PCTU

Why Clinical Trials are Like Bicycles

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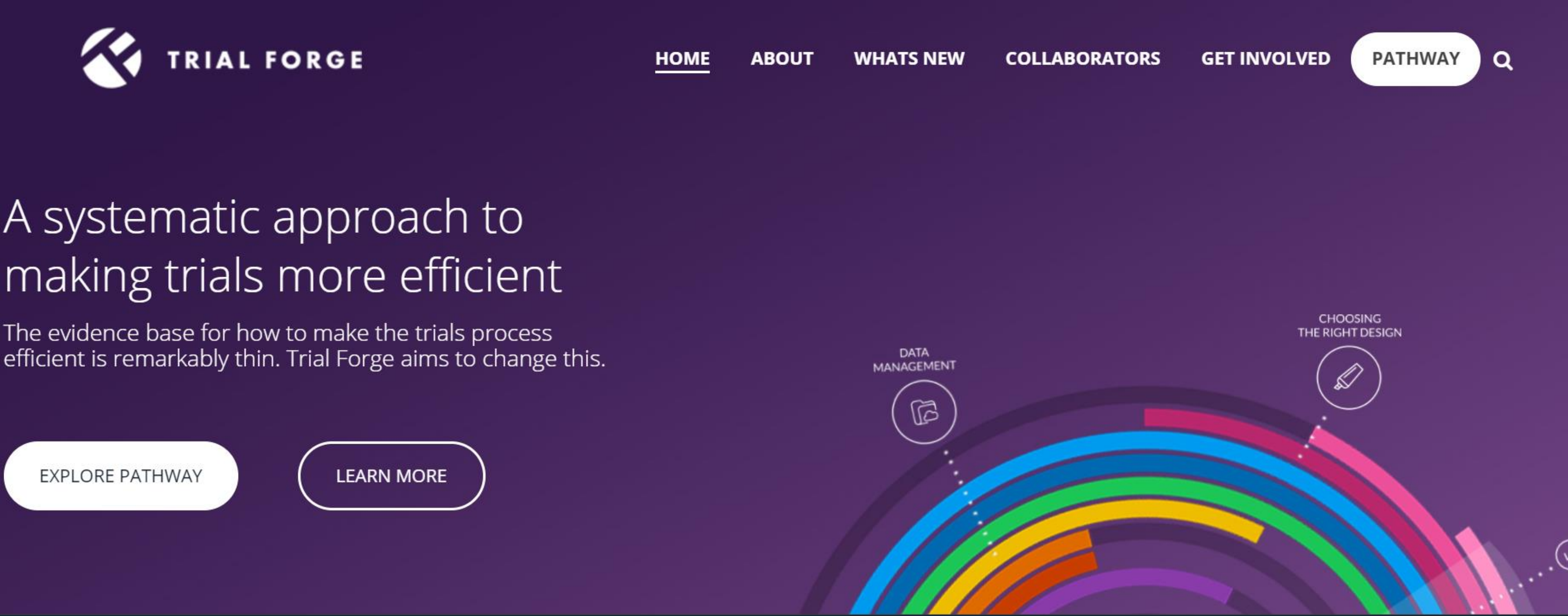
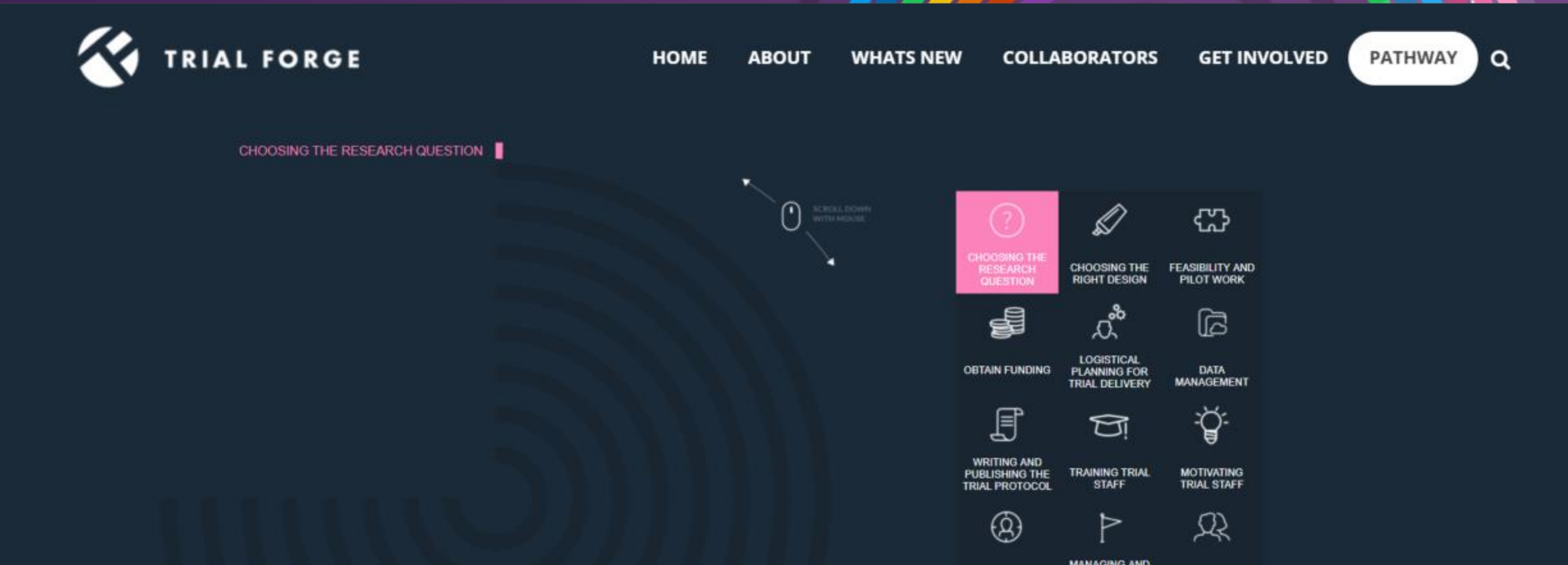


A systematic approach to making trials more efficient

The evidence base for how to make the trials process efficient is remarkably thin. Trial Forge aims to change this.



Marginal Gains

"The whole principle came from the idea that if you broke down everything you could think of that goes into riding a bike, and then improved it by 1%, you will get a significant increase when you put them all together."

