



International Seminar on Integrated
WATER-Related
Disease Control

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Sørhellinga Building
Norwegian University of Life Sciences, Ås



Cluster-Randomized Trials for Integrated Water-Related Disease Control

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Overview

- Rationale for cluster randomization and applicability to Integrated Water-Related Disease Control (IWRDC)
- Review of development of cluster-randomized trials (CRTs)
- Summary of analysis methods
- Review of published water-related CRTs

Why randomize by cluster?

- The intervention may, by definition, not apply at the individual level.
 - e.g. services delivered by clinics
- The intervention it is difficult or impossible to deliver at the individual level.
 - e.g. educational information
- Some interventions may affect people other than those receiving them.
 - e.g. educational interventions, or those targeting infectious diseases
- Now a couple of examples...



TB/HIV at the
clinic: 257,698



Enhanced Case
Finding: 148,090

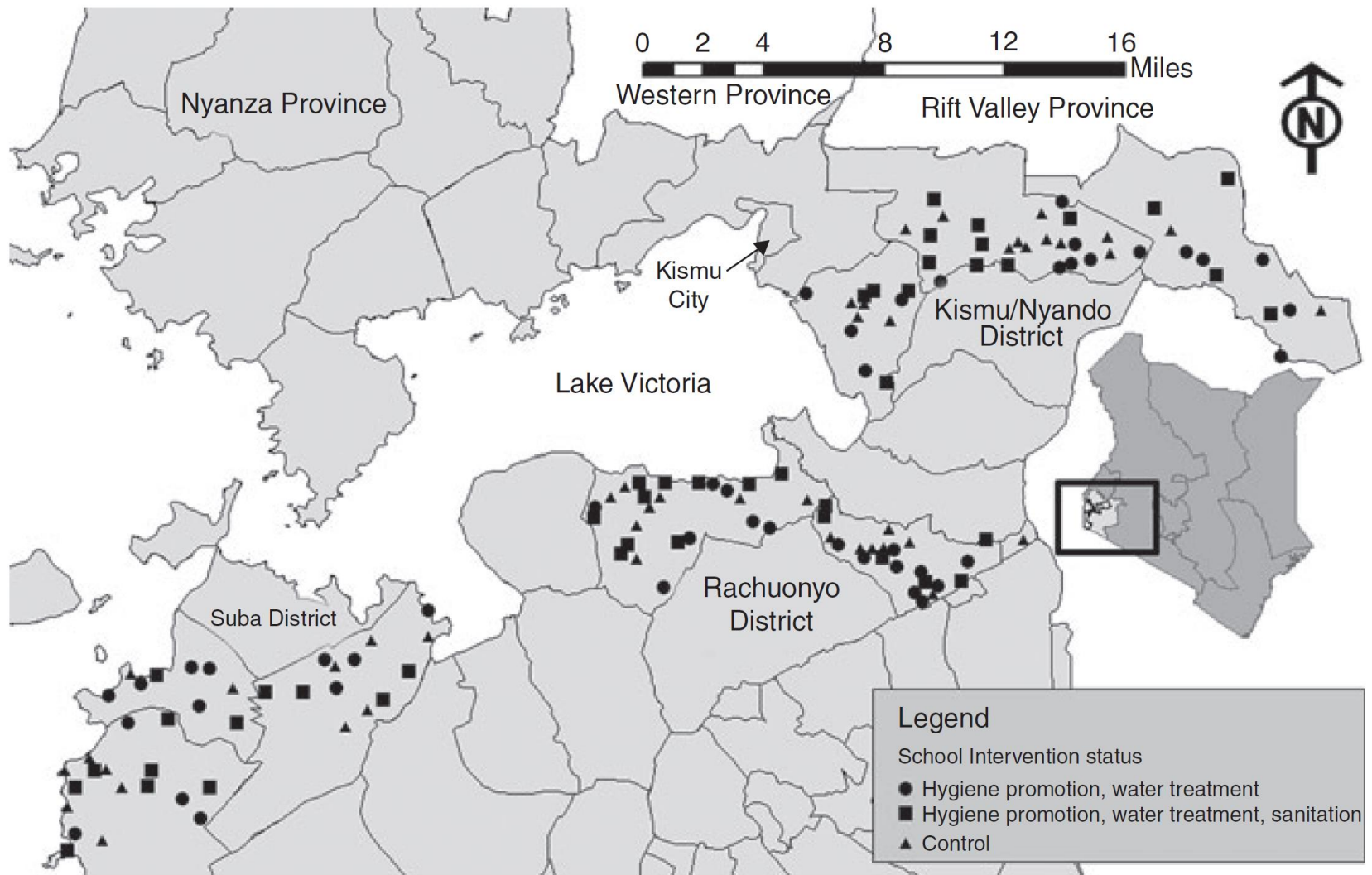


Household:
257,729

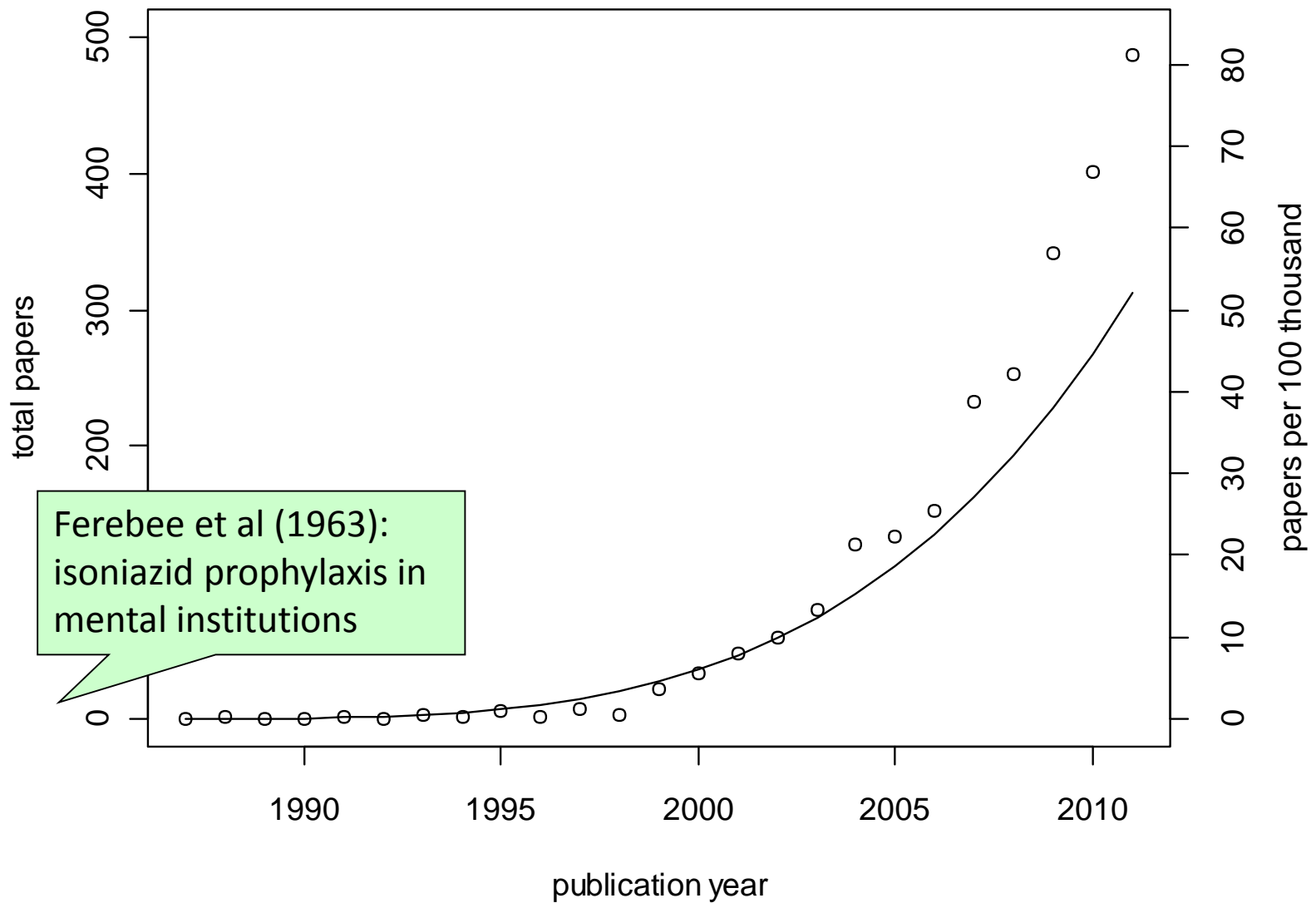


ECF & Household:
299,138

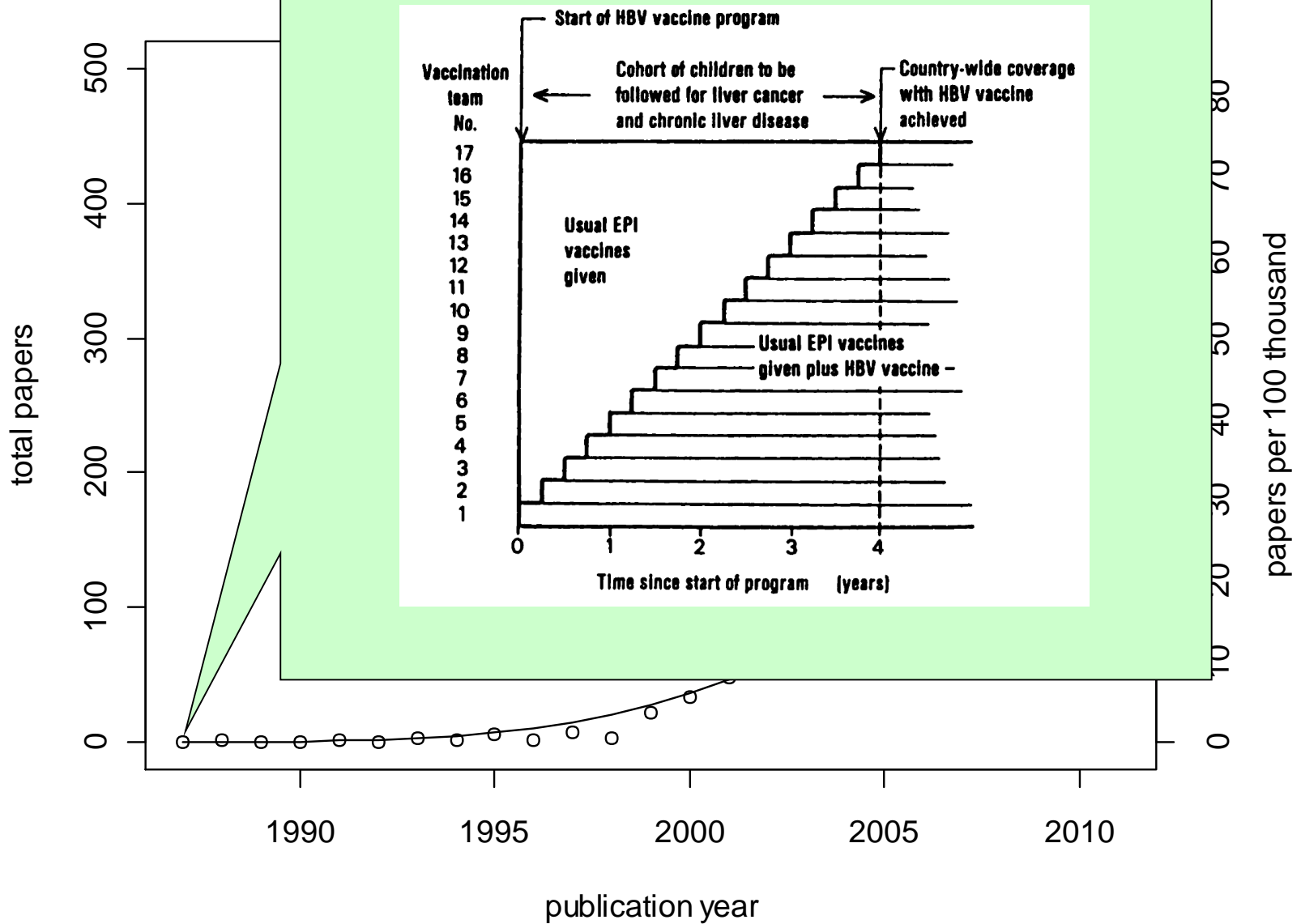
Ayles et al 2013



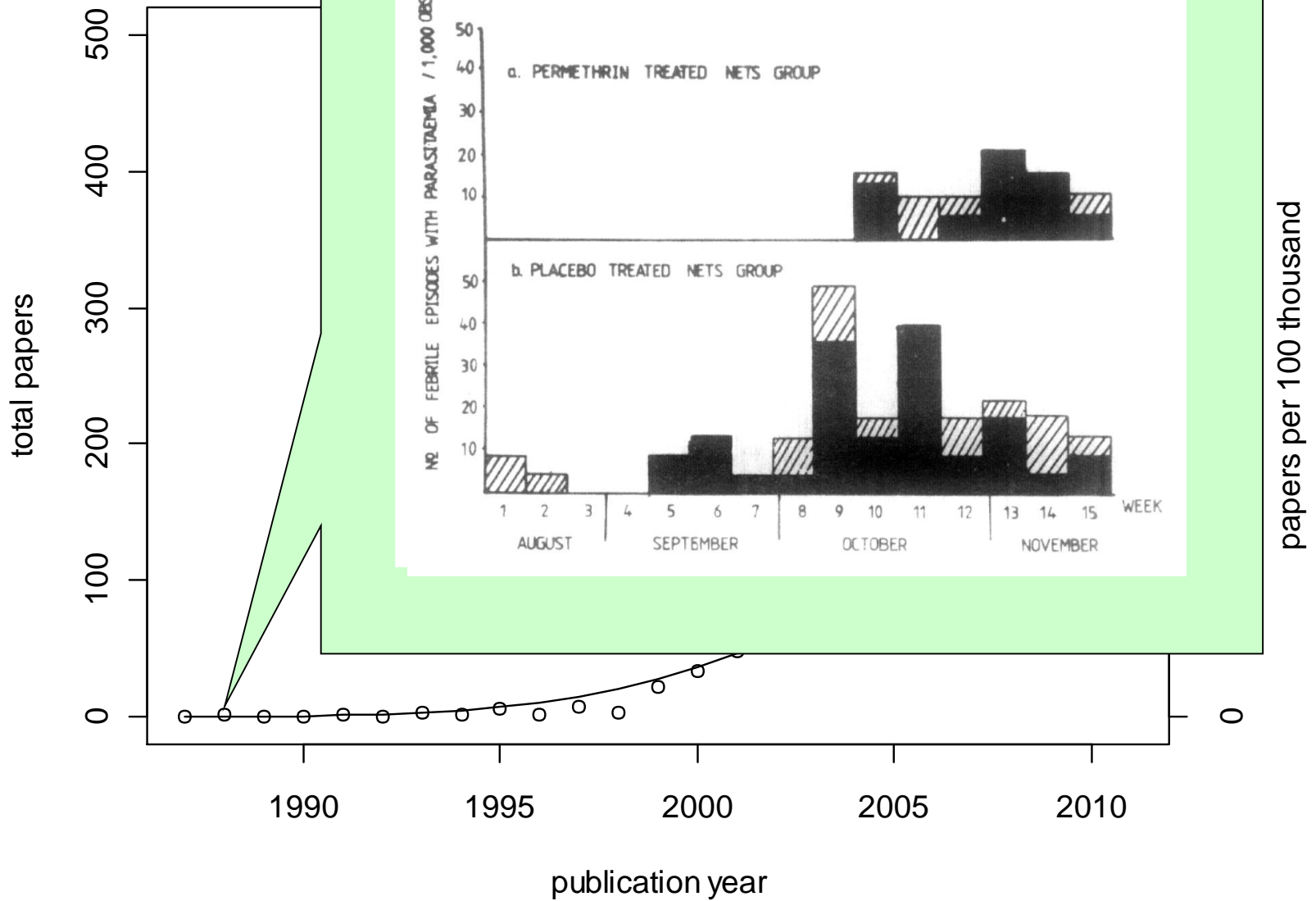
Cluster-randomized Trials in PubMed

