

In cluster randomised trials with binary outcomes, plausible values of

- (i) the intra-cluster correlation coefficient (ICC)
- & (ii) the standard deviation (SD) of true cluster prevalences

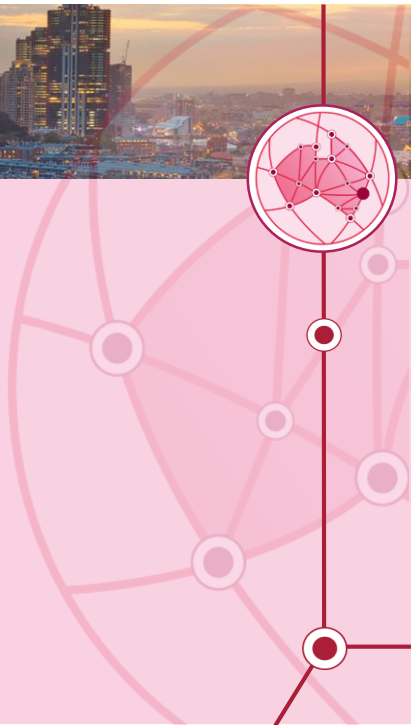
are bounded by the overall prevalence, its complement, and  $1/3$

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## Disclosure

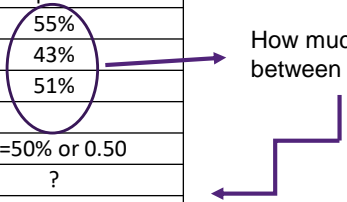
**The presenter has advised that the following presentation is subject to no conflicts of interest and has nothing to disclose.**



## Setting 1

	True prevalence of primary outcome, "cluster prevalence"
Cluster 1 (Control)	55%
Cluster 2 (Control)	43%
Cluster 3 (Control)	51%
...etc	
Overall or Mean	$\mu = 50\%$ or 0.50
SD	?
ICC	?

How much variation between these??



### Example.

Clusters: primary care clinics in Ibadan, Nigeria

Patients: moderate to severe depression (scoring  $\geq 11$  on PHQ-9)

Primary Outcome: remission of depression at 12 months (score  $\leq 6$  on the PHQ-9)

[Lancet Glob Health 2019; 7: e951-e960]

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## Background

In sample size / power calculations of cluster randomised trials with a binary primary outcome, the anticipated amount of between-cluster variation in the prevalence of the outcome

(i.e. variation between "cluster prevalences")

is often specified by the intra-cluster correlation coefficient (**ICC**)

### Problem?

- ICC is **not** an **intuitive** measure
- ICCs are often estimated with **little precision**
- ICCs are sometimes confused with an "**alternative definition**" which gives higher numbers (Stata users beware! Mixed effects logistic regression, followed by -estat icc- will give you the latter!)

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## Aims

To help trialists, at trial design,

1. better appreciate the amount of between-cluster variation anticipated
2. appreciate how much variation is plausible

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## Methods

1. Created graphs showing the distribution\* of cluster prevalences (for various amounts of between-cluster variation), when the overall prevalence is:

50% (setting 1)

14% (setting 2)

1% (setting 3)

**\*beta distribution** assumed – fully specified given (i) overall prevalence & (ii) SD or ICC

2. Consider maximum plausible\* amount of variation to be described by the

### **maximum entropy distribution**

i.e. the *least informative* distribution among all continuous distributions that are supported in the interval [0%, 100%] with (i) a specified overall prevalence

-> it turns out to be like the exponential distribution [source: stackexchange]

\*Yes, considerations of plausibility are necessarily tentative, subjective and subject-specific