Dave Brailsford, 2012

Great Britain led the cycling medal table at the 2008 and 2012 Olympic Games, winning eight golds at both, while British cyclists won 59 World Championships across different disciplines from 2003 to 2013

Treweek *et al. Trials* (2015) 16:261
DOI 10.1186/s13063-015-0776-0

TRIALS

METHODOLOGY **Open Access**

Making randomised trials more efficient: report of the first meeting to discuss the Trial Forge platform

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What if I just gave you a bicycle that went 30% or 40% faster?

What statisticians usually mean by "relative efficiency"

The inverse ratio of sample sizes required by two different trial designs to answer the same research question.

e.g.

Study design X needs 50 participants

Study design Y needs 75 participants

Relative efficiency of X compared with Y = 75/50 = 1.5

X is 50% more efficient than Y.

Randomised Controlled Trials – Year Zero

1948 The MRC streptomycin for tuberculosis trial

Austin Bradford Hill

Group Sequential Designs

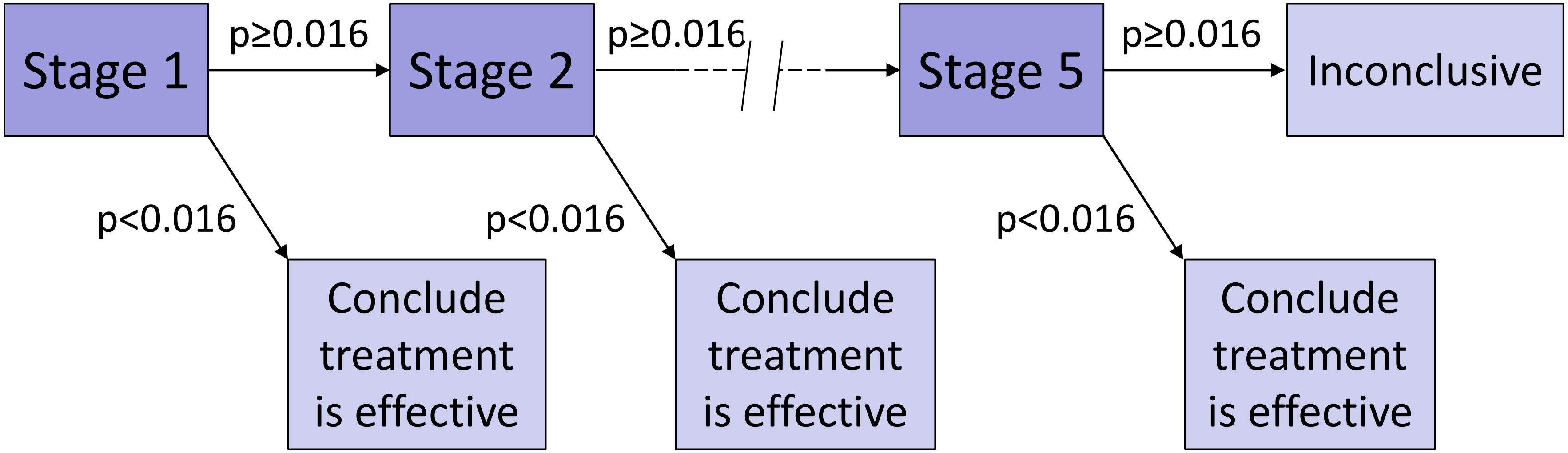
Pocock (1977) and O'Brien & Fleming (1979)

As outcome data accrue, we carry out a number of interim analyses

Group sequential methods are also the basis for **adaptive trial designs**, in which aspects of the protocol can be altered following interim analysis

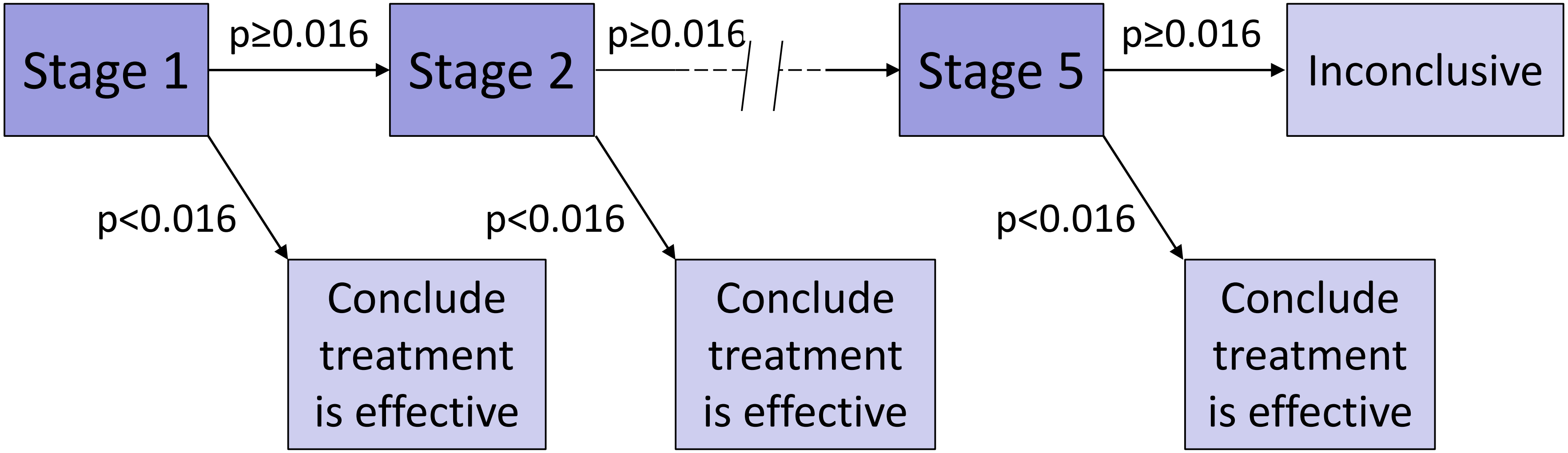
Group Sequential Designs

Pocock design with 5 stages:



Group Sequential Designs

Pocock design with 5 stages:



e.g. to detect a mean difference of 1.0 with standard deviation 2.0 in each arm, with 90% power:

