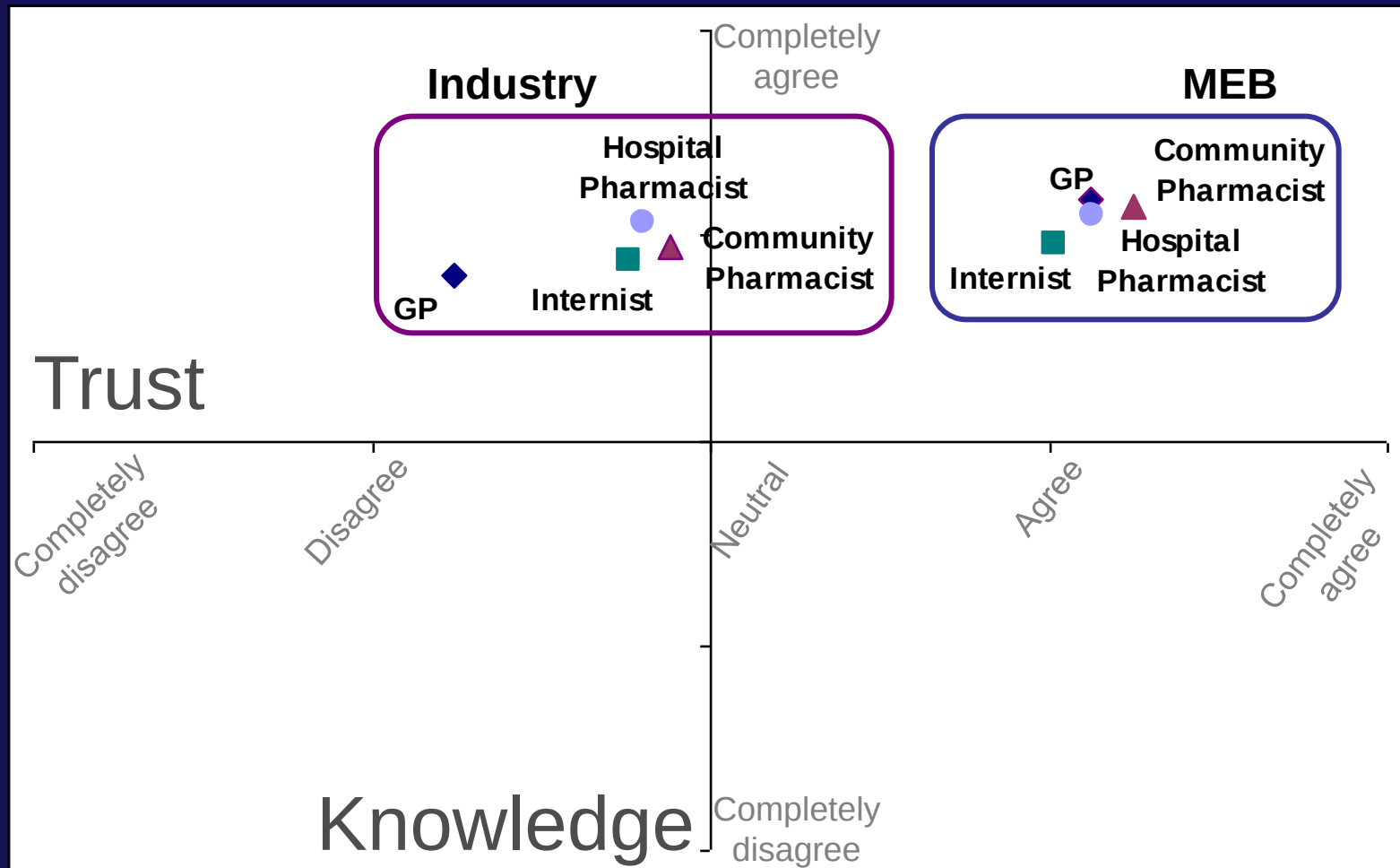


# Trust & Knowledge in Industry and MEB





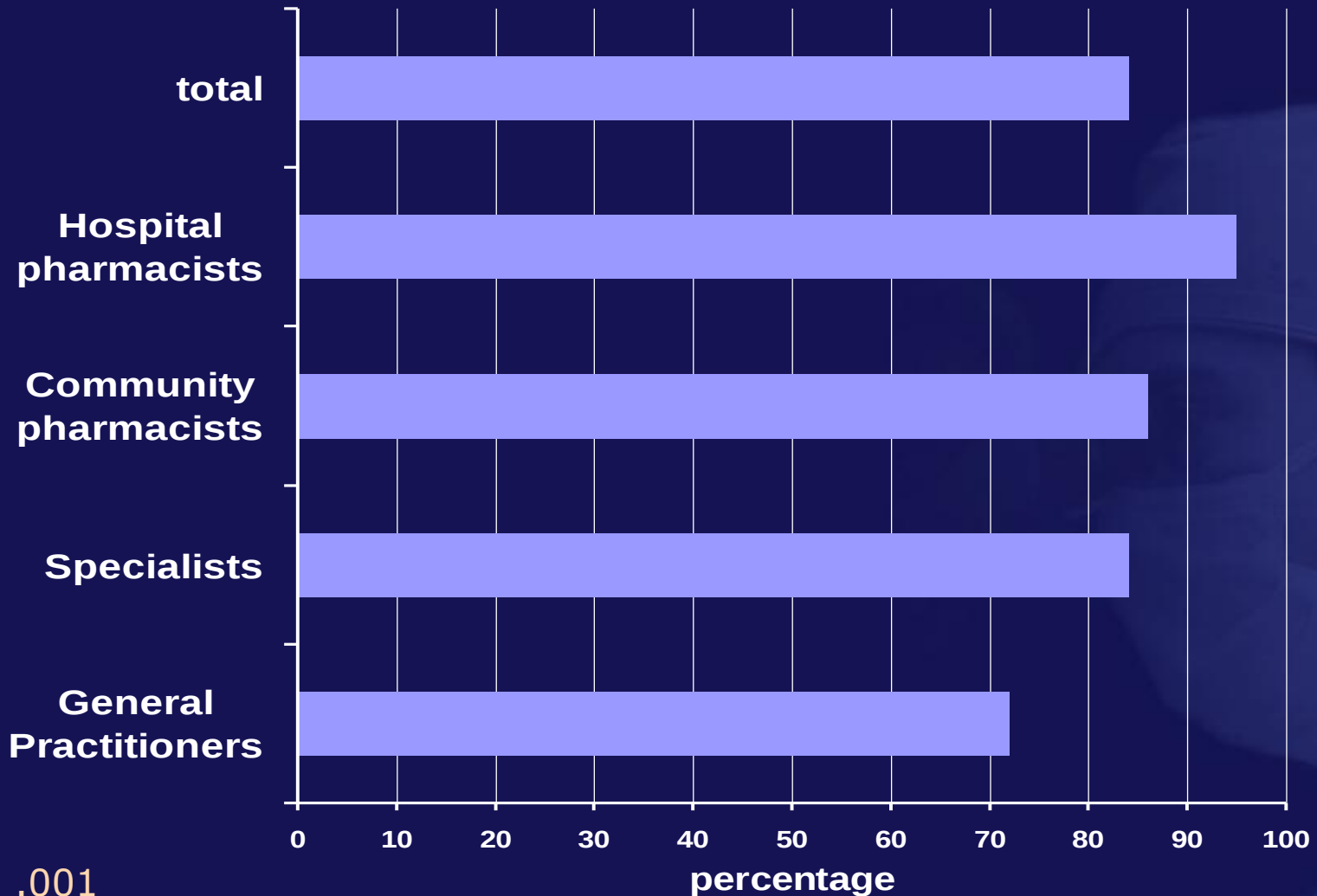