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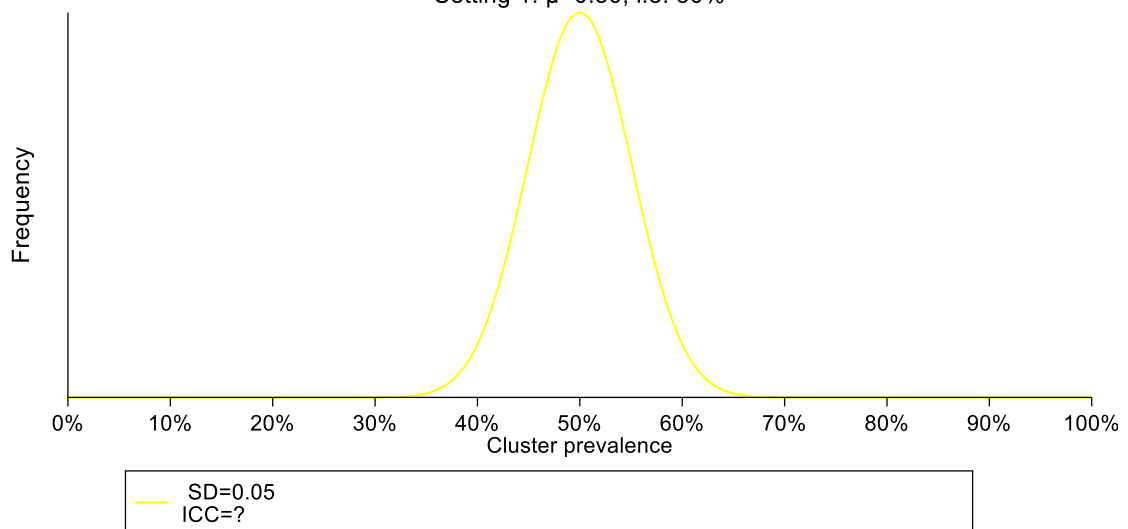
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## Distribution of cluster prevalences

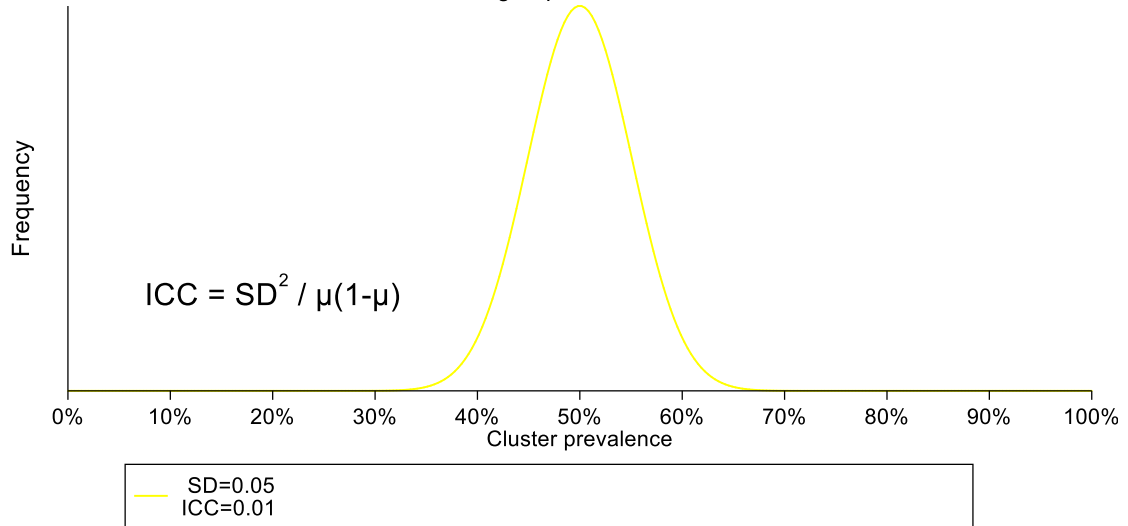
Setting 1:  $\mu = 0.50$ , i.e. 50%



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### Distribution of cluster prevalences

