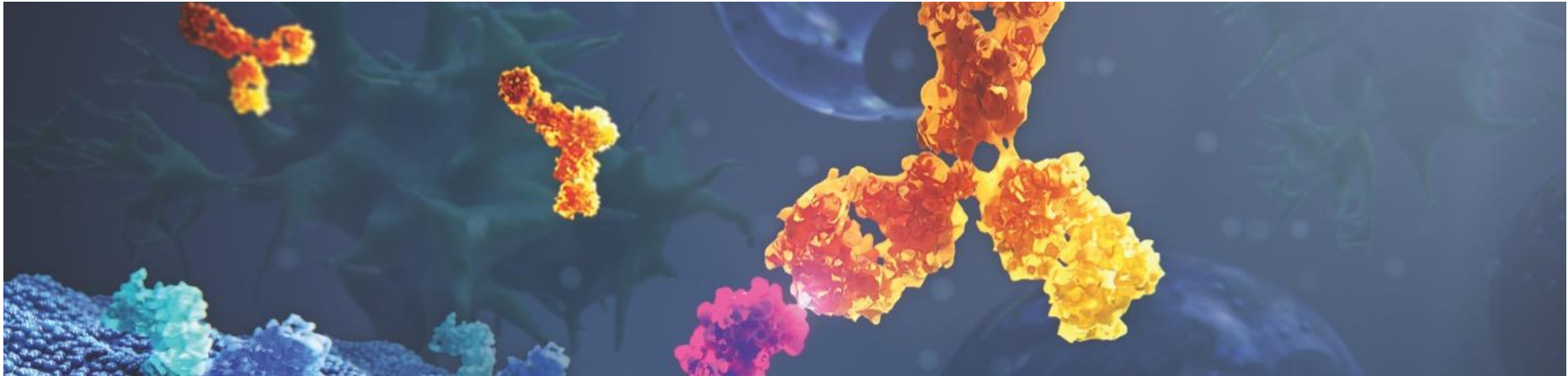


Becoming a change agent

Dr Natasha Karp

Quantitative Biology, Discovery Science, IMED Biotech Unit, AstraZeneca, UK

22nd May 2019



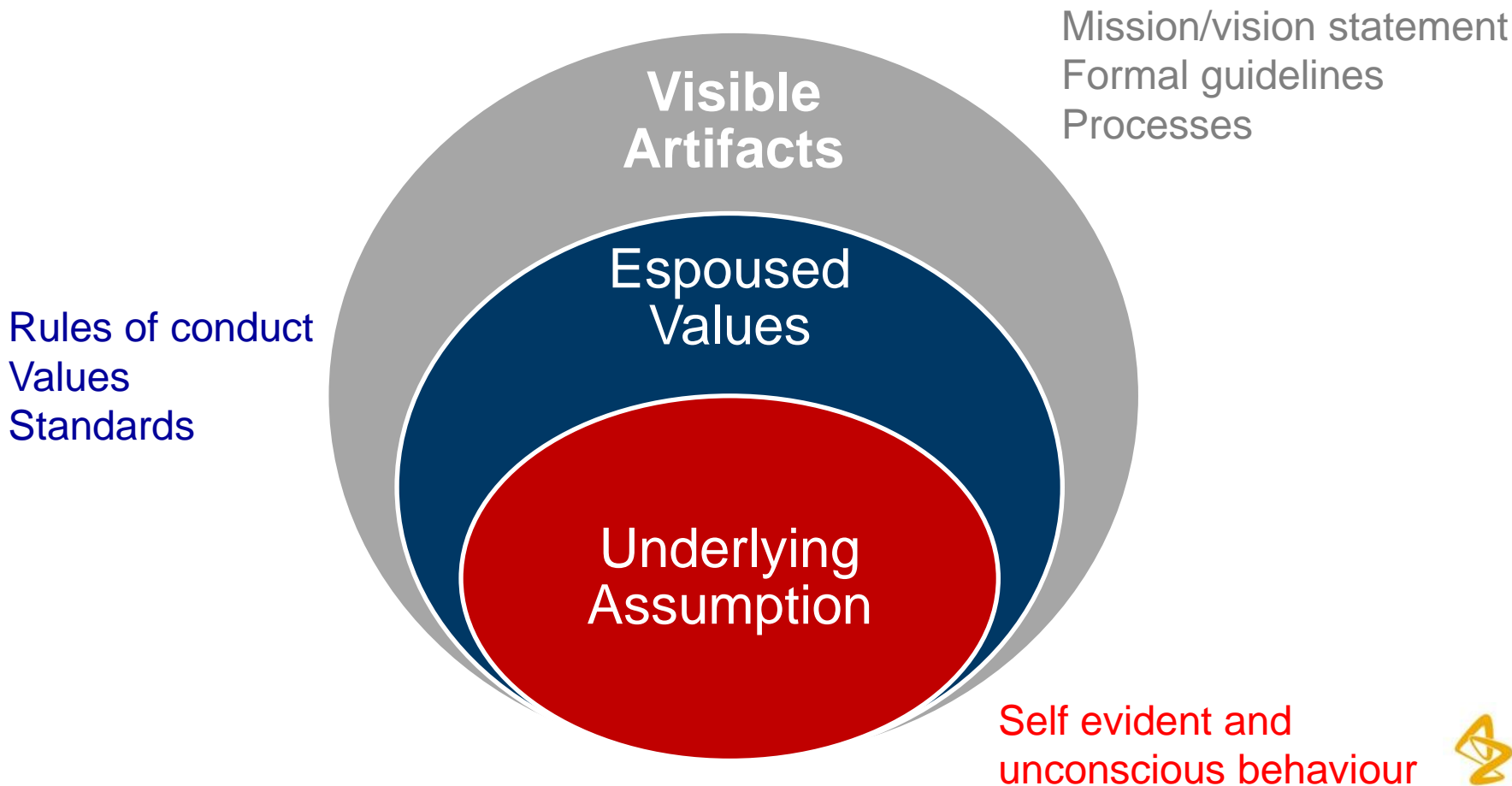
CHALLENGES OF DRIVING AND EMBEDDING CHANGE