# Trust & Knowledge in Industry and MEB





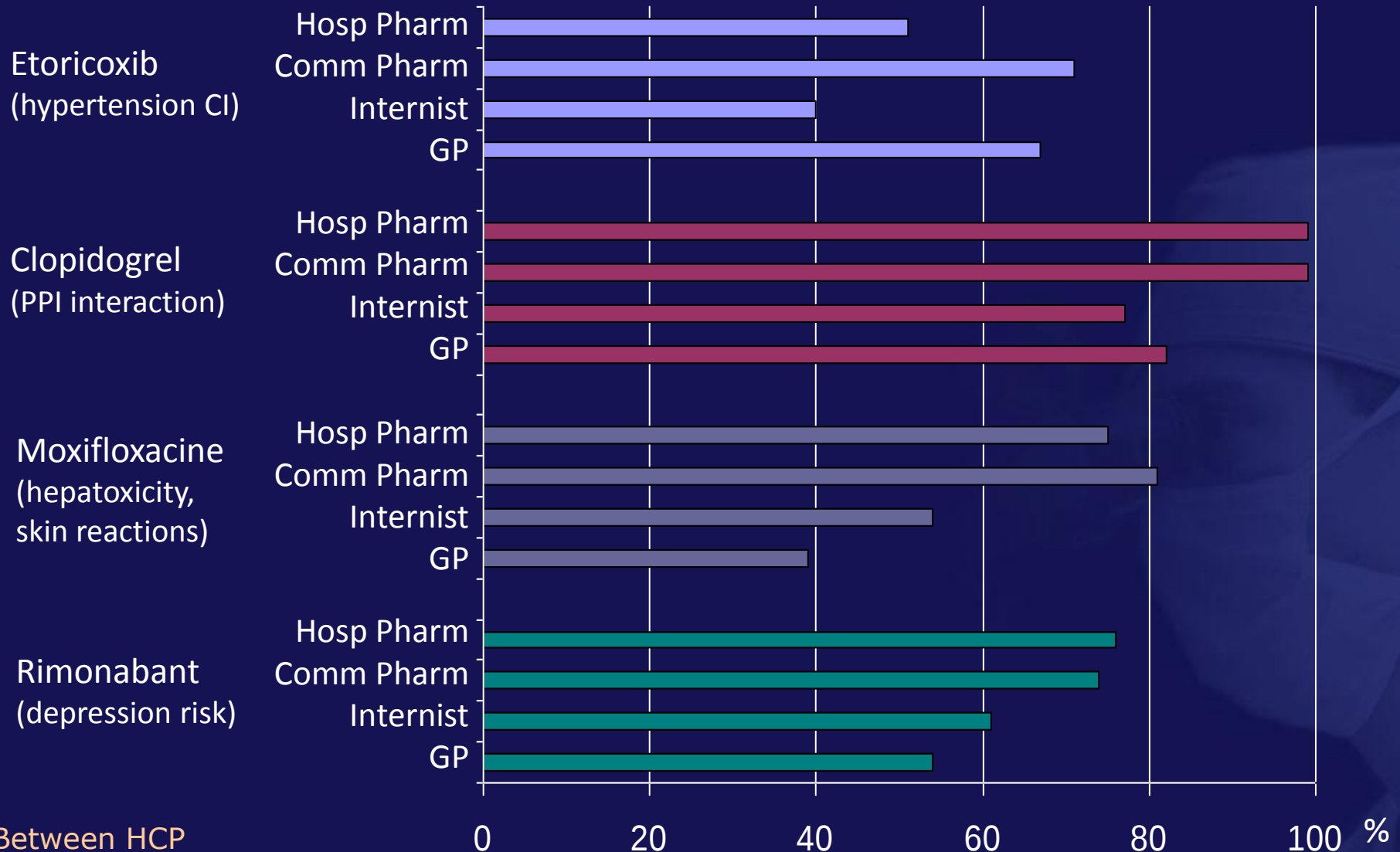
# Awareness of DHPCs

Yes, I