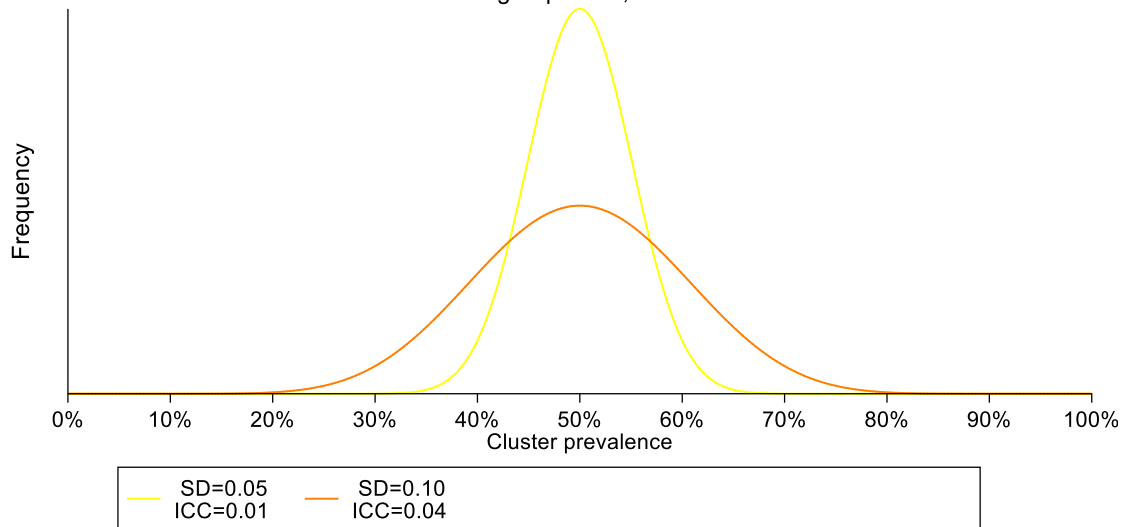
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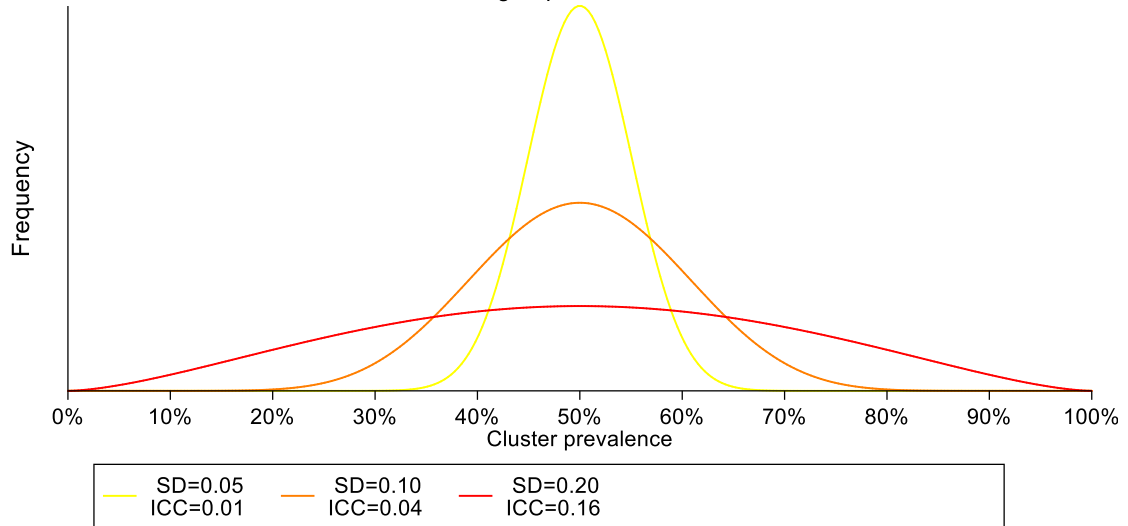
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