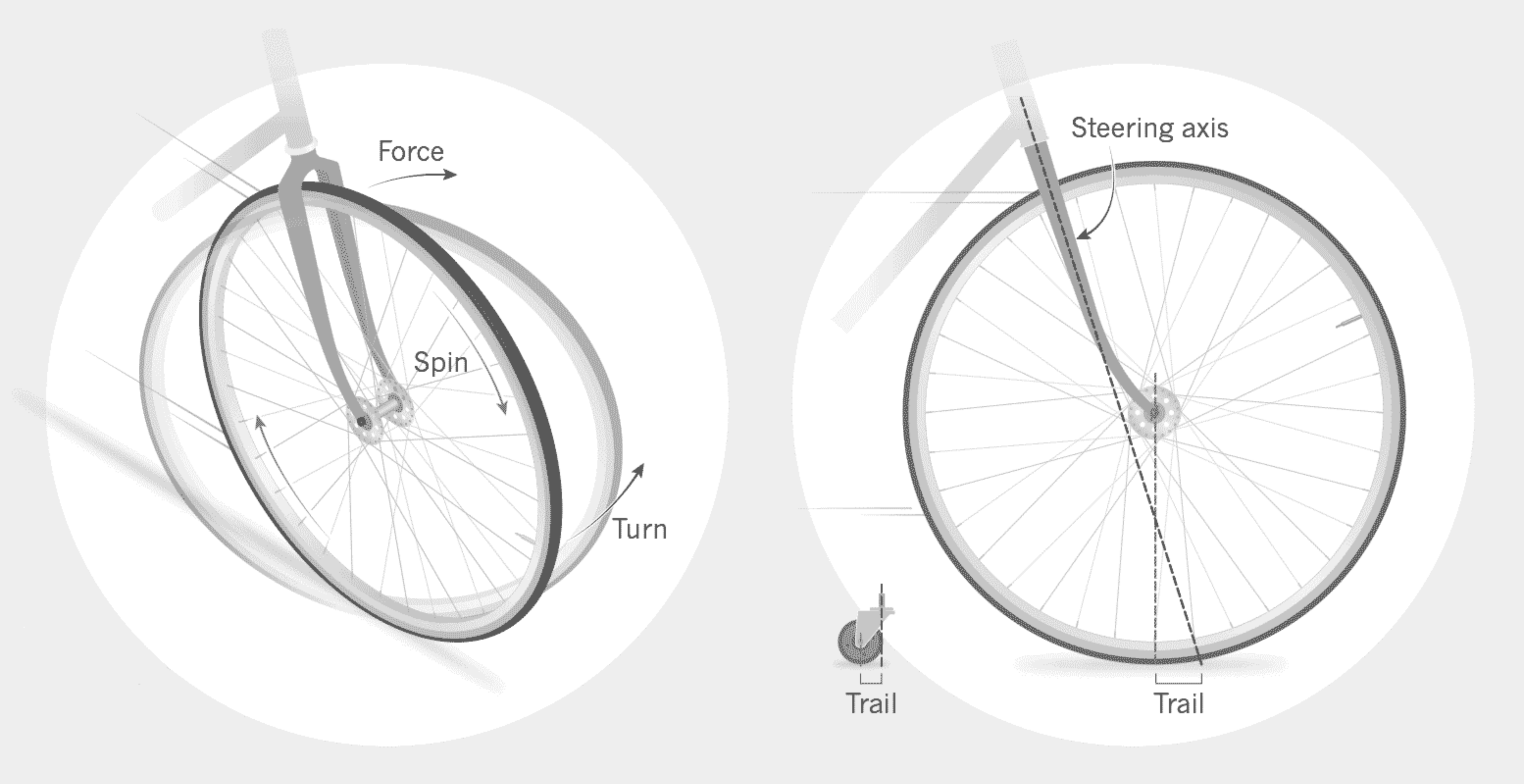
Pocock design is **45% more efficient** than a one-stage design

PHYSICS ON TWO WHEELS

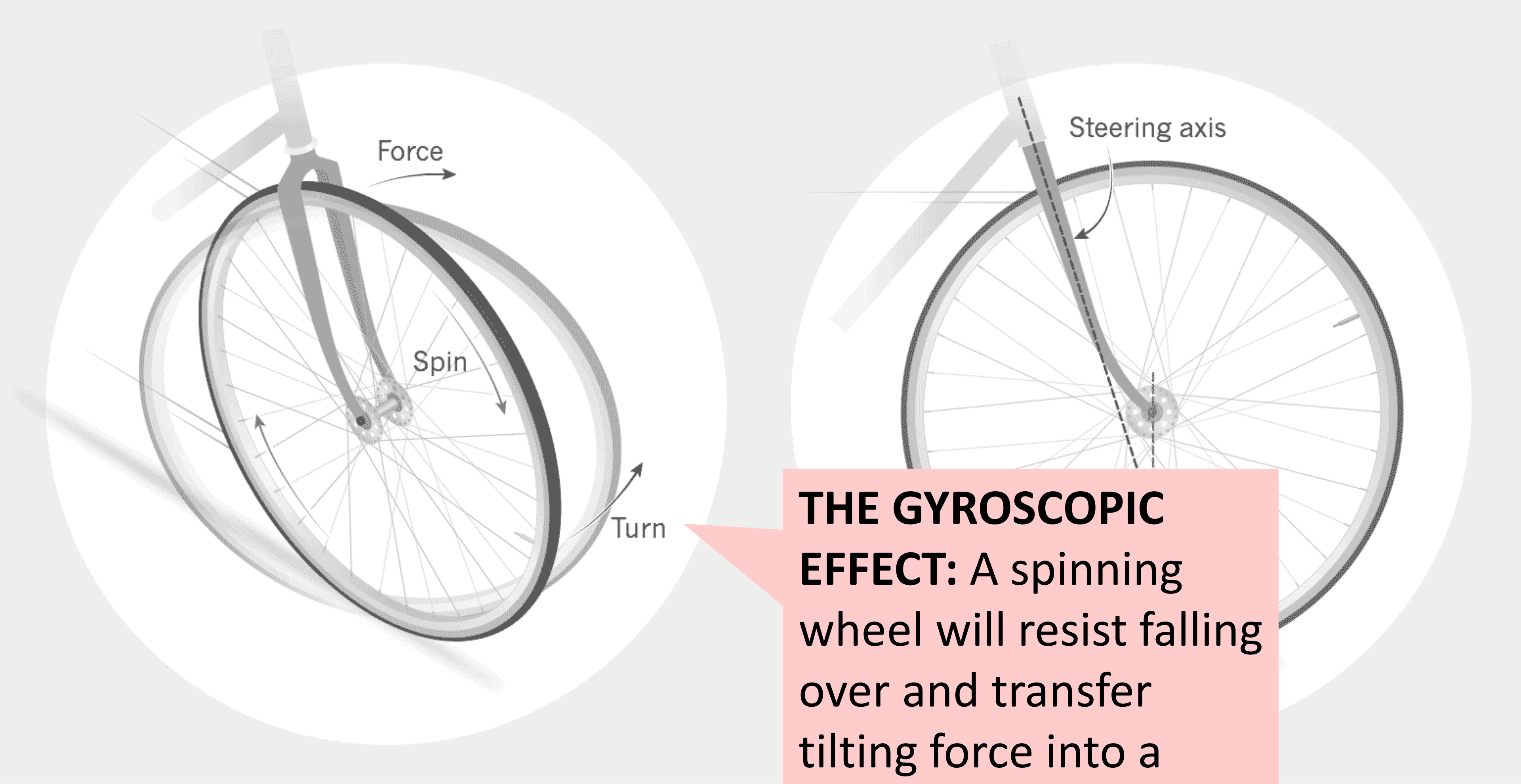
Nature 2016;535:338-341

> “Everybody knows how to ride a bike, bit no one knows how we ride bikes.”
>
> Jim Papadopoulos

WHAT KEEPS A RIDERLESS BIKE UPRIGHT?