have seen a DHPC before





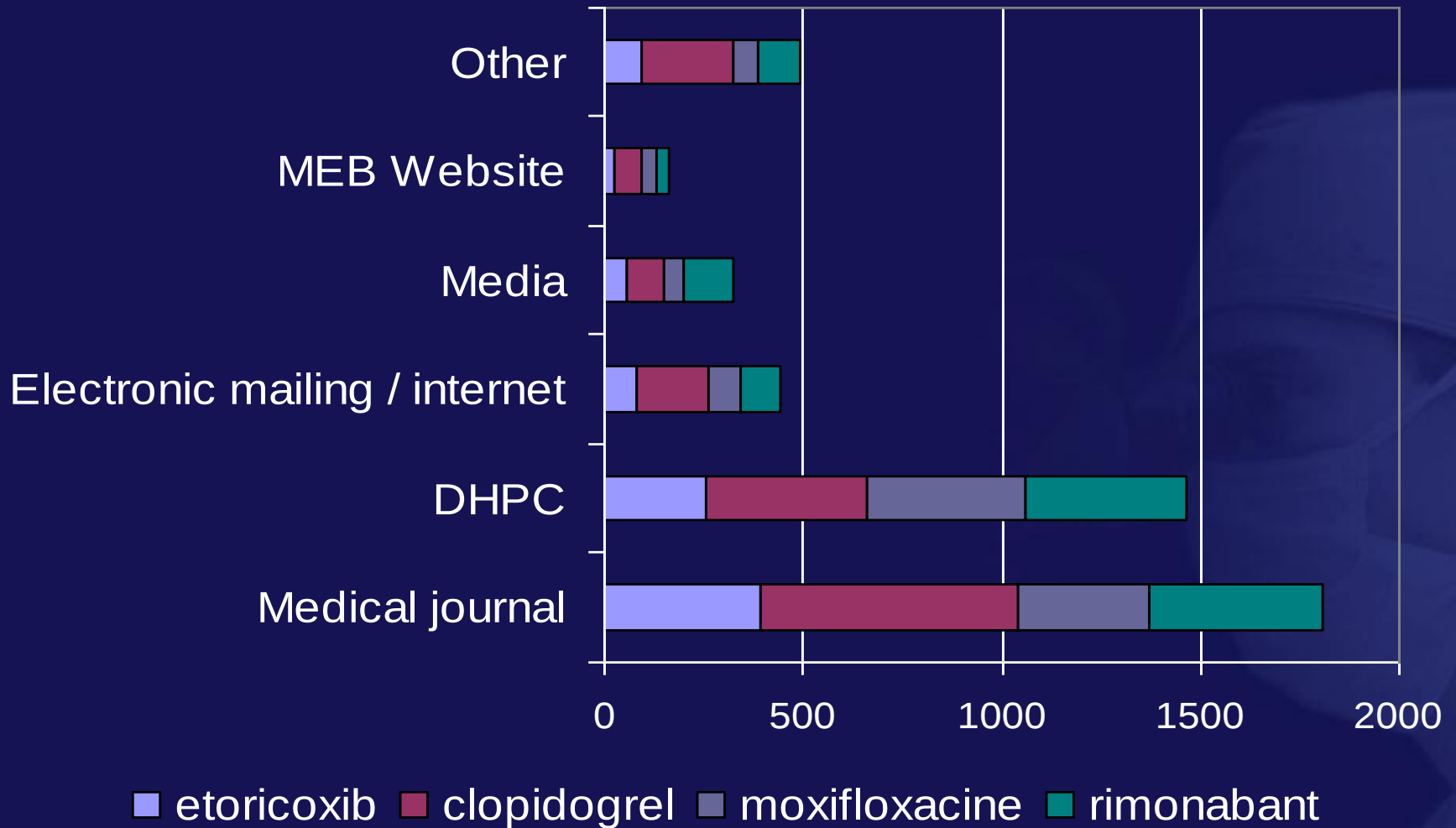
# Awareness of specific safety issues



Between HCP  