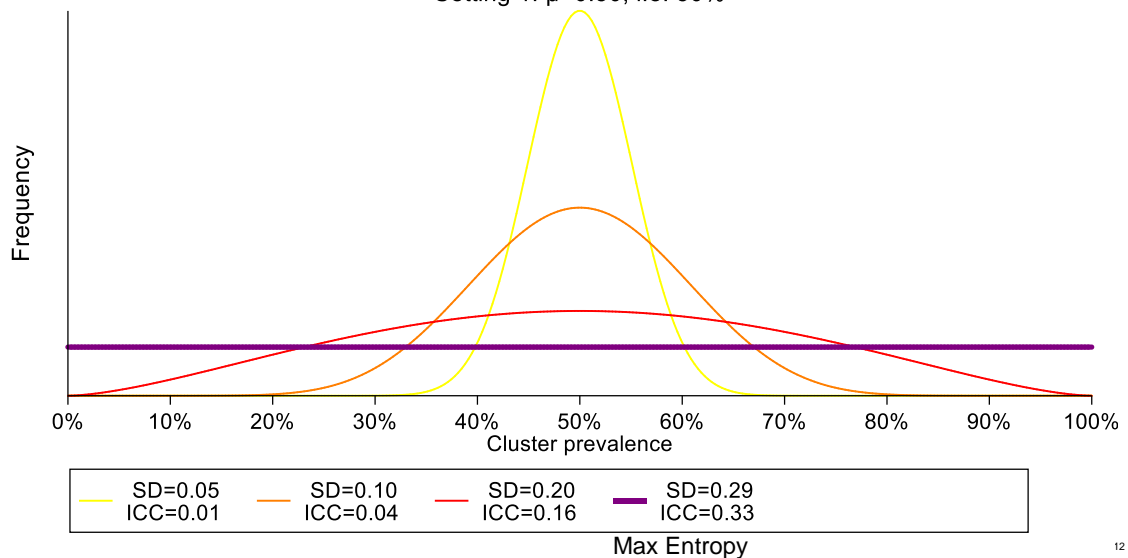
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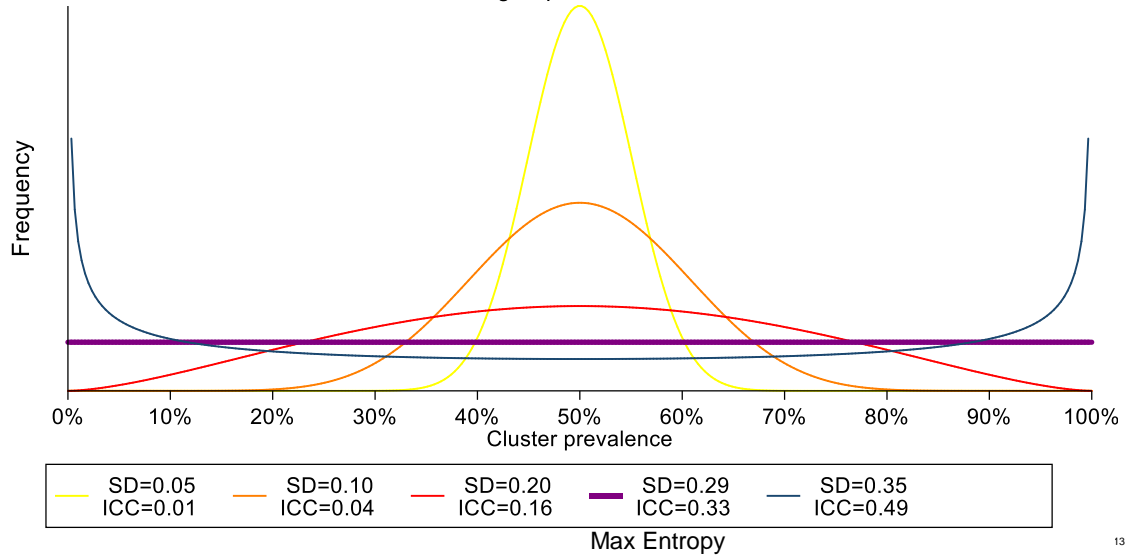
Setting 1:  $\mu=0.50$ , i.e. 50%