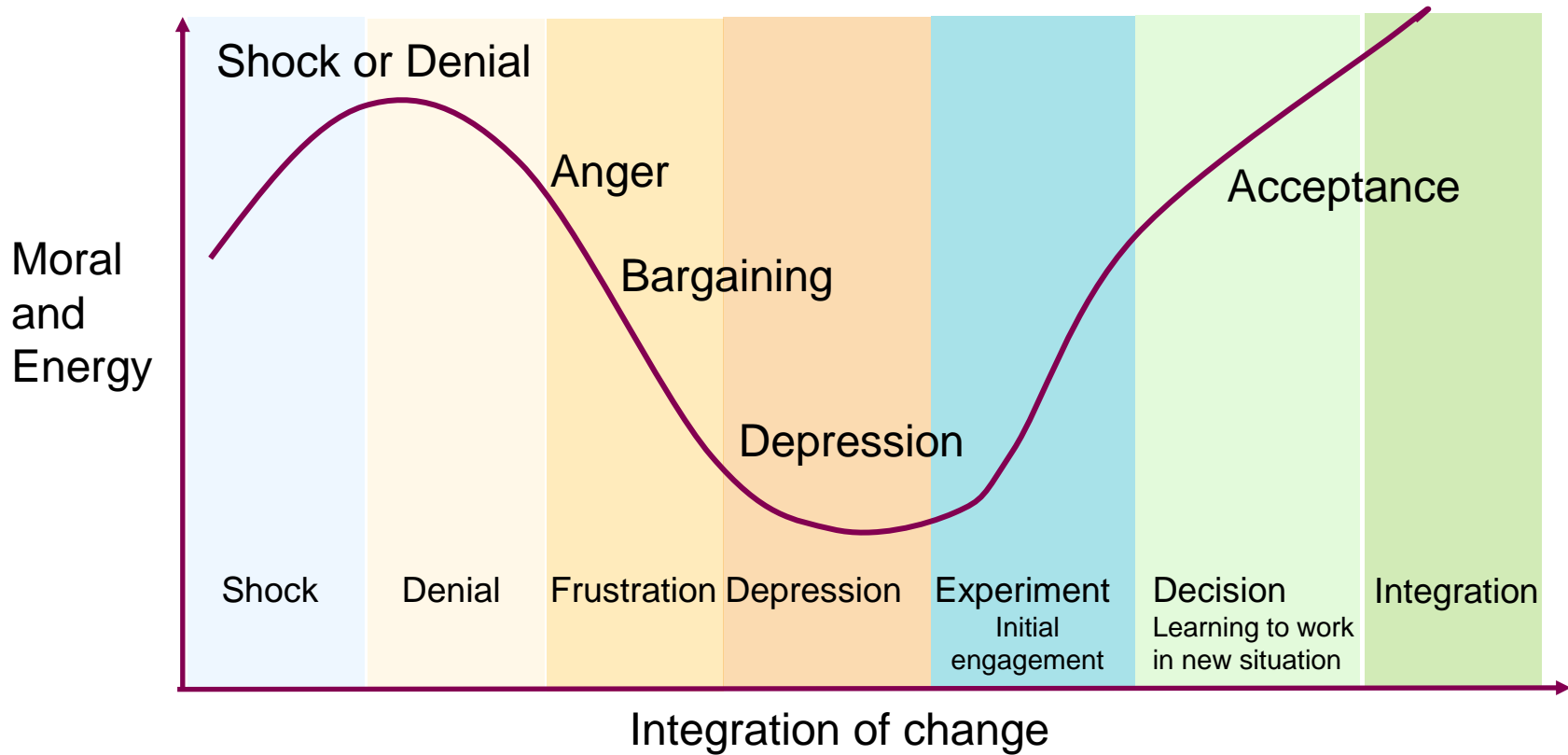
Step 1 - recognising that this is CHANGE