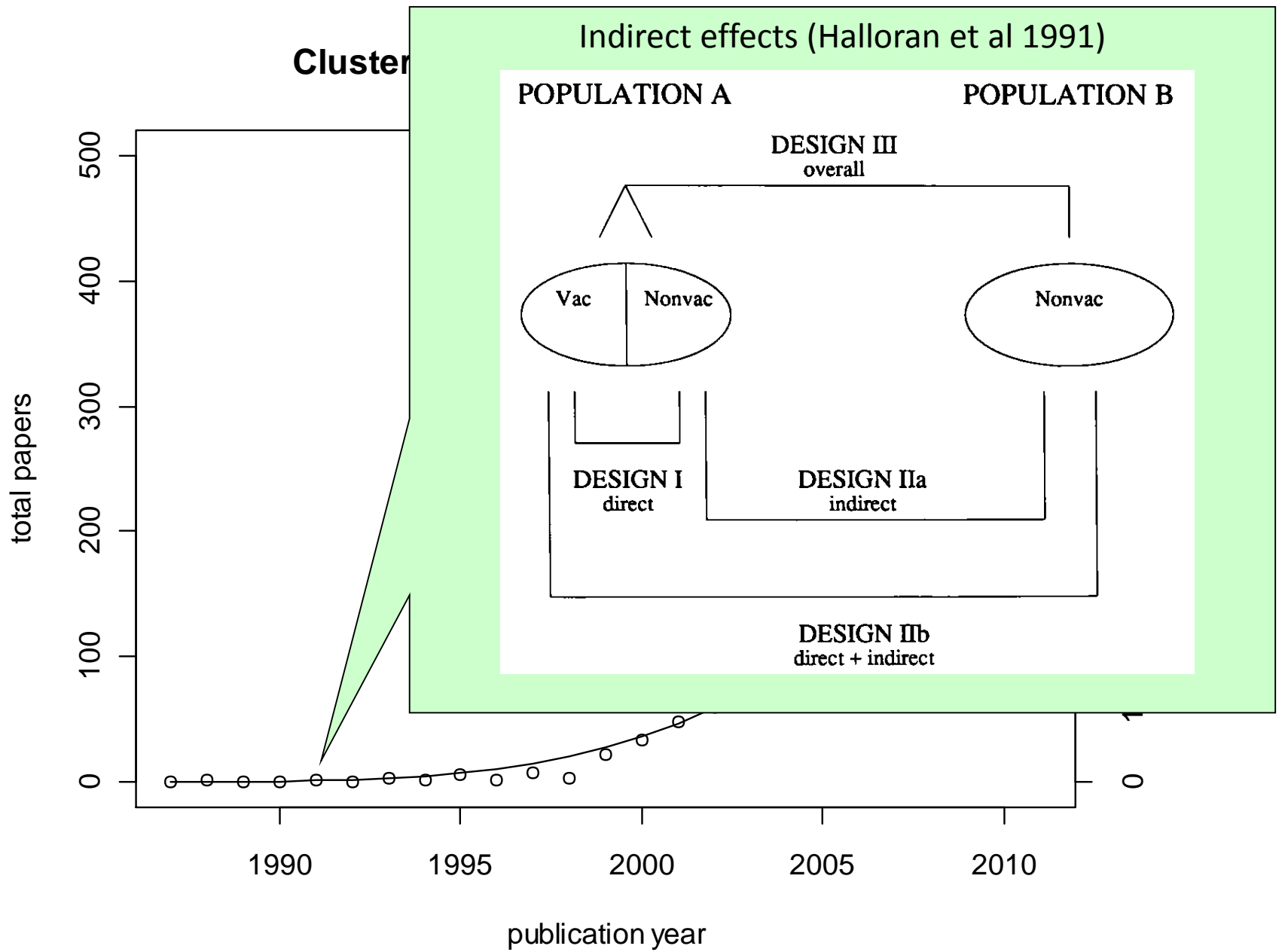


The Gambia Hepatitis Intervention Study (1987)



Bednets in Gambian villages (Snow et al 1988)





Analysis methods

- General principle is to allow for intra-cluster correlation
- Individual-level analysis
 - generalized estimating equations (GEE)
 - random effects models (multilevel modelling)
 - more statistical power, although require model checking, and may be unreliable with small numbers of clusters

- Cluster level analysis
 - one summary measure is calculated for each cluster, and these are compared using standard methods
 - e.g. *t* test, analysis of variance, generalized linear models
 - does not remove need for model checking but is easier to do and more likely to be met
 - e.g. *t* test has been shown to be robust
 - we specified this approach for main analyses of HealthPlatform trial (Overgaard et al 2012)