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## Distribution of cluster prevalences

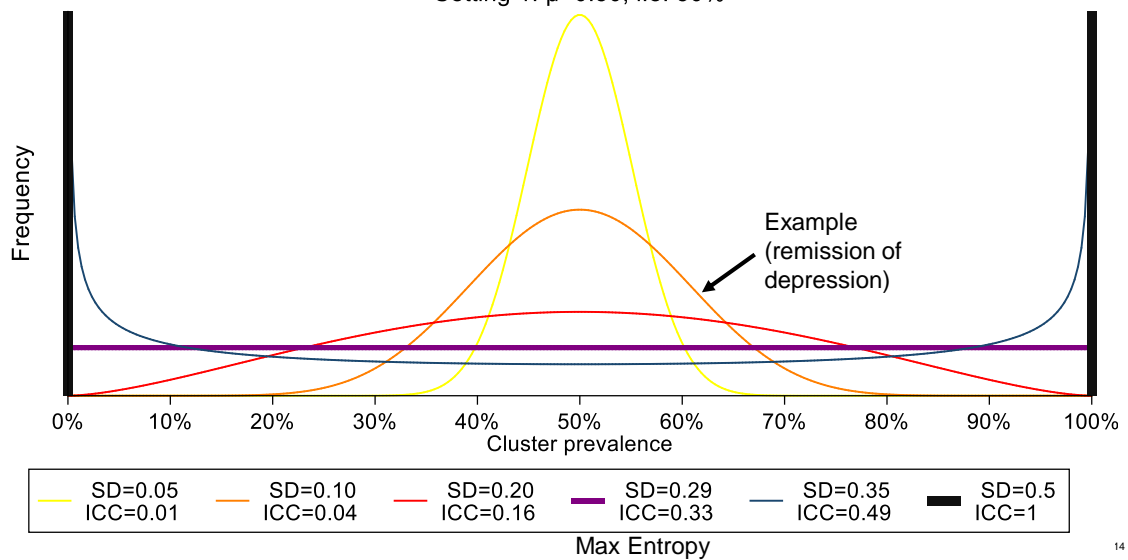
Setting 1:  $\mu=0.50$ , i.e. 50%



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## Distribution of cluster prevalences

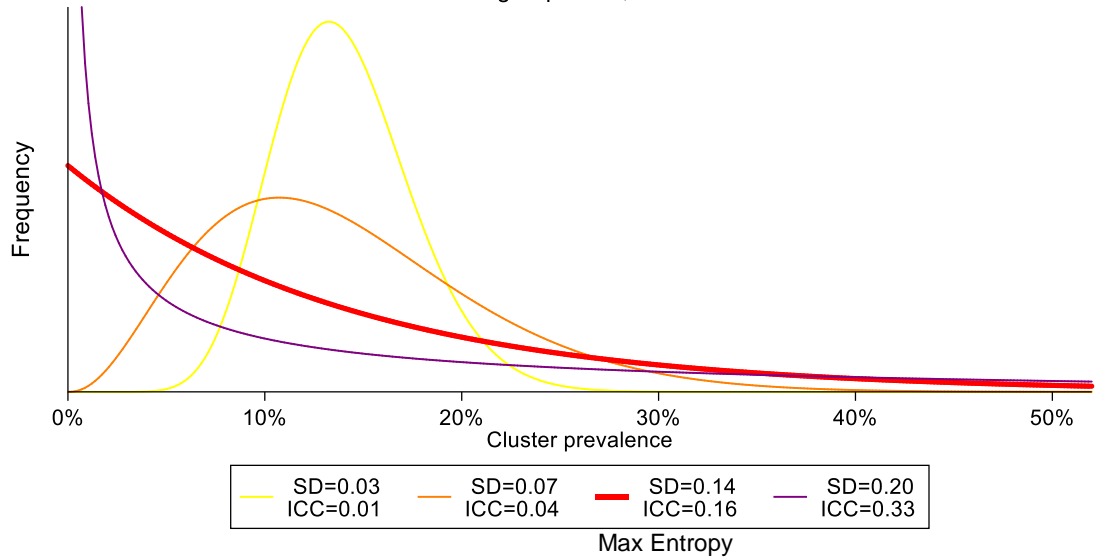
Setting 1:  $\mu=0.50$ , i.e. 50%



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### Distribution of cluster prevalences