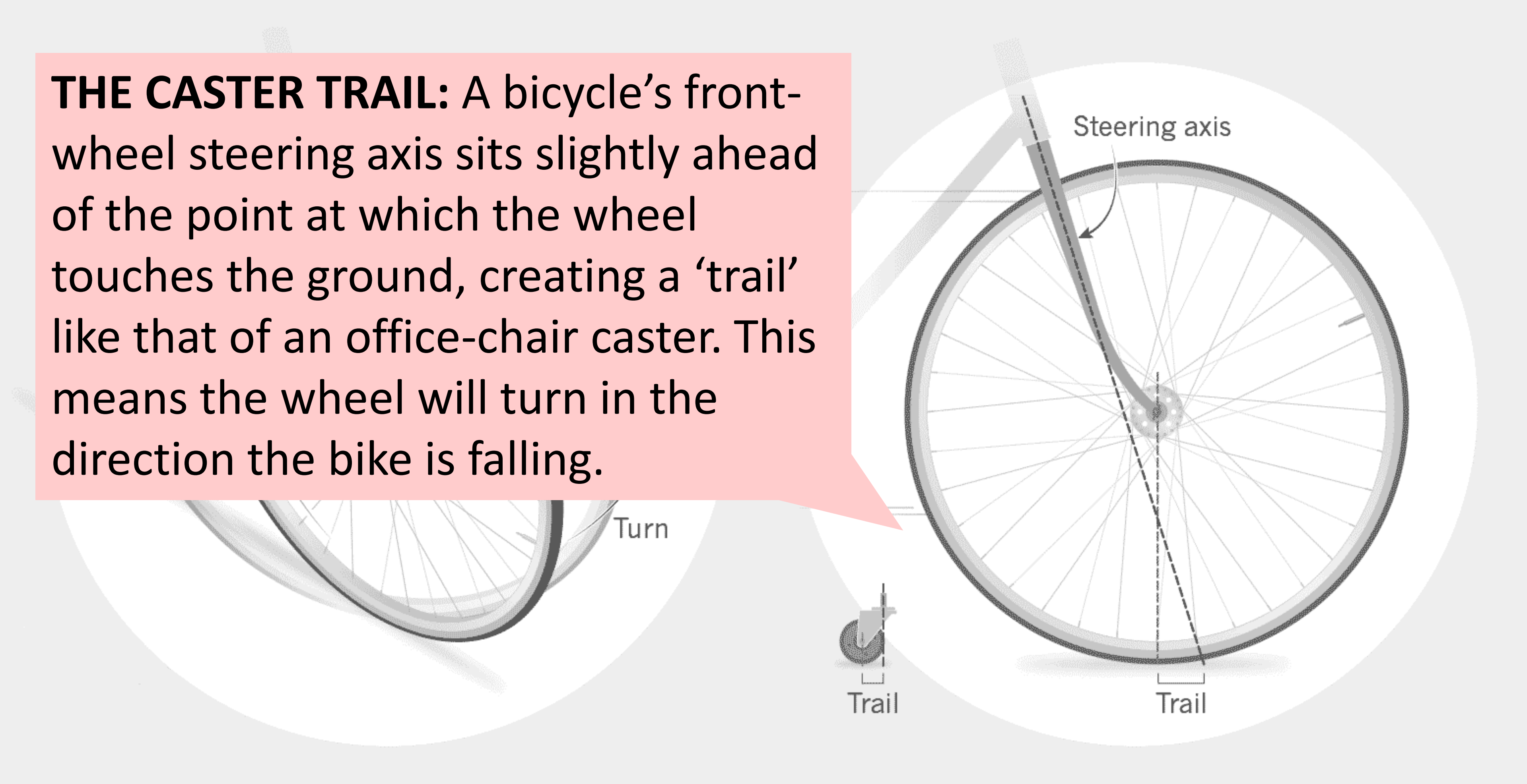


WHAT KEEPS A RIDERLESS BIKE UPRIGHT?