Spatial analysis

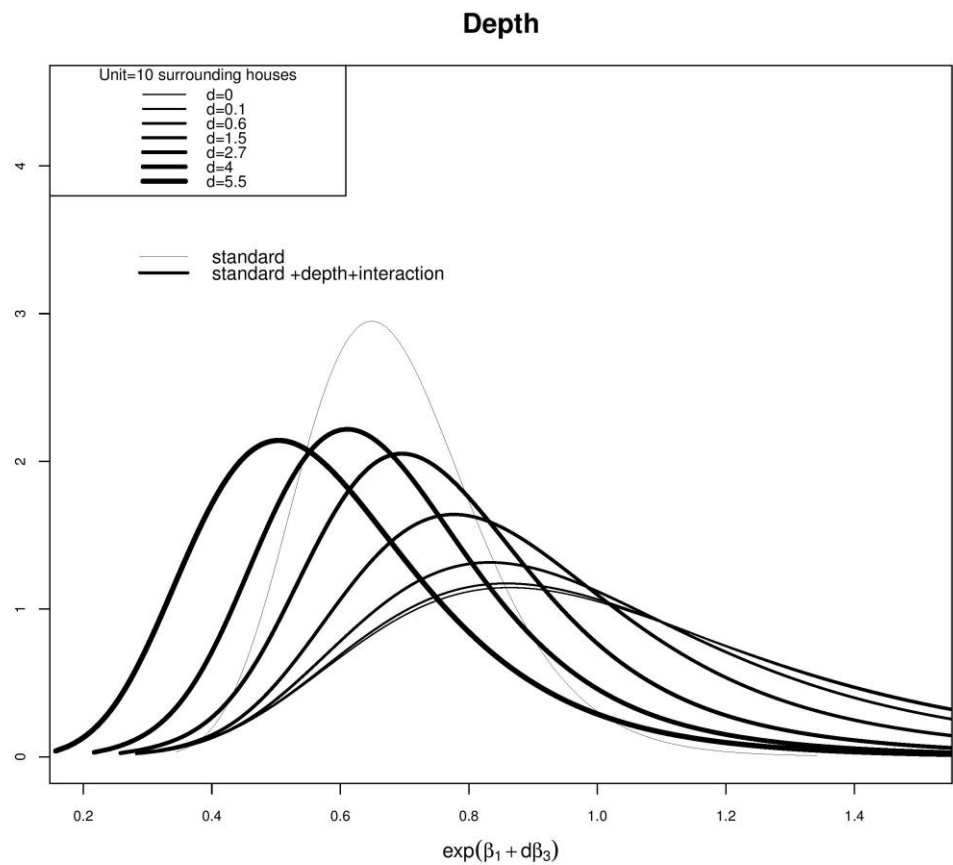
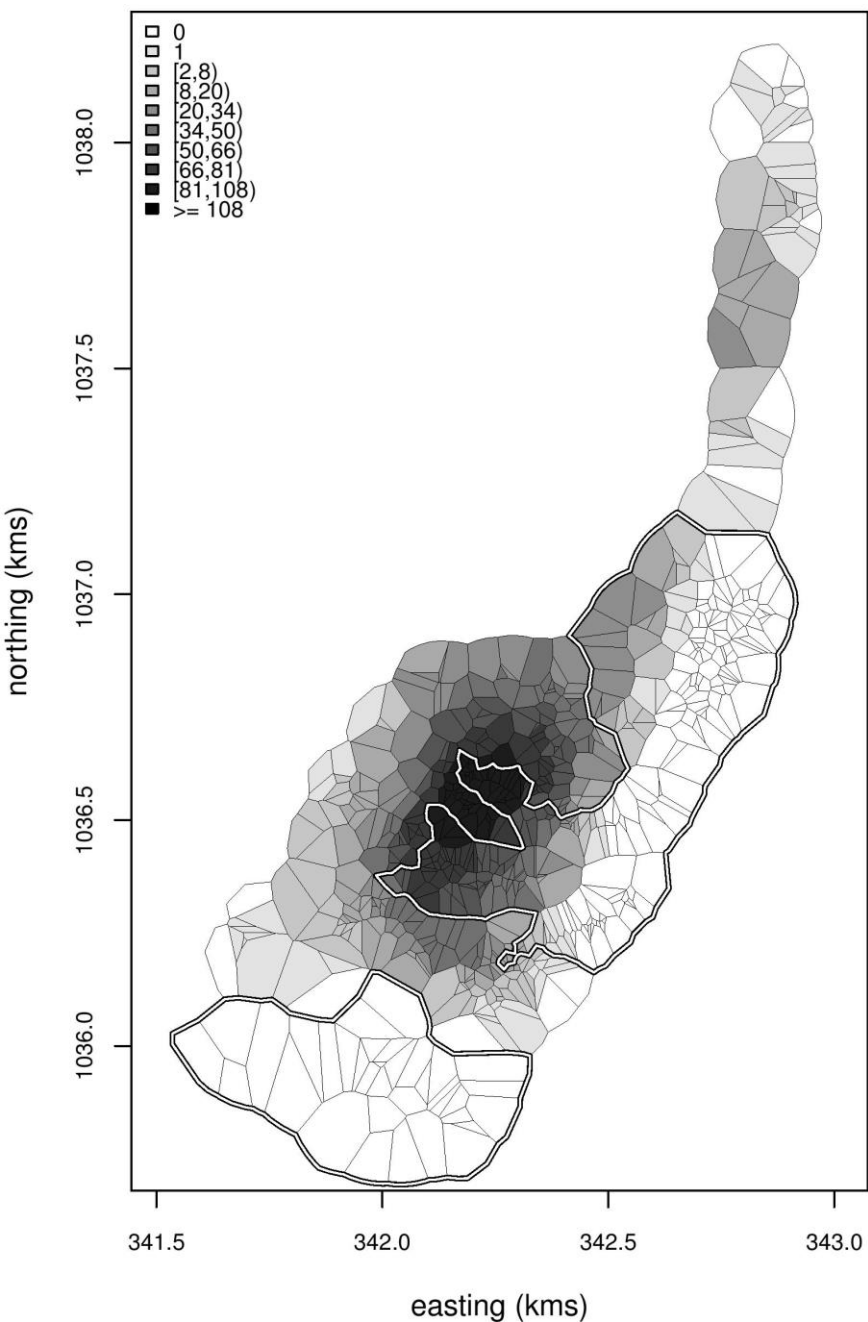


