NUFFIELD DEPARTMENT OF
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HEALTH SCIENCES

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In children under 16 in the Asia-Pacific region, would administration of the new dengue vaccine, rather than a placebo, lead to lower mortality/morbidity?

Student EBM presentations

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The question

You are working in a hospital on elective in Thailand. A mother comes in with her 5 year old child asking whether the child should be given the new dengue vaccine. She is worried about her child getting dengue, but has concerns about the side effects of the vaccine.

"In children under 16 in the Asia-Pacific region, would administration of the new dengue vaccine, rather than a placebo, lead to lower mortality/morbidity?"

P	Children under the age of 16 in the Asia-Pacific region
I	Sanofi Pasteur dengue vaccine
C	Placebo
O	1) Virologically confirmed dengue 2) Adverse reactions to vaccine 3) Hospitalisation or death

The search and search results

- Search in PubMed
  - (((dengue vaccin*) AND dengue fever) AND child*) AND Asia
  - 50 results
- First result = descriptive rather than investigative
- Used second result
  - *Clinical efficacy and safety of a novel tetravalent dengue vaccine in healthy children in Asia: a phase 3, randomised, observer-masked, placebo-controlled trial (Capeding et al, 2014)*

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The study appraisal

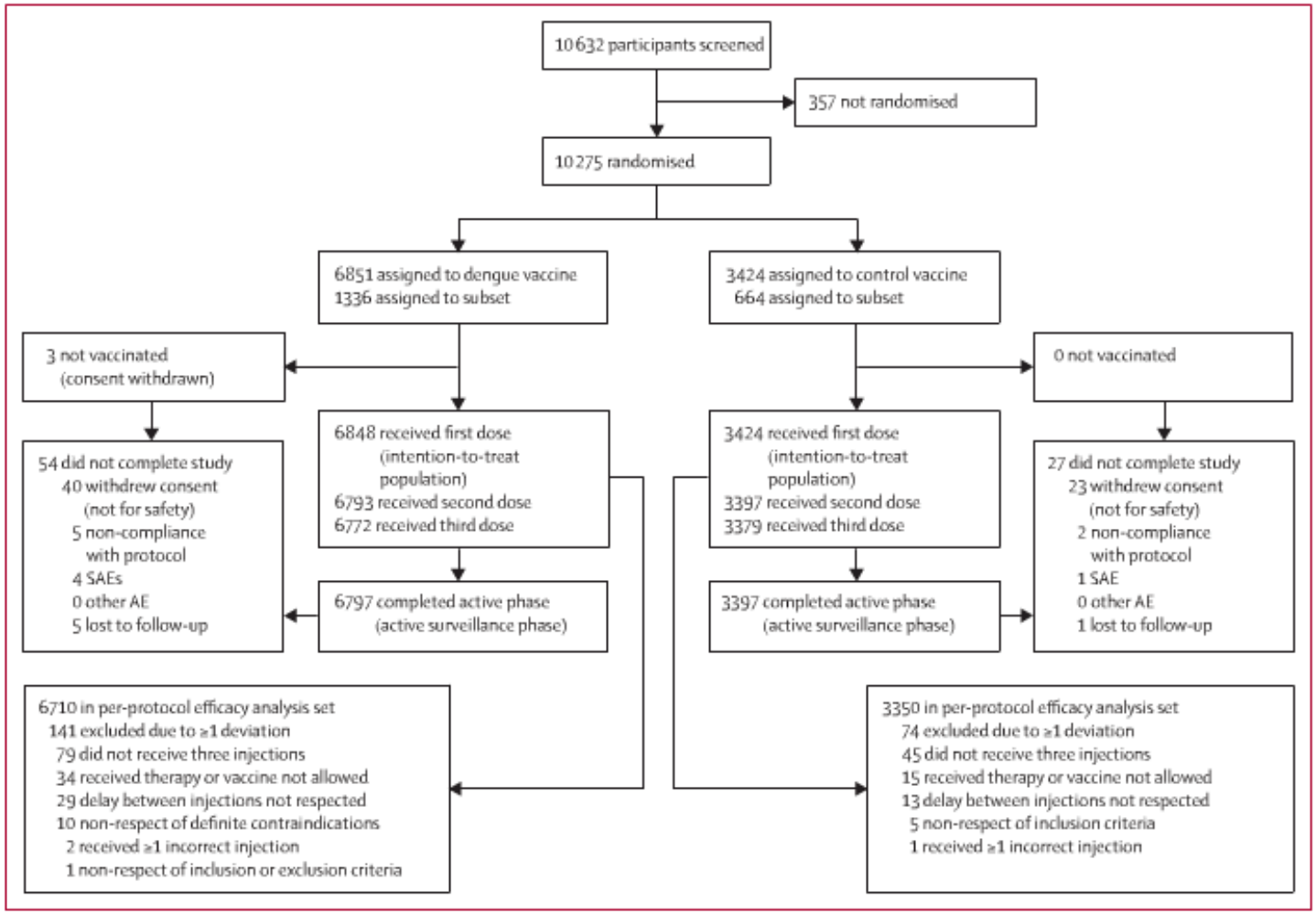

Figure 1: **Trial profile**
The safety analysis set included all participants who had received at least one injection, and participants were analysed in the group corresponding to the injection received. SAE=serious adverse event. AE=adverse event.

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The study appraisal

- Recruitment
  - Unbiased, decided in advance
- Allocation/blinding
  - Computer-generated allocation, but groups not concealed from trial staff → blinding could be broken
- Maintenance
  - Similar at start for age, sex, seropositivity for Japanese Encephalitis and dengue
  - Remained similar throughout
- Measurement of outcomes
  - Full reporting of pre-specified outcomes, with both per-protocol and intention-to-treat analysis

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The Results