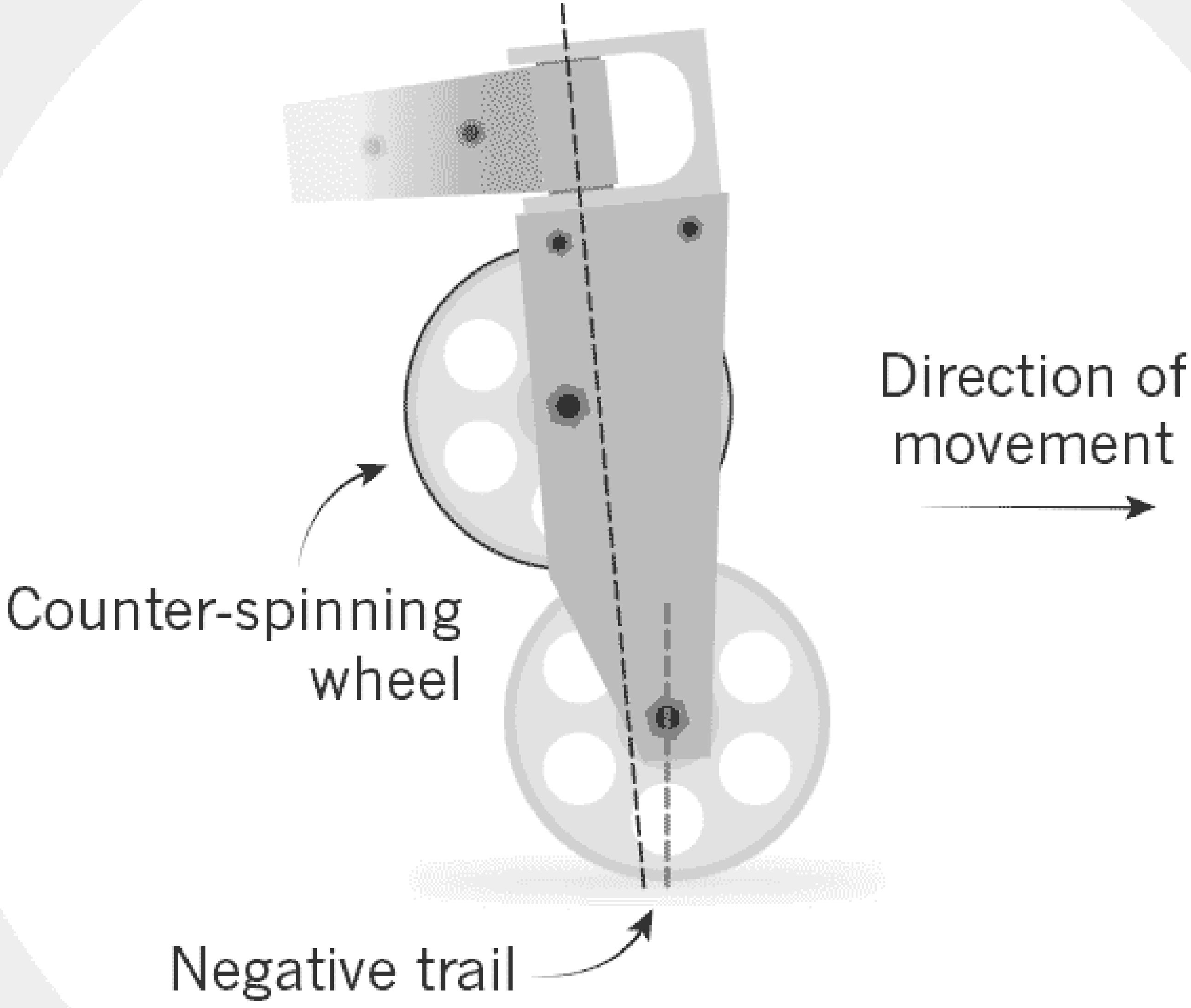


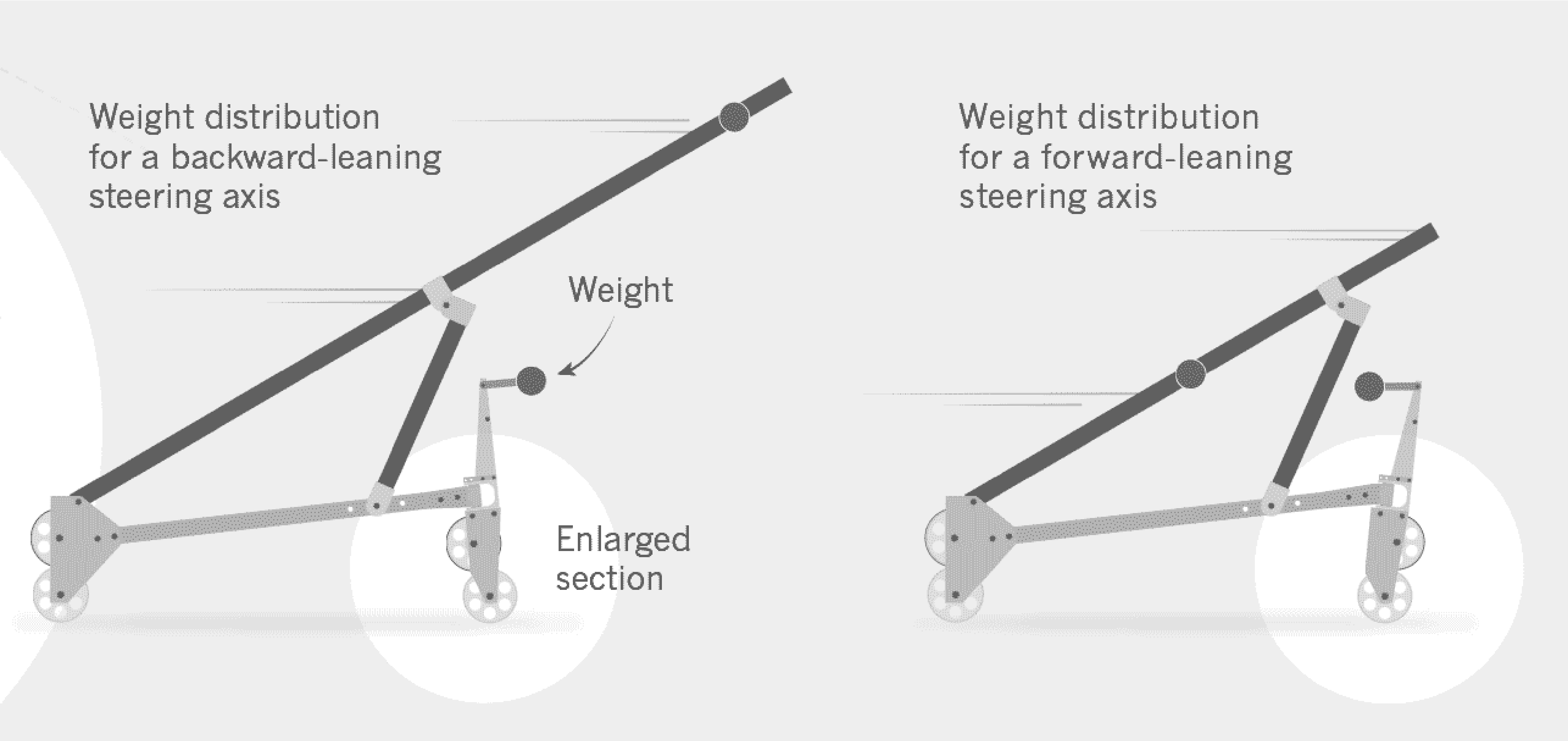
THE GYROSCOPIC EFFECT: A spinning wheel will resist falling over and transfer tilting force into a turn. This could help to right a bike.

WHAT KEEPS A RIDERLESS BIKE UPRIGHT?