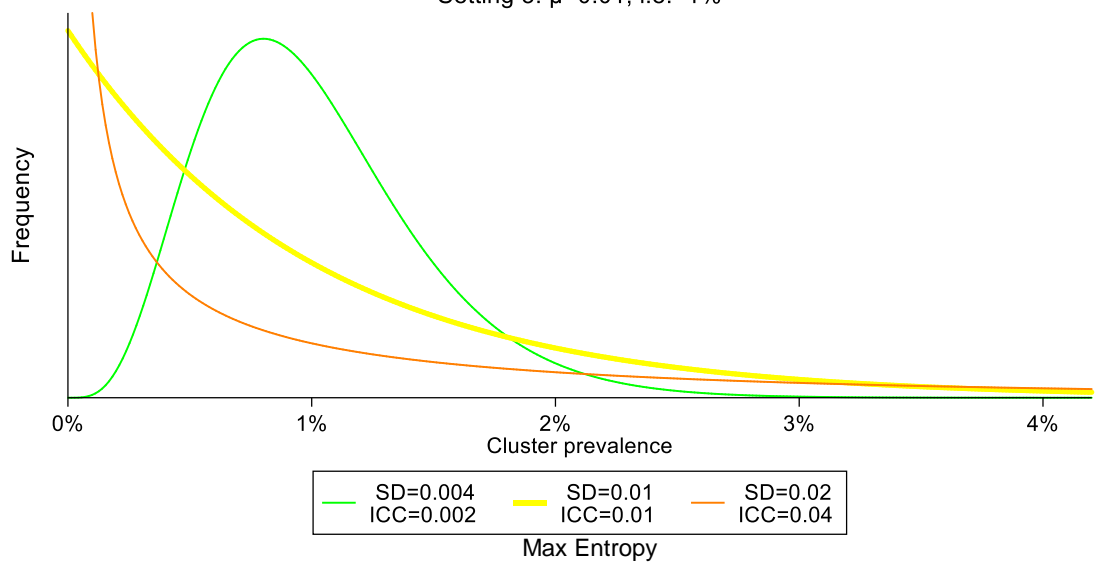
Setting 2:  $\mu=0.14$ , i.e. 14%



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### Distribution of cluster prevalences