	Vaccine group (N=6848)			Control group (N=3424)			Vaccine efficacy (% [95% CI])
	Cases* (n)	Person-years at risk†	Incidence density‡ (95% CI)	Cases (n)	Person-years at risk	Incidence density (95% CI)	
Primary analysis (per-protocol)§	117	6526	1·8 (1·5–2·1)	133	3227	4·1 (3·5–4·9)	56·5% (43·8–66·4)
Intention-to-treat analysis¶	286	13 571	2·1 (1·9–2·4)	309	6623	4·7 (4·2–5·2)	54·8% (46·8–61·7)

	Vaccine group (N=6848)			Control group (N=3424)			Vaccine efficacy (% [95% CI])
	Cases* (n)	Person-years at risk†	Incidence density‡ (95% CI)	Cases (n)	Person-years at risk	Incidence density (95% CI)	
Efficacy against VCD, more than 28 days after third injection in all participants who had received three injections							
Serotype 1	51	6548	0·8 (0·6 to 1·0)	50	3210	1·6 (1·2 to 2·0)	50·0% (24·6 to 66·8)
Serotype 2	38	6561	0·6 (0·4 to 0·8)	29	3253	0·9 (0·6 to 1·3)	35·0% (−9·2 to 61·0)
Serotype 3	10	6613	0·2 (0·1 to 0·3)	23	3281	0·7 (0·4 to 1·1)	78·4% (52·9 to 90·8)
Serotype 4	17	6605	0·3 (0·2 to 0·4)	34	3265	1·0 (0·7 to 1·5)	75·3% (54·5 to 87·0)
Unserotyped	2	6634	<0·1 (0·0 to 0·1)	3	3309	<0·1 (0·0 to 0·3)	66·7% (−190·3 to 97·2)
Efficacy against VCD, from baseline in all participants who had received at ≥1 injection (intention to treat)							
Serotype 1	116	13 742	0·8 (0·7 to 1·0)	126	6796	1·9 (1·5 to 2·2)	54·5% (40·9 to 64·9)
Serotype 2	97	13 766	0·7 (0·6 to 0·9)	74	6856	1·1 (0·8 to 1·4)	34·7% (10·4 to 52·3)
Serotype 3	30	13 835	0·2 (0·1 to 0·3)	43	6895	0·6 (0·5 to 0·8)	65·2% (43·3 to 78·9)
Serotype 4	40	13 826	0·3 (0·2 to 0·4)	72	6874	1·0 (0·8 to 1·3)	72·4% (58·8 to 81·7)
Unserotyped	7	13 858	<0·1 (0·0 to 0·1)	8	6926	0·1 (0·0 to 0·2)	56·3% (−38·0 to 86·5)

The Results (interpretation of findings)

- Calculated relative risk as a ratio of annual incidence of dengue in vaccine group : control group
    - 1 – RR = vaccine efficacy
- 54.8% [46.8 – 61.7] vaccine efficacy
  – Not as high as hoped

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The Implications

- Positive
  - 54.7% chance that vaccine would prevent dengue
  - No notable side effects
- Negative
  - 3 doses
  - Still relatively high chance of getting dengue after effort of getting vaccine
  - Couldn’t use this vaccine to completely eradicate dengue, but more to reduce disease burden

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