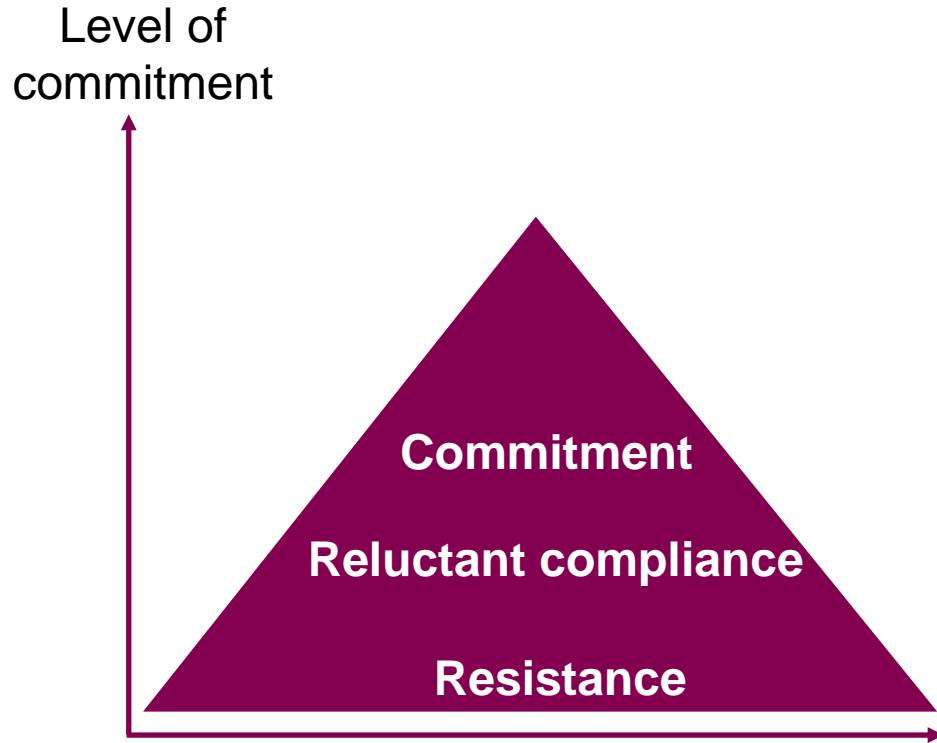
Organisational Culture ‘the way we do things around here’.