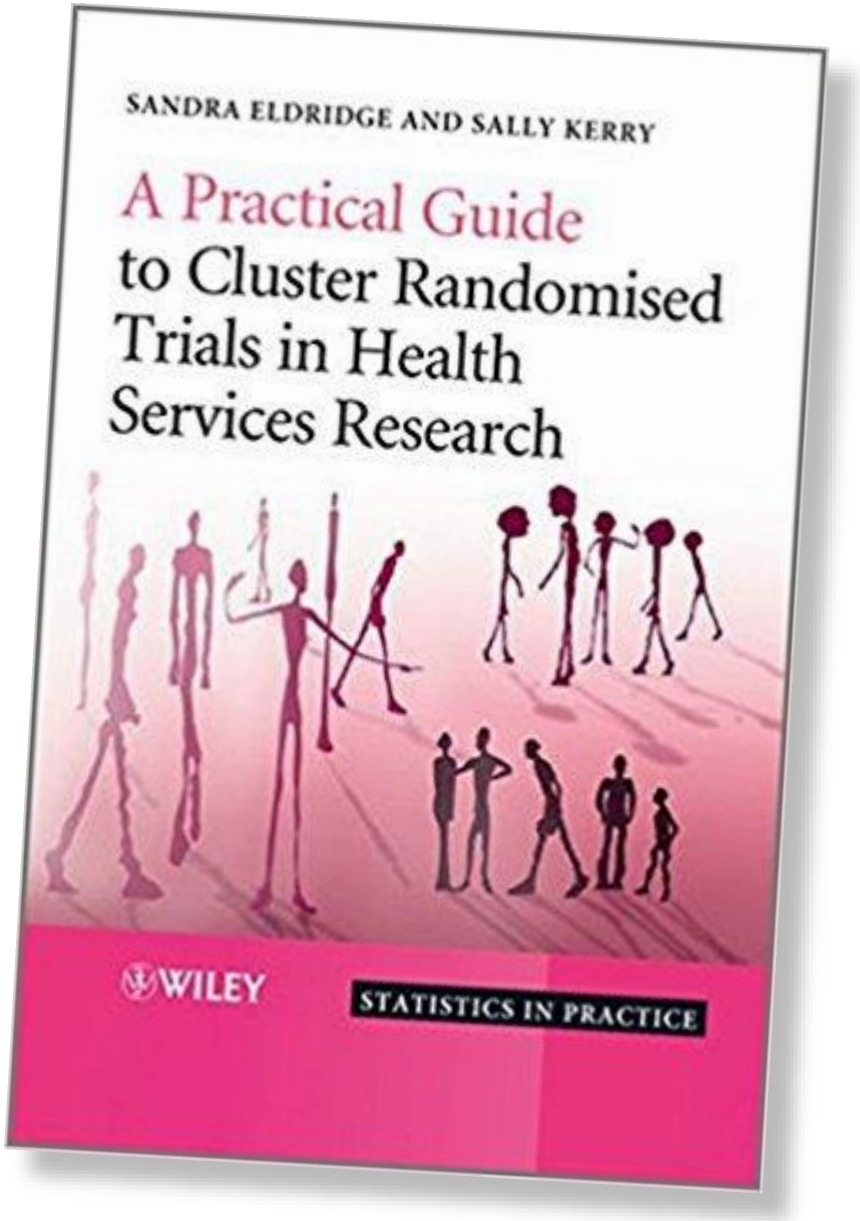


THE CASTER TRAIL: A bicycle's front-wheel steering axis sits slightly ahead of the point at which the wheel touches the ground, creating a 'trail' like that of an office-chair caster. This means the wheel will turn in the direction the bike is falling.


Direction of movement
Counter-spinning wheel
Negative trail


Weight distribution for a backward-leaning steering axis
Weight
Enlarged section
Weight distribution for a forward-leaning steering axis