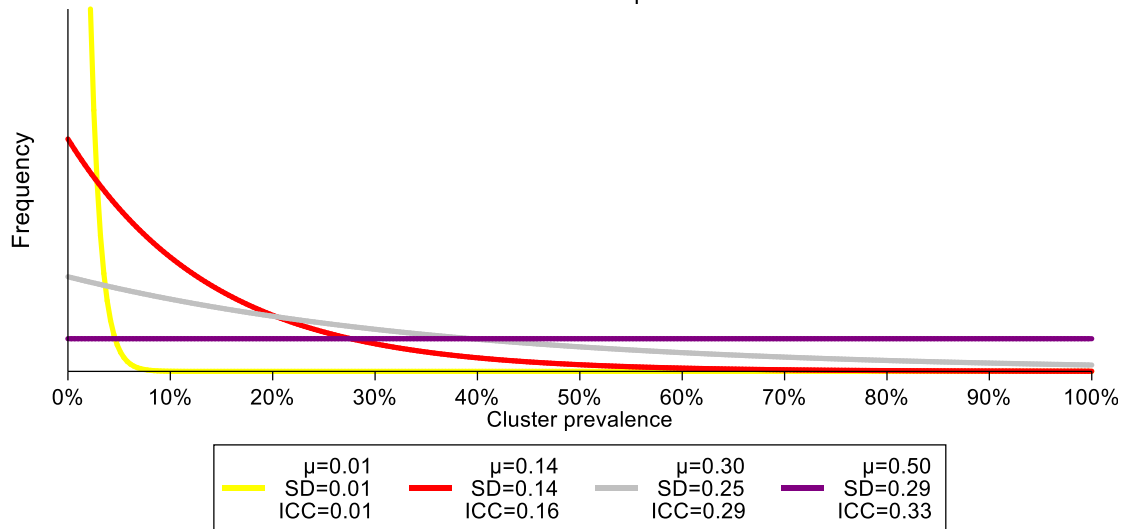
Setting 3:  $\mu=0.01$ , i.e. 1%



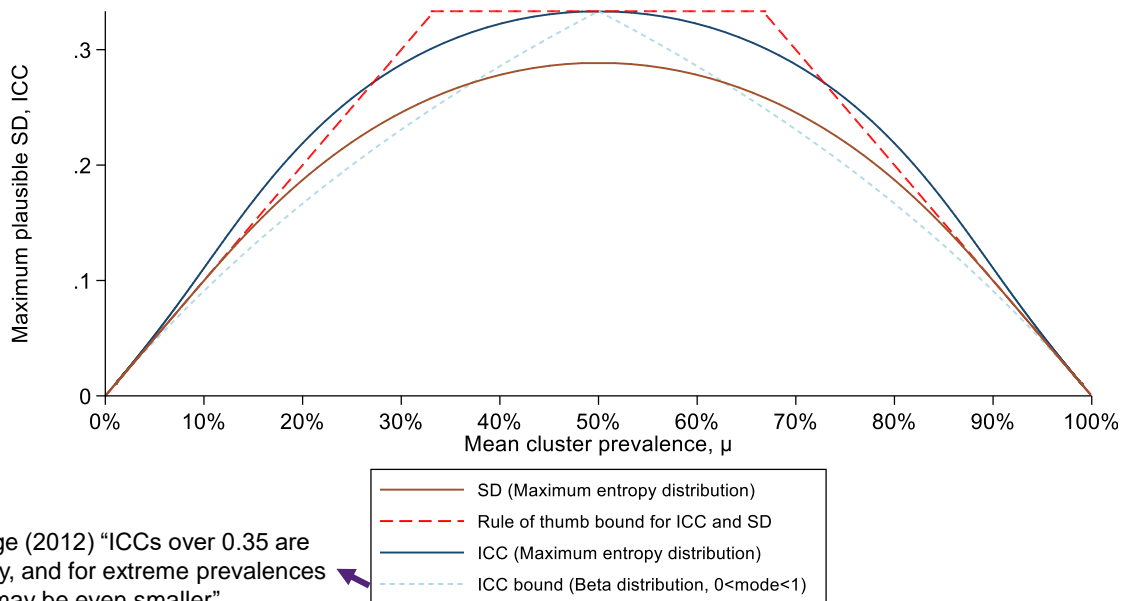
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## Maximum entropy distribution for various $\mu$



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Eldridge (2012) "ICCs over 0.35 are unlikely, and for extreme prevalences ICCs may be even smaller"

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## Typical ICCs seen are less than our proposed bounds

Gulliford et al. quantified the relationship between overall prevalence and the observed ICC.

Two databases mined:

- [General Practice Research Database \(GPRD\)](#)
- [Health Technology Assessment \(HTA\)](#) - outcomes in community and health services settings from a review

	Overall prevalence, $\mu$		
	1%	14%	50%
Maximum plausible ICC (maximum entropy distribution)	0.01	0.14	0.33
Median ICC - GPRD	0.008	0.032	0.075
Median ICC - HTA	0.002	0.013	0.046

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## Aims revisited

To help trialists, at trial design,

1. better appreciate the anticipated amount of between-cluster variation (in the prevalence of the primary outcome)

ICC -> graph (beta) distribution of cluster prevalences, and/or

ICC -> calculate SD

NB Much variation in true cluster prevalences was seen for ICCs as low as 0.04 (especially when the overall prevalence nears 0% or 100%)

2. appreciate how much variation is plausible

rule of thumb: **plausible** ICCs and SDs of true cluster prevalences are **bounded by ...**

Perhaps safer to say: ICCs and SDs are **rarely higher than ...**

...the overall prevalence, its complement (100% - overall prevalence), and 1/3

**Check your reasoning if you are proposing higher ICCs!**

Variation will often be much lower than these bounds!