Küber-Ross Change Curve

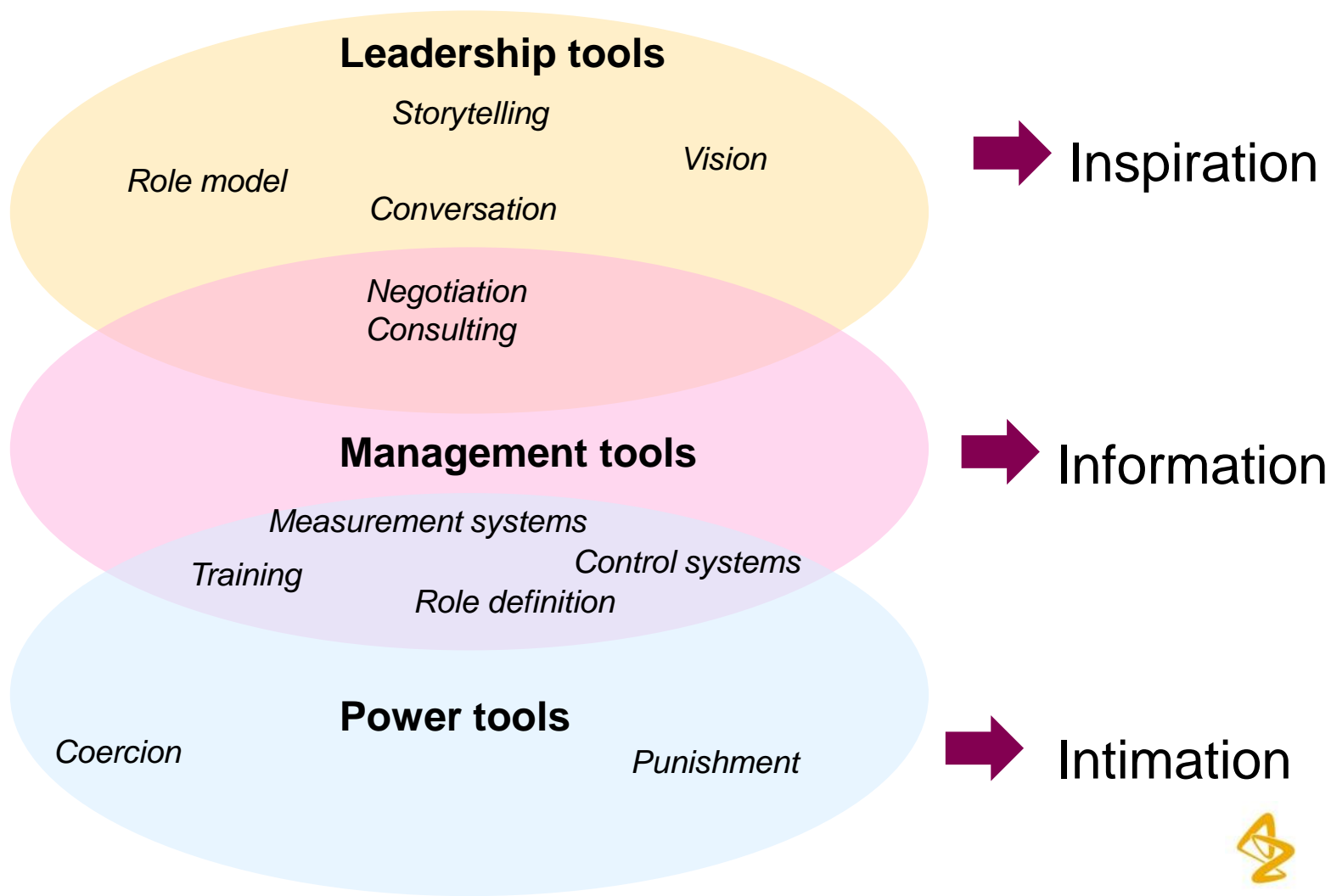


Influence tactics

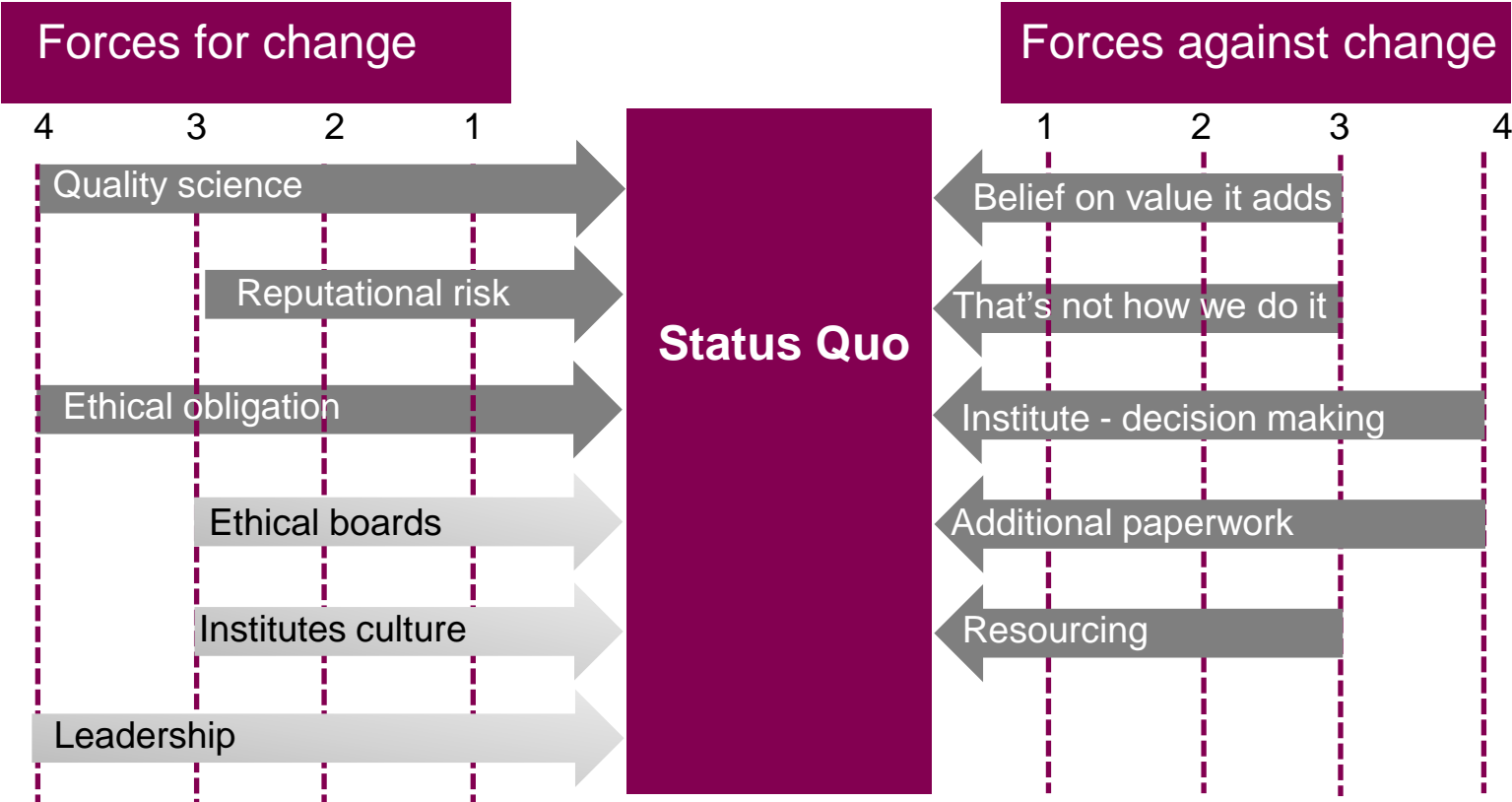


Tactics	
Negative	Pressure
	Legitimising
	Coalition Building
Positive	Rational Persuasion
	Exchange
	Consultation
	Inspirational Appeal