ANOVA:  $P < 0.001$



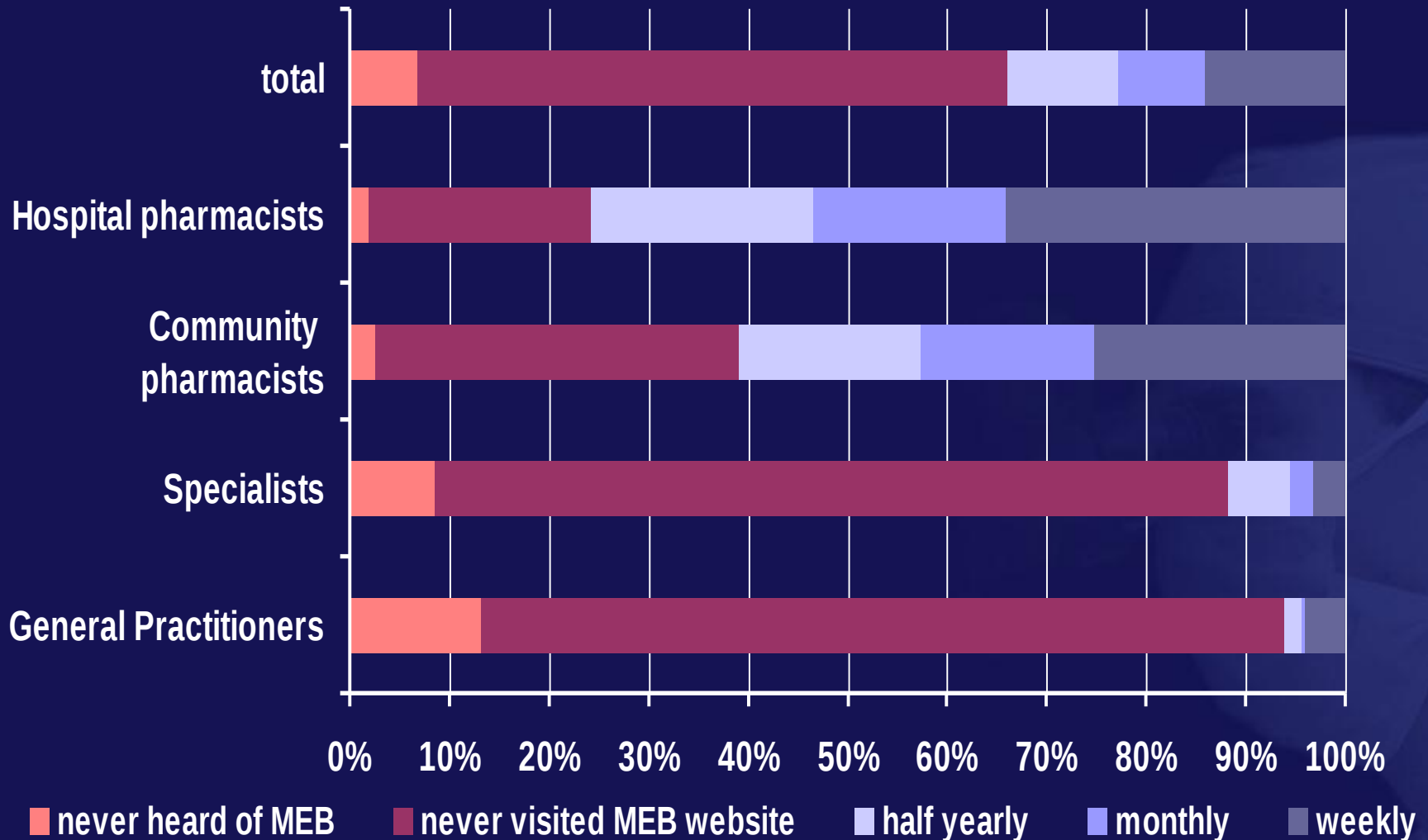
## Awareness of specific safety issues - sources\*