- Although the clusters should ideally be far enough apart to be independent, this may not be practical
 - e.g. because ‘enough’ may not be quantifiable a priori.
- Hence some trials may show ‘spillover’ effects



Fitting a 'tapatanque' in Trujillo (Kroeger et al 2006, photo Elci Villegas)

Depth (minimum number of surrounding sites)



Conclusions

- For HealthPlatform trial, primary analyses have been specified to be on summary measures
 - reporting needs to follow CONSORT CRT extension
- For additional secondary analyses, and/or future trials, may use other methods

- In PubMed:

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((cluster AND randomi*) AND trial AND water) OR  
(cluster-randomi* AND trial AND water)
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- Limitations

- may not find all water-related interventions e.g. if they refer to ‘sanitation’ but not ‘water’
- May be randomized by cluster without calling it such, either by using a phrase such as group-randomized, or by randomizing a unit which can be considered as a cluster, such as a household

- 107 results

- 7 of these also contain ‘integrated’

Inclusion criteria

- Interventions applied to people
 - e.g. not veterinary
- Interventions physically related to water
 - e.g. not purely educational
- Reporting a cluster-randomized trial, or systematic review
 - e.g. papers on design, or analytical methods, were excluded
- Either a) health, developmental, infection or contamination outcome
 - e.g. hand contamination with *E. coli*, but not *E. coli* in water
- or b) vector outcome
 - e.g. pupae per person



- 21 with trial results
- of which, 1 self-described as integrated
 - Vanlerberghe et al 2009, 'A community based environmental management embedded in a routine control programme was effective at reducing levels of *Aedes* infestation'
- 2 Cochrane systematic reviews

Two systematic reviews

- Mosquito larval source management for controlling malaria (Tusting et al 2013)
 - ‘In Africa and Asia, LSM is another policy option, alongside LLINs and IRS, for reducing malaria morbidity in both urban and rural areas where a sufficient proportion of larval habitats can be targeted’
- Interventions to improve water quality and supply, sanitation and hygiene practices, and their effects on the nutritional status of children (Dangour et al 2013)
 - ‘suggestive of a small benefit of WASH interventions (specifically solar disinfection of water, provision of soap, and improvement of water quality) on length growth in children under five years of age’

21 CRT reports

- 16 reported health-related outcomes, 5 reported vector outcomes
- In the former, health-related outcomes included:
 - diarrhoea occurrence (8)
 - *E. coli* hand contamination (2)
 - prevalence of overweight (2)
 - surgical site infection (1)
 - helminth infection (1)
 - flu-like illness (1)
 - global development quotient (1)

- In the 16 with health-related outcomes, interventions included
 - one or more water, sanitation, and hygiene (WASH) interventions including SODIS (14)
 - promotion of water consumption (2)
- In the 5 with vector outcomes, all related to *Aedes* pupae per person and *Stegomyia* indices, the interventions being environmental management or ITMs

Conclusions from review



- Some of these CRTs showed integration of interventions, but little in the way of programmatic integration (over diseases)