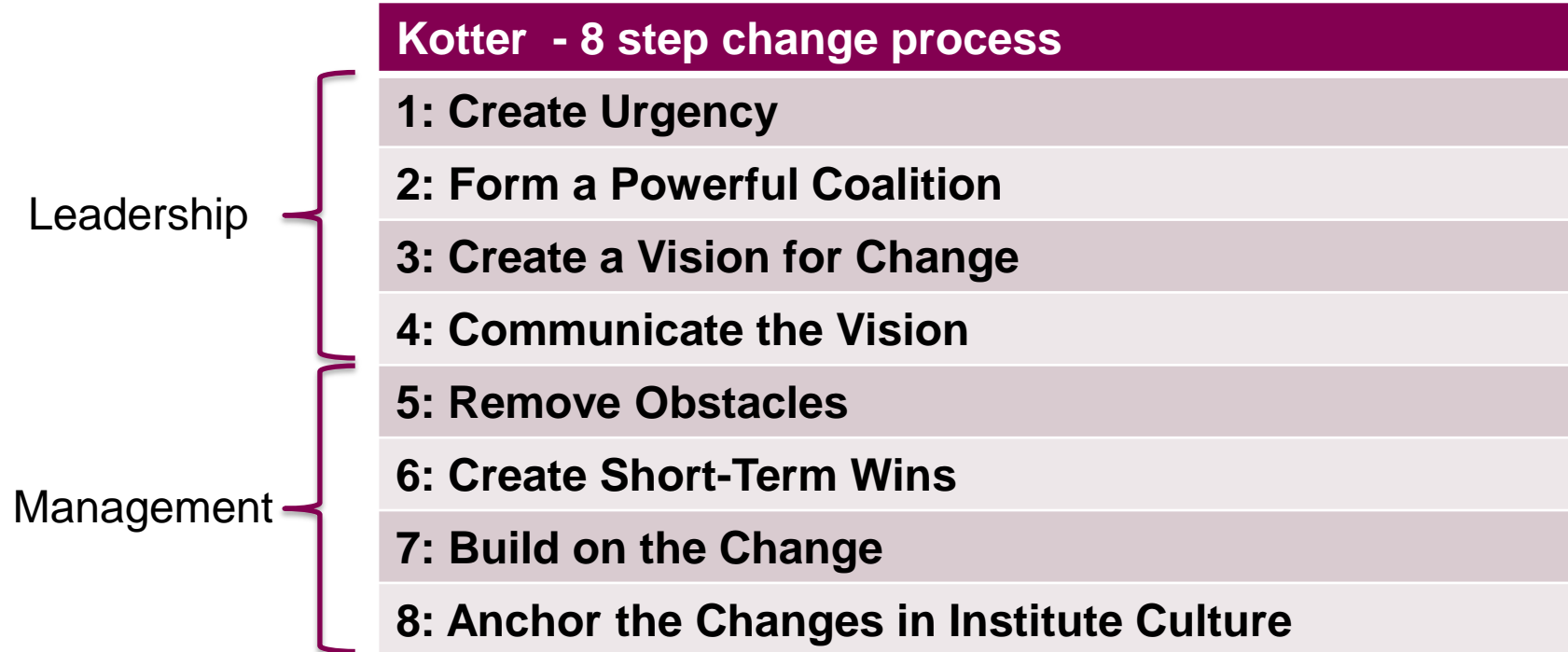




Force field analysis




Institute level plan




CASE STUDY: INITIATING “GOOD STATISTICAL PRACTICE”



Significant media focus on replicability

 BROWSE PUBLISH ABOUT

SEARCH 

advanced search

 OPEN ACCESS

ESSAY

Why Most Published Research Findings Are False

John P. A. Ioannidis

Published: August 30, 2005 • <https://doi.org/10.1371/journal.pmed.0020124>

68,836 Save	3,858 Citation
2,653,975 View	10,480 Share

“Simulations show that for most study designs and settings, it is more likely for a research claim to be false than true.”



A burning platform

Financial Times
Sept 2007

“Flaws in use of
animal tests for
new drugs”

Dr Macleod also reported the results of an investigation into NXY-059, AstraZeneca’s experimental stroke treatment. The company dropped NXY-059 when it showed no benefit in a clinical trial involving more than 3,000 patients, after very promising animal studies.