\* Several answers possible



# Awareness of (website of) Dutch MEB

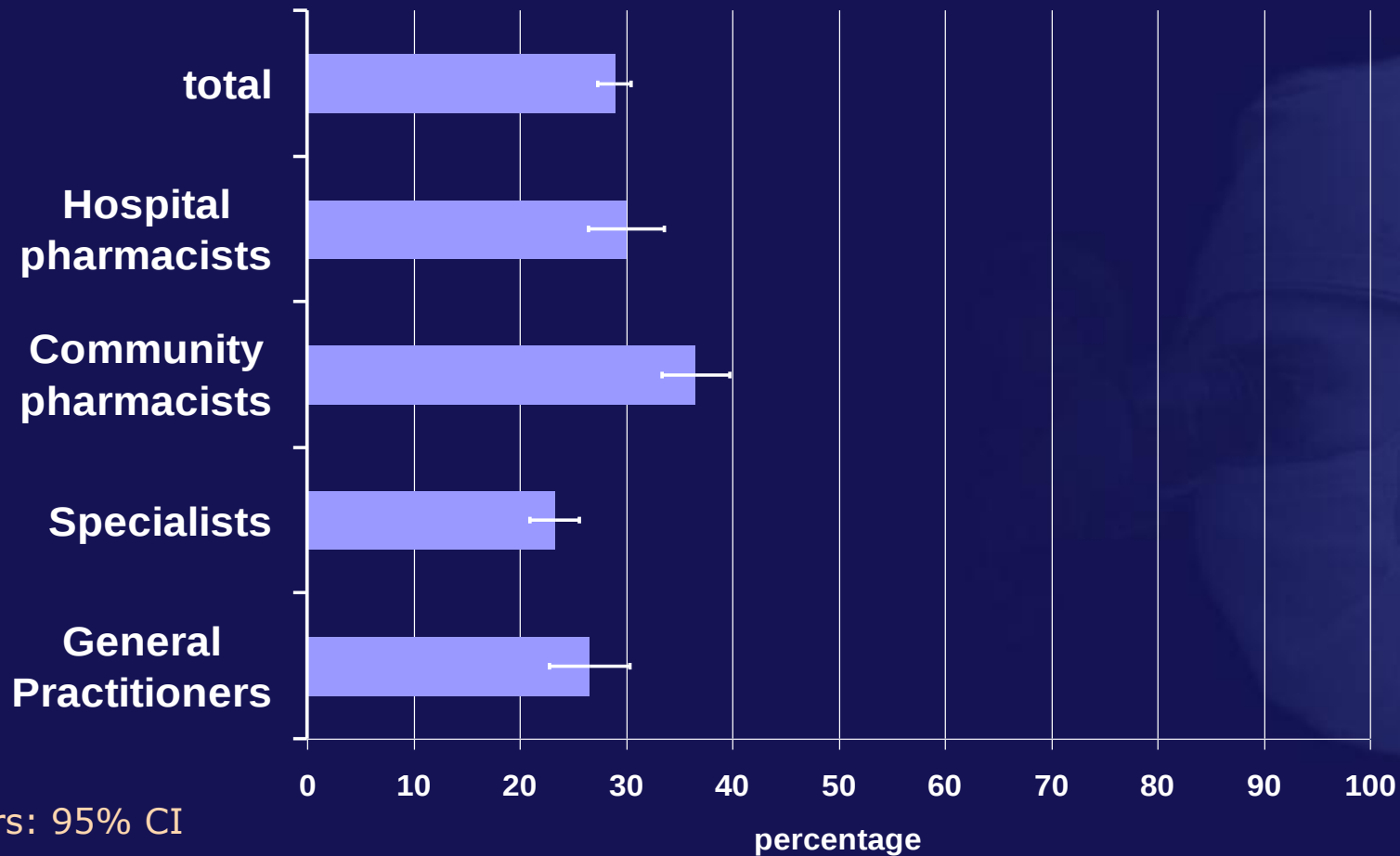


Between HCP  
ANOVA:  $P < 0.001$



# Reported behavior

Estimated % DHPCs that lead to action



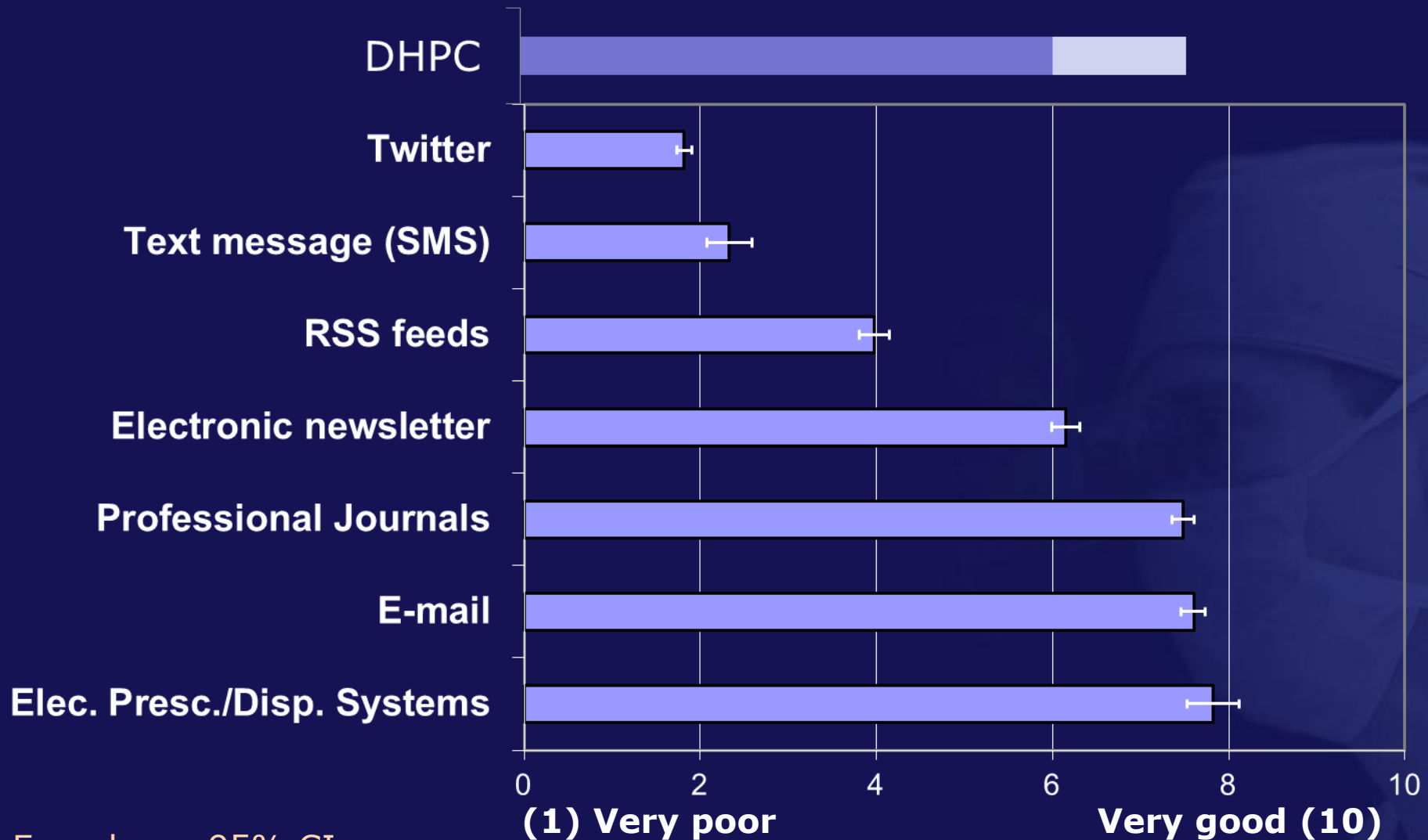
Error bars: 95% CI

Between HCP

ANOVA:  $P < 0.001$



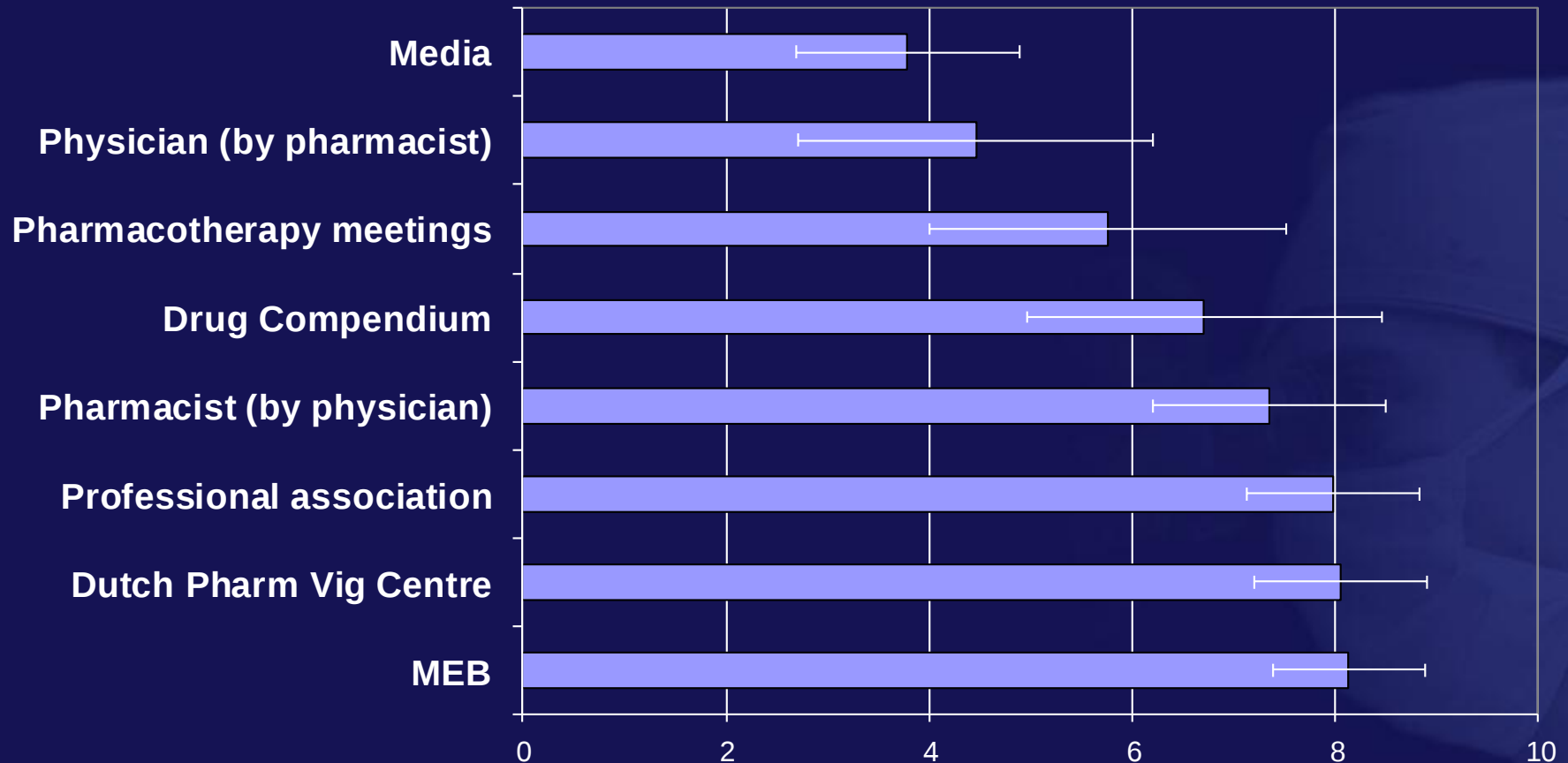
# Preferences (channels)



Error bars: 95% CI



# Preferences (sources)



Error bars: 95% CI

(1) Very poor

Very good (10)



# Summary

- HCPs have more trust in info from MEB than industry
- Appr. 30% of GPs has never seen DHPC
- Awareness of safety issues mainly from
  - 1) Medical journals
  - 2) DHPCs
- Most physicians never visit MEB website
- HCPs take action in appr. 30% of DHPCs
- Preferred channels: electronic systems/e-mail
  - 84% of HCPs prepared to submit email address to MEB
- Preferred sources: independent organisations





## Conclusion

Safety information does not always reach HCPs  
through DHPCs.

Changes are needed to improve  
current risk communication of  
safety issues of drugs.