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AUSTRALIA

CREATE CHANGE

# Thank you

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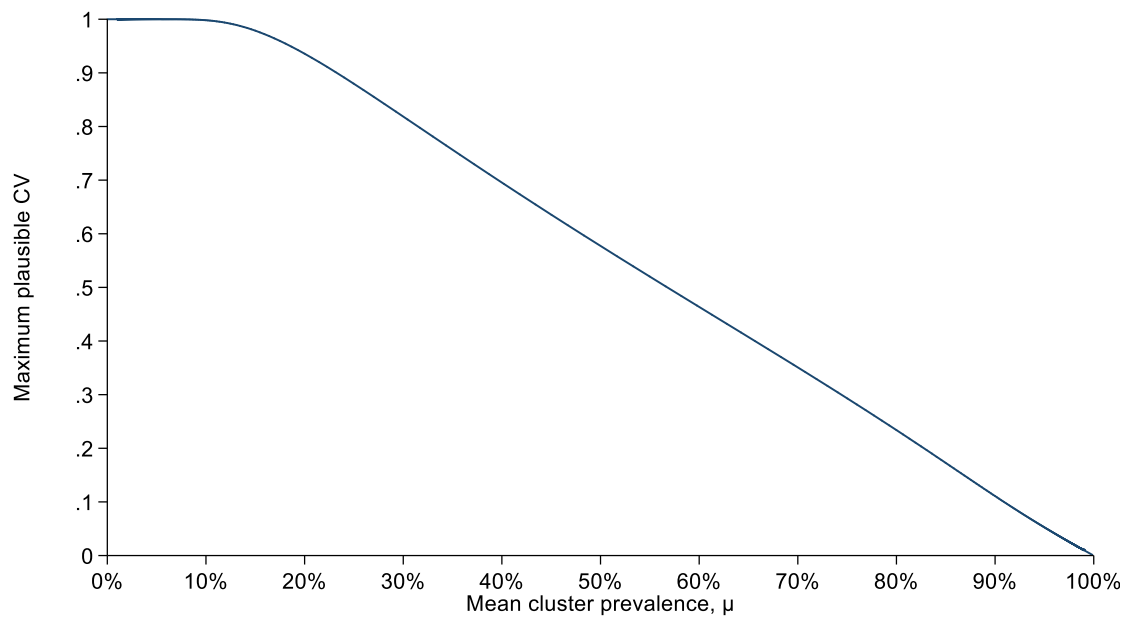
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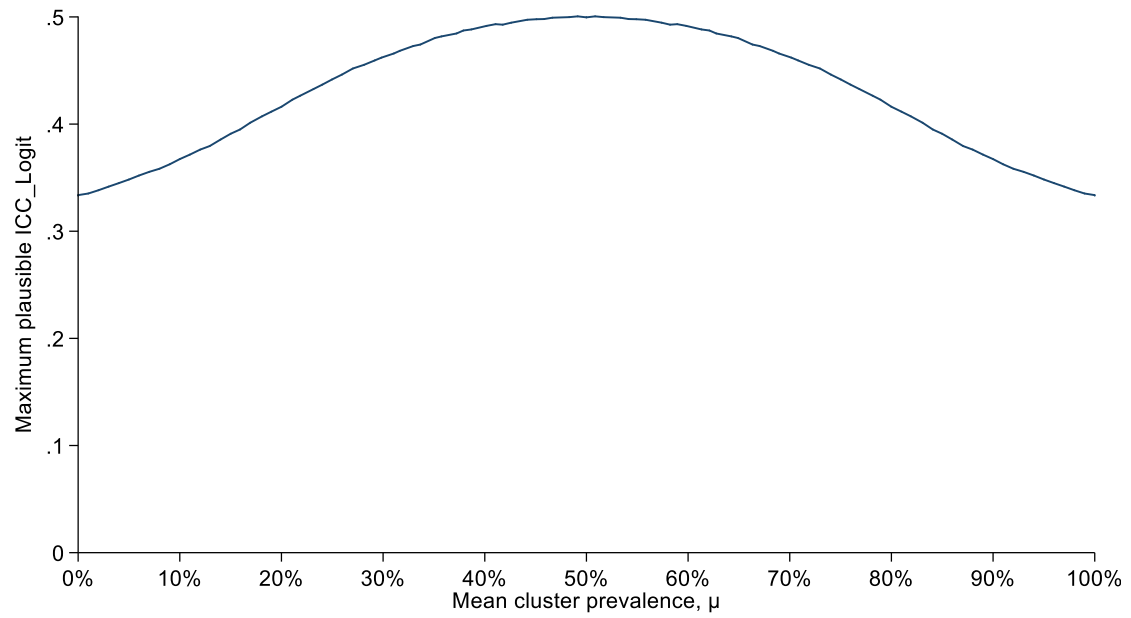
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