Back to Trials



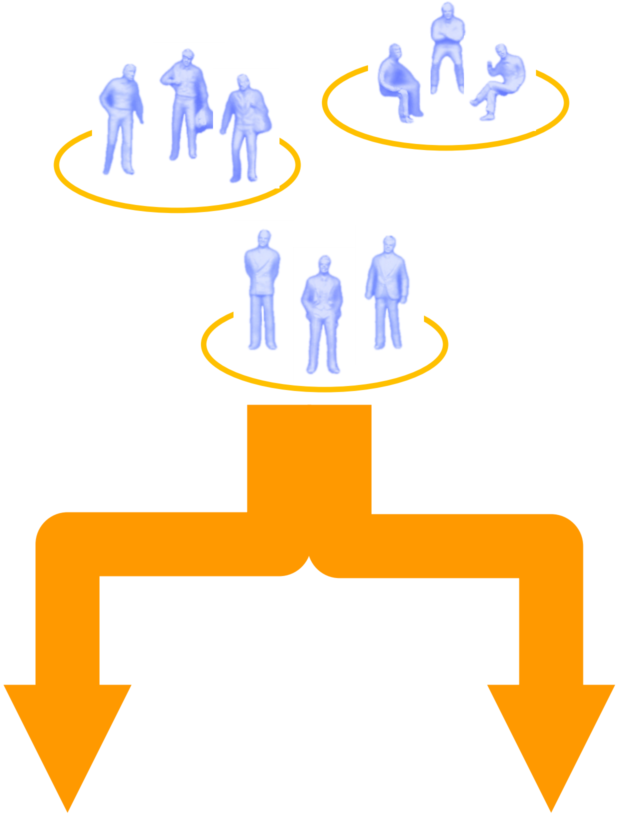
SANDRA ELDRIDGE AND SALLY KERRY

A Practical Guide to Cluster Randomised Trials in Health Services Research

WILEY

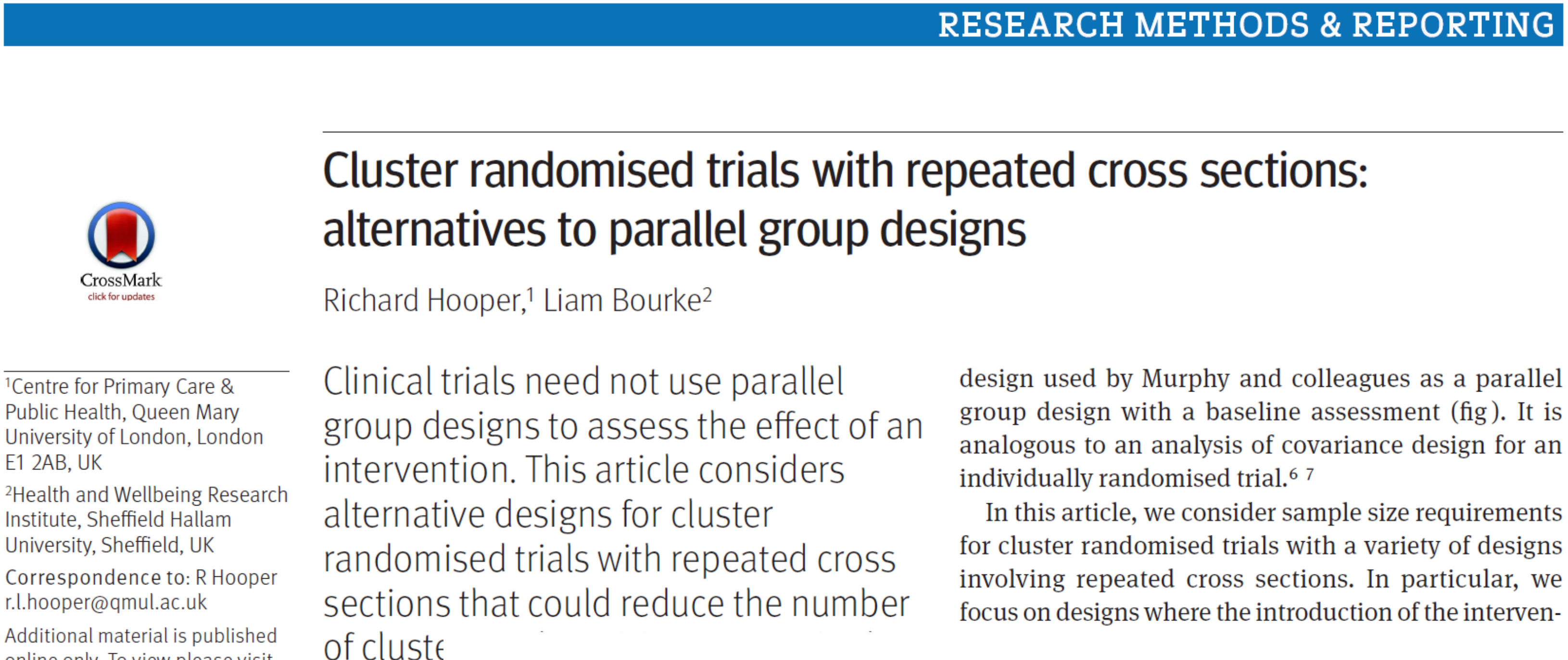
STATISTICS IN PRACTICE

Cluster Randomising



Active treatment

Control or comparator



Cluster randomised trials with repeated cross sections: alternatives to parallel group designs

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Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/bmj.h2925)

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Clinical trials need not use parallel group designs to assess the effect of an intervention. This article considers alternative designs for cluster randomised trials with repeated cross sections that could reduce the number of cluste

In 1948, the
trial establis
and for lo
recruited cc

design used by Murphy and colleagues as a parallel group design with a baseline assessment (fig). It is analogous to an analysis of covariance design for an individually randomised trial.[6 7]

In this article, we consider sample size requirements for cluster randomised trials with a variety of designs involving repeated cross sections. In particular, we focus on designs where the introduction of the interven-

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Int. J. Epidemiol. Advance Access published January 22, 2014

International Journal of Epidemiology, 2014, 1–7
doi: 10.1093/ije/dyt281
Original article

Original article

The dog-leg: an alternative to a cross-over design for pragmatic clinical trials in relatively stable populations

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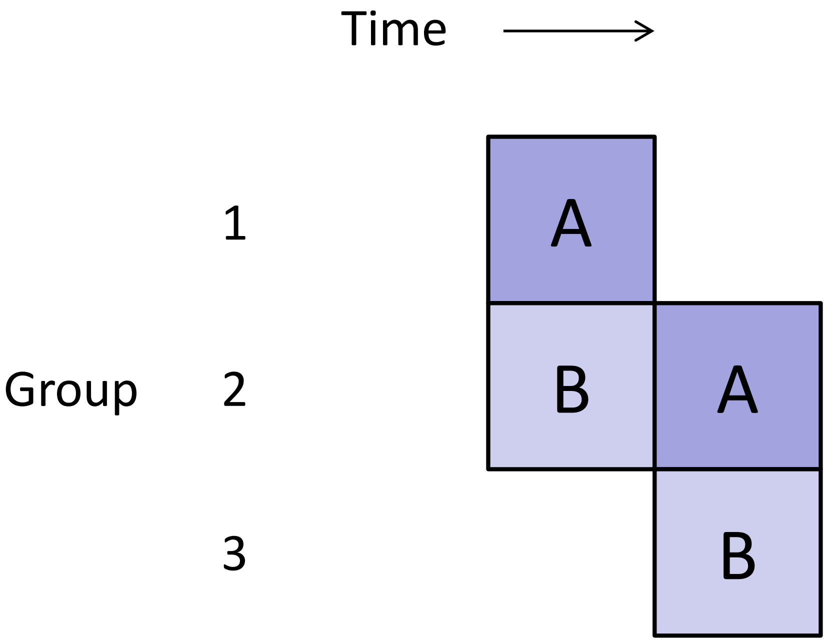
Cluster Randomised Dog-Leg Design

Schedule of assessments (B = before intervention, A = after):