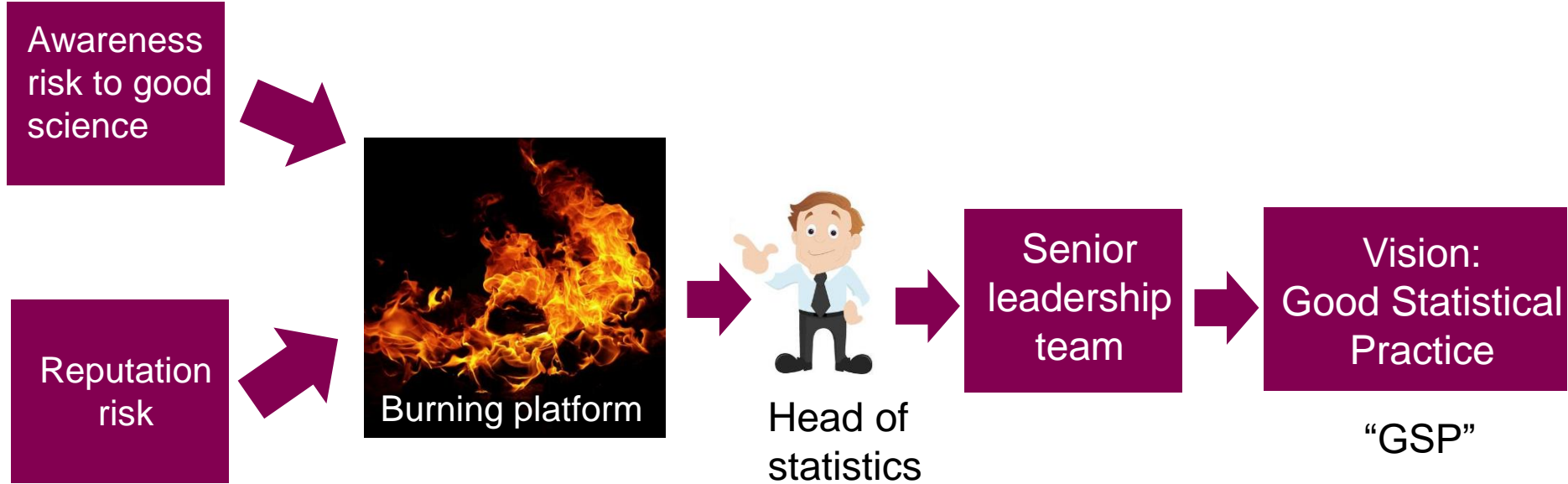
Overall, NXY-059 improved outcome in animals with stroke by 44 per cent, Dr Macleod said: “However, when we looked in more detail, disturbing patterns appeared.”

For example, studies that did not randomise animals said NXY-059 improved outcome by more than 50 per cent; those that did not estimated the effect at only 20 per cent. Studies that did not blind the assessment of outcome said it improved that outcome by almost 50 per cent; those that did not estimated the effect at less than 30 per cent.

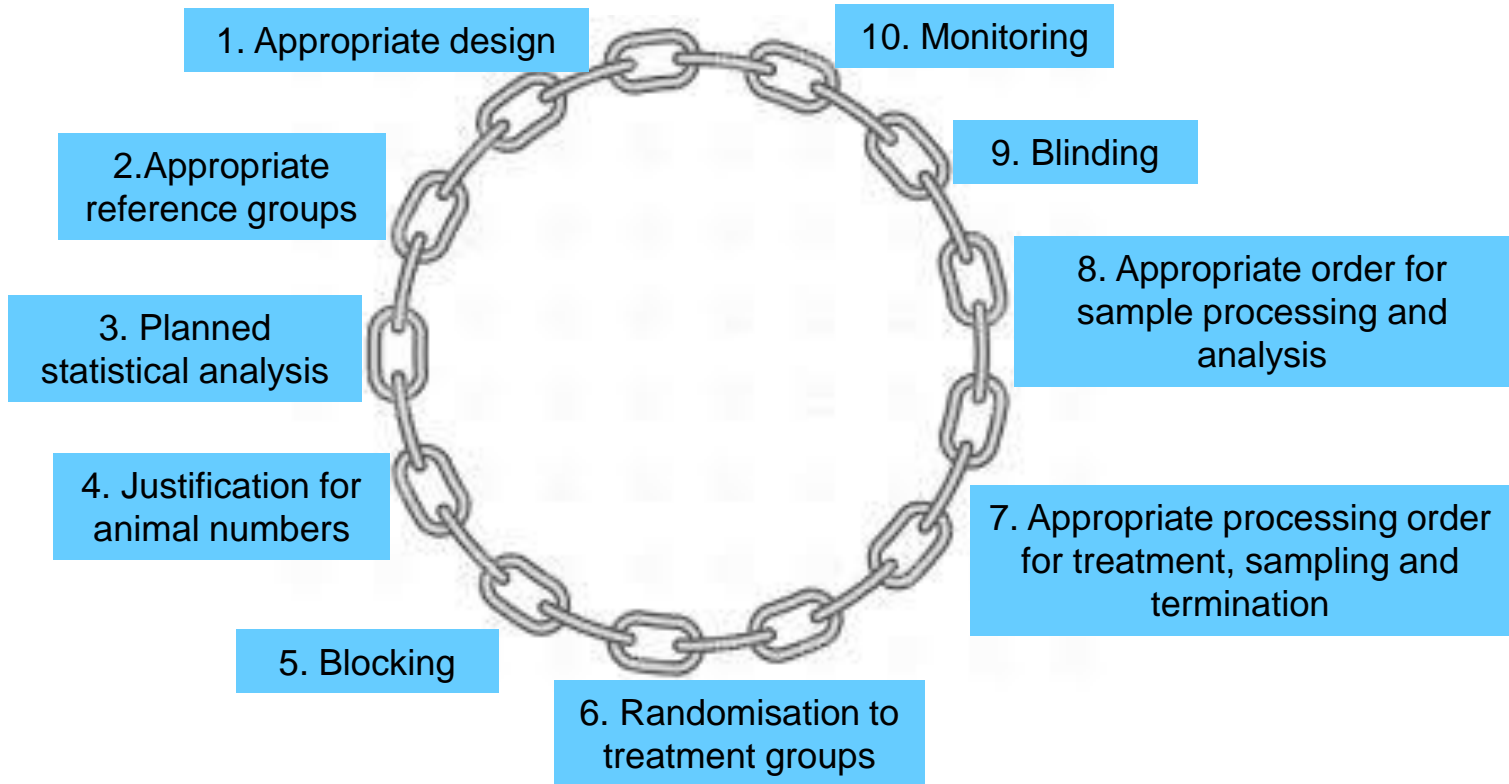
“We have reported similar findings for other interventions, but what is disturbing about the data for NXY-059 is that for a drug where most of the published work was funded by the drug manufacturers the impact of poor study quality was much more pronounced,” said Dr Macleod. He emphasised that he was not opposed to animal experiments – indeed he uses them in his own work – but wanted them to be designed to the same high standard as human clinical trials.