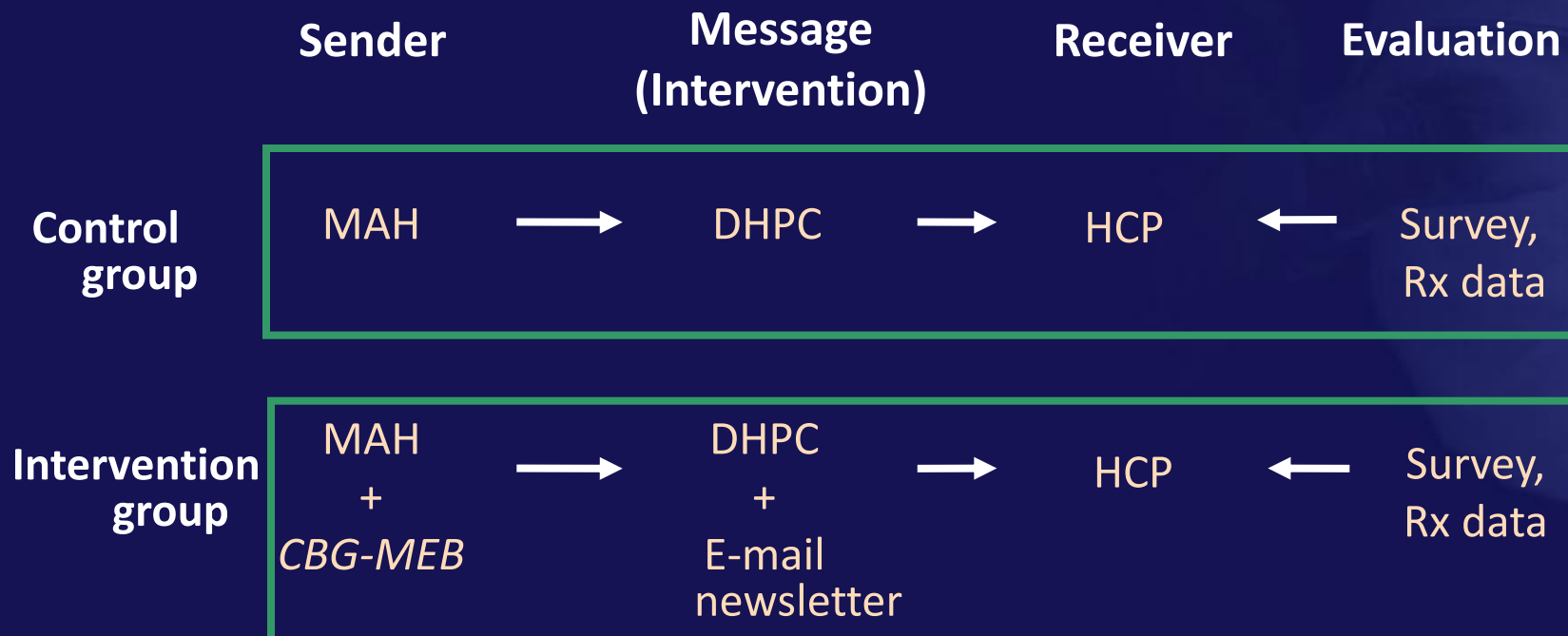
## Recommendations

- (Additional) Electronic channels could be used to disseminate drug safety information
- Safety information coming from professional bodies like the Dutch MEB or Pharmacovigilance Centre (LAREB) should be considered
- Tailor made approach can be used to reach GPs



# Intervention study (ongoing work)

- Does an additional e-mail, sent by CBG-MEB, lead to better knowledge & behaviour?
- Study design: controlled trial





# Intervention

## Outcome measures:

- Survey: Web-based questionnaire
  - Awareness and knowledge of safety issue
    - Eg.: 'Can you indicate which new safety issue was identified for drug X?'
  - Undertaken action in response to safety issue
    - Eg.: 'Did you adjust treatment of your patients because of the safety issue?'
- Results expected later this year...



# Take home message

- Point of reference
  - 34% DHPCs affect new use
- Facilitating impact
  - More (!?) serious ADEs
  - Already decreasing use before the DHPC
  - Newer DHPCs
- Target group
  - Specialists respond differently from GPs
    - GP's less informed, more critical of source (knowledge gap)
    - Specialists more reluctant to change (behaviour issue)





# The way forward

- How to improve Risk Communication
  - Independent source (e.g. national authority)
  - Other/additional channels (e.g. e-mails)
  - *intervention study....*
- Caveats for future work
  - Recruitment: Low response to surveys; especially when online and/or from industry
  - Generalizability of findings across Europe
    - Differences in healthcare systems
    - Differences in HCP knowledge & perception of authorities / industry
  - 'Actionable recommendations'





Thank you for your attention