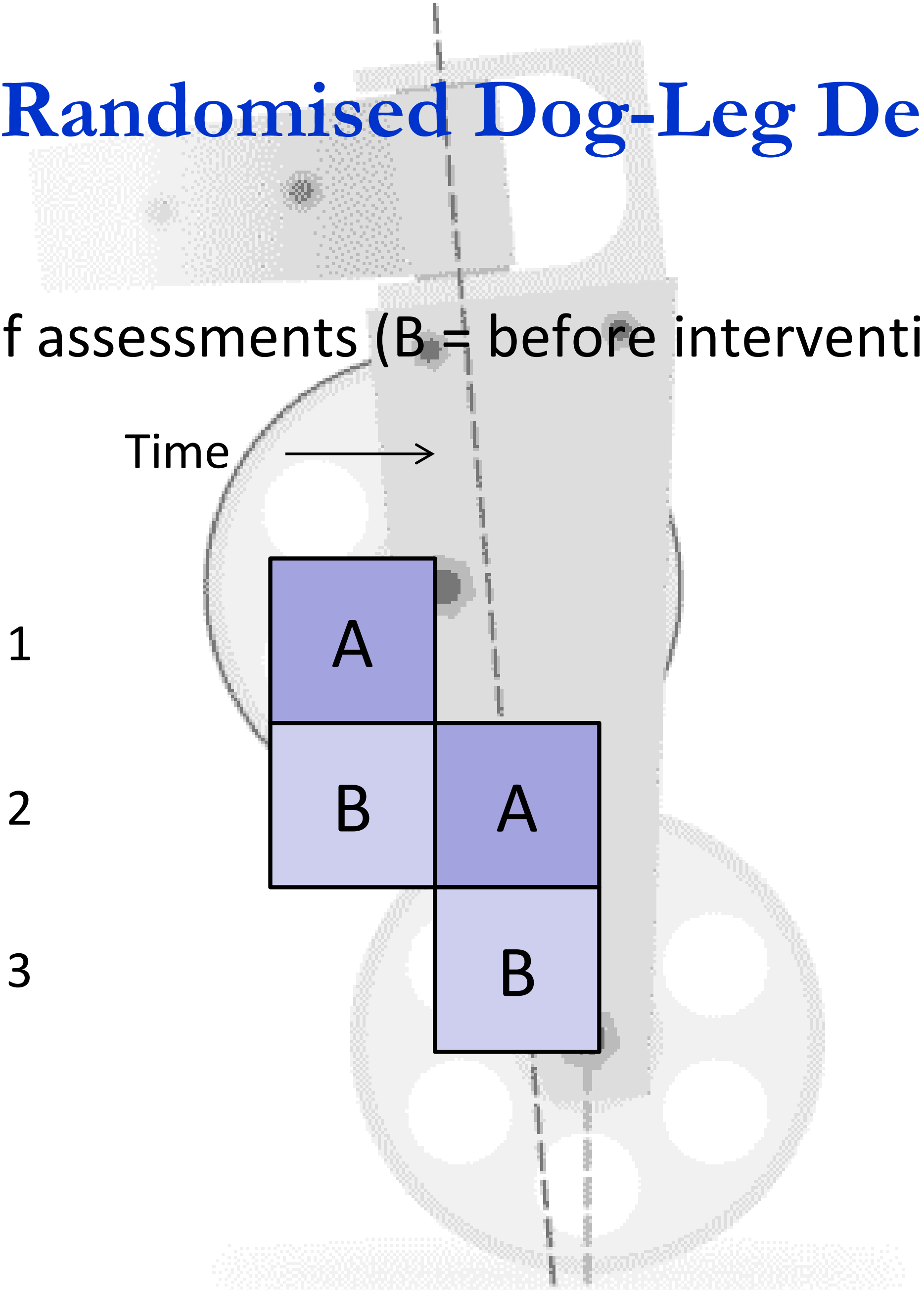


Time →

	1	A	
Group	2	B	A
	3		B

Cluster Randomised Dog-Leg Design

Schedule of assessments (B = before intervention, A = after):



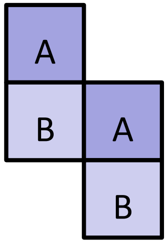
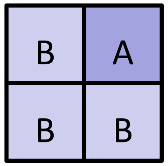
Time →

	1	A	
Group	2	B	A
	3		B

Cluster Randomised Dog-Leg Design

Example from *BMJ* paper:

Evaluating a free breakfast programme in schools

Required sample size*:	Schools	Pupils
	**63**	**4,200**
	**88**	**8,800**

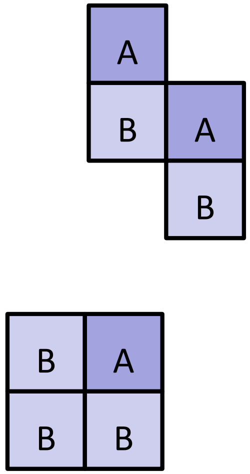
* To achieve 80% power at the 5% significance level to detect a mean difference equal to 0.11 standard deviations, assuming cluster size 50, intracluster correlation 0.02, and cluster autocorrelation 0.8.

Cluster Randomised Dog-Leg Design

Example from *BMJ* paper:

Evaluating a free breakfast programme in schools

Required sample size*: Schools Pupils



Schools: **40% more efficient**

Pupils: **110% more efficient**

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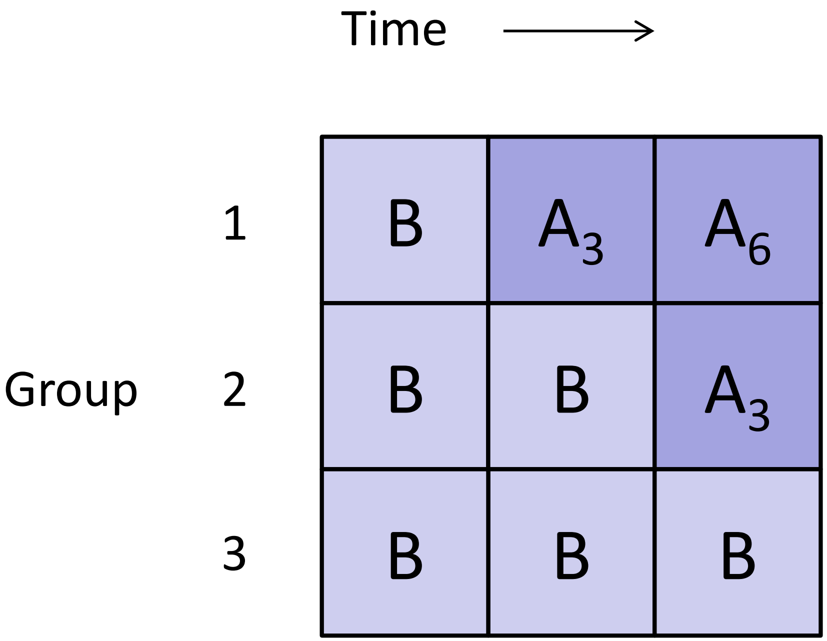
* To achieve 80% power at the 5% significance level to detect a mean difference equal to 0.11 standard deviations, assuming cluster size 50, intracluster correlation 0.02, and cluster autocorrelation 0.8.

An individually randomised trial with staggered introduction of the intervention

Schedule of assessments:

(B = before, A_3 = 3 months after, A_6 = 6 months after)



Time →

	1	B	A_3	A_6
Group	2	B	B	A_3
	3	B	B	B

An individually randomised trial with staggered introduction of the intervention

Schedule of assessments:
(B = before, A_3 = 3 months after, A_6 = 6 months after)

Time →

	1	B	A_3	A_6
Group	2	B	B	A_3
	3	B	B	B

For estimating 3-month effect, **56%–77% more efficient** than

B	A_3	A_6
B	B	B

- Re-design

- Re-design
- Be creative

- Re-design
- Be creative
- Break the rules

- Re-design
- Be creative
- Break the rules
- Take giant leaps

- Re-design
- Be creative
- Break the rules
- Take giant leaps

Keep building better bicycles

Thank you