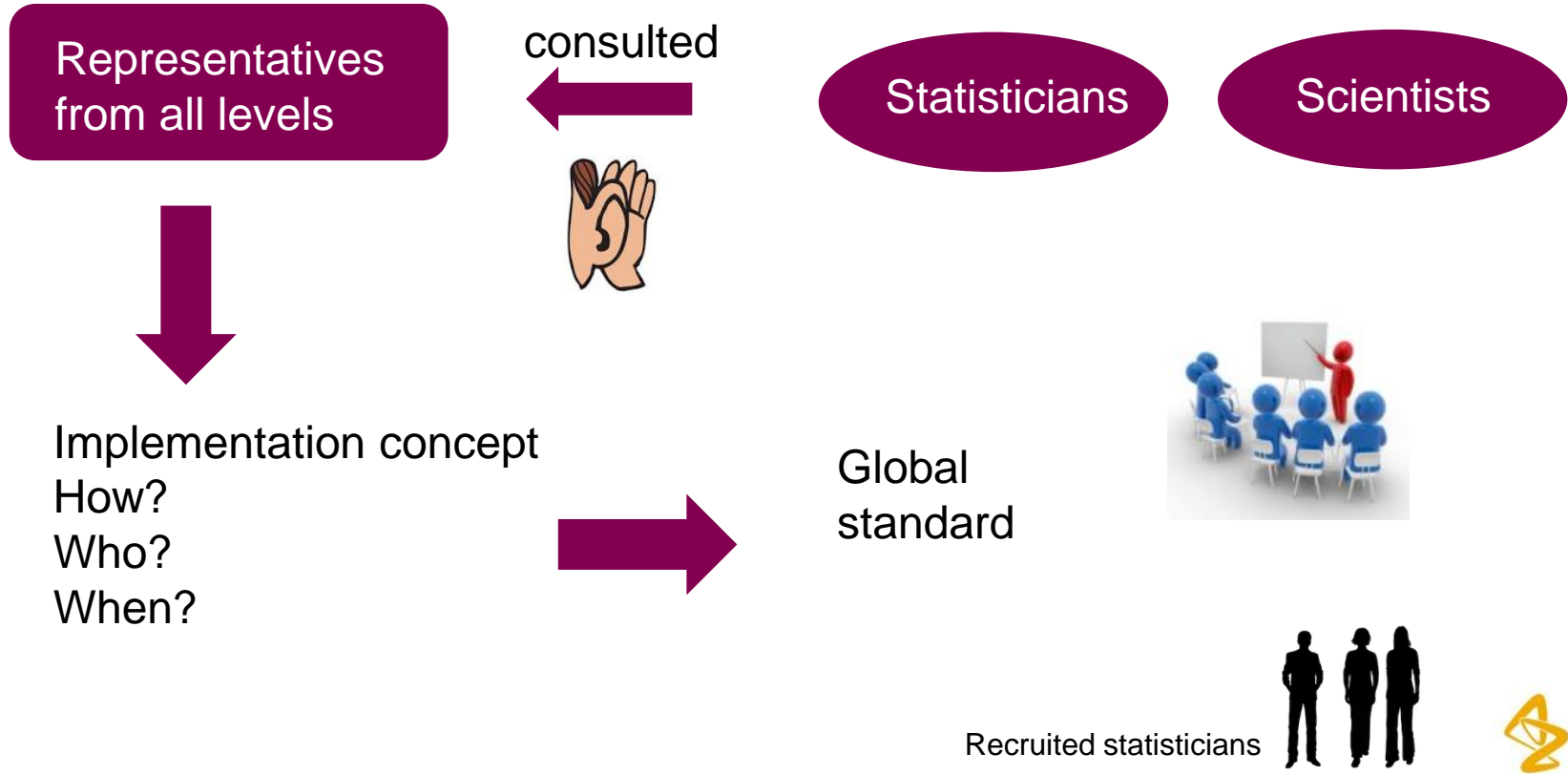
Initiating a new vision



Vision: formal review of 10 principles of all *in-vivo* studies



Coalition construct to develop implementation plan



Requirements and who's responsible?

REQUIRED

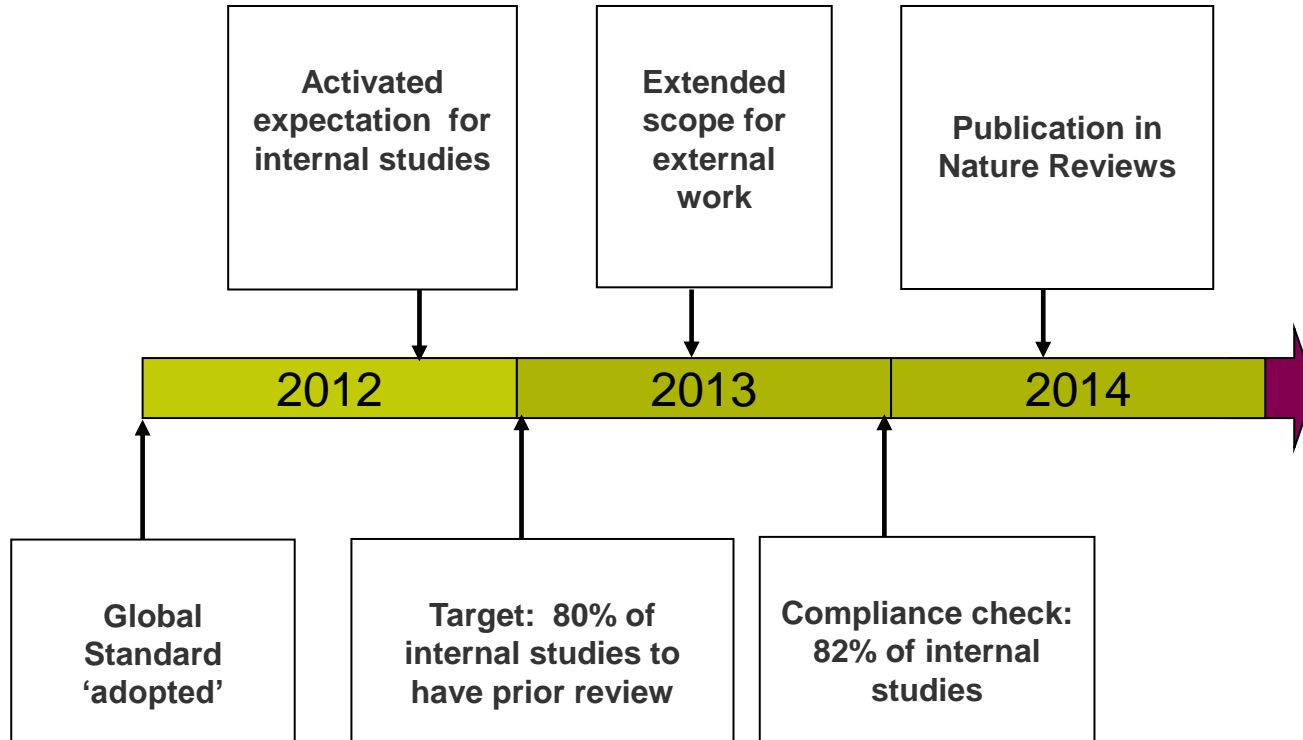
- A documented review prior to study starting
- GSP principles must also be summarised in the formal reporting
- Any deviations must be reviewed and documented



- **Responsible scientist:** applying GSP & engaging statistician
- **Scientist's line manager:** ensuring studies are planned and conducted in accordance with GSP
- **Statistician:** providing expert statistical input to animal studies



Implementation: focused expectations with short terms wins



Process had tracking used to demonstrate value added

Principle	% protocols amended (n=255)
Animal number	57%
Analysis	28%
Randomisation	20%
Experiment procedures	19%
Design	18%
Blocking	13%
Monitoring	7%
Controls	6%
Blinding	4%

50% of reviews



meaningful change in
at least one of the
principles



**MAINTAINING:
“GOOD STATISTICAL PRACTICE”**



Challenges of maintaining momentum in changing world

Scientists?



Change



Statistical support?

- Relocation
- Reorganisation
- Huge staff turn over
- Distraction
- Loss of experience and knowledge of systems

- Complete turn over statistics support team.
- 70% loss of staff
- Change in focus to Bayesian/AI



Focus: a sign of quality

Training

Monitoring

Case studies of value
added

Evolution: simplification



Conclusions

- Change isn't just about the processes but about culture.
- Successful change requires both leadership and management.
- You need senior leadership advocacy.
- Consulting is an essential component to understanding the resisting forces and where you need to focus attention.
- There are challenges in embedding changes and ensuring the change sticks.



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