Public Health England

PROUD

MRC Clinical Trials Unit

Pragmatic Open-Label Randomised Trial of Pre-Exposure Prophylaxis: the PROUD study

http://www.proud.mrc.ac.uk/

Disclaimers

- Gilead Sciences plc provided drug free of charge, and distributed it to participating clinics
- Gilead Sciences plc provided funds for the additional diagnostics including the pharmacokinetic sub-study

Sexual health service in England

- ~220 sexual health clinics, linked through professional guidelines
- Accessed by 110,000 HIV negative gay men per year
- Diagnoses made and services provided reported to Public Health England

Rationale

- **To determine whether PrEP worked as well as iPrEx in this setting (44% reduction in HIV)**

- **Why might effectiveness be less in real world?**
- Adherence less
  - trial schedules monthly
  - well resourced for adherence support

- Behaviour riskier
  - participants constantly reminded that they could be on placebo, and that effectiveness was unknown
  - well resourced for behaviour change interventions

PROUD Pilot

GMSM reporting UAI last/next 90days; 18+;
and willing to take a pill every day

↓

Randomize HIV negative MSM
(exclude if treatment for HBV/Truvada contra-indicated)

↓

Risk reduction includes Truvada **NOW**

Risk reduction includes Truvada **AFTER 12M**

↓

Follow **3 monthly** for up to 24 months

Main endpoints in Pilot: recruitment and retention
From April 2014: HIV infection in first 12 months

Designed to mimic real-world

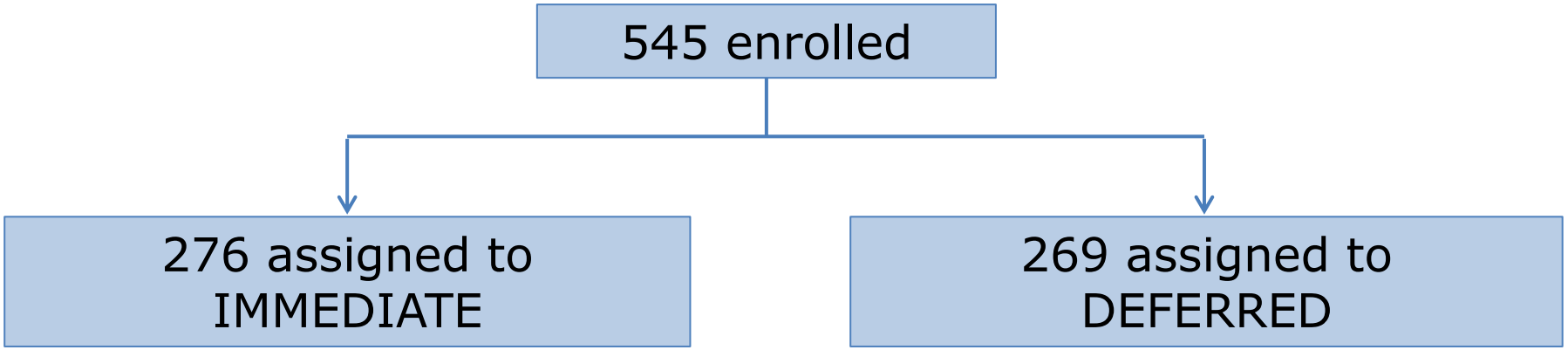
- Eligibility: routine clinic data and p24Ag/Ab serology at enrolment (no PCR)
- Safety: serum creatinine when starting and annually; additional tests if 1+ protein on dipstick
- STIs: (mainly) quarterly HIV, syphilis, HCV, gonorrhoea and chlamydia according to routine clinic
- Behaviour change interventions according to routine clinic (sexual risk, adherence, addiction)

- **Study procedures: web-randomisation, data entry, participant-completed questionnaires**

Results:

Population, Prescribing, Tolerability

Participant randomization



Baseline demographics[1]

Characteristics		Immediate	Deferred
Age, median (IQR)		35 (30 – 43)	35 (29 – 42)
Ethnicity	White	80%	82%
Born UK	No	40%	40%
Education	University	59%	60%
Employment	Full-time	70%	73%
Sexuality	Gay	96%	94%
Current relationship	No	53%	55%
Recreational drug use[2]	Yes	76%	64%

[1] 539/545 (99%) questionnaires returned
[2] in the last 90 days

Prescriptions of PrEP and PEP

Immediate	Deferred
• 14 (5%) **never started PrEP**	• Anecdotally, **rare use of PrEP**
• 156 (56%) prescribed sufficient drug for 100% daily dosing	
• Overall, drug prescribed covered 86% of days in follow-up	
• 13 (5%) prescribed **PEP** (total 15 prescriptions)	• 83 (31%) prescribed **PEP** (total 174 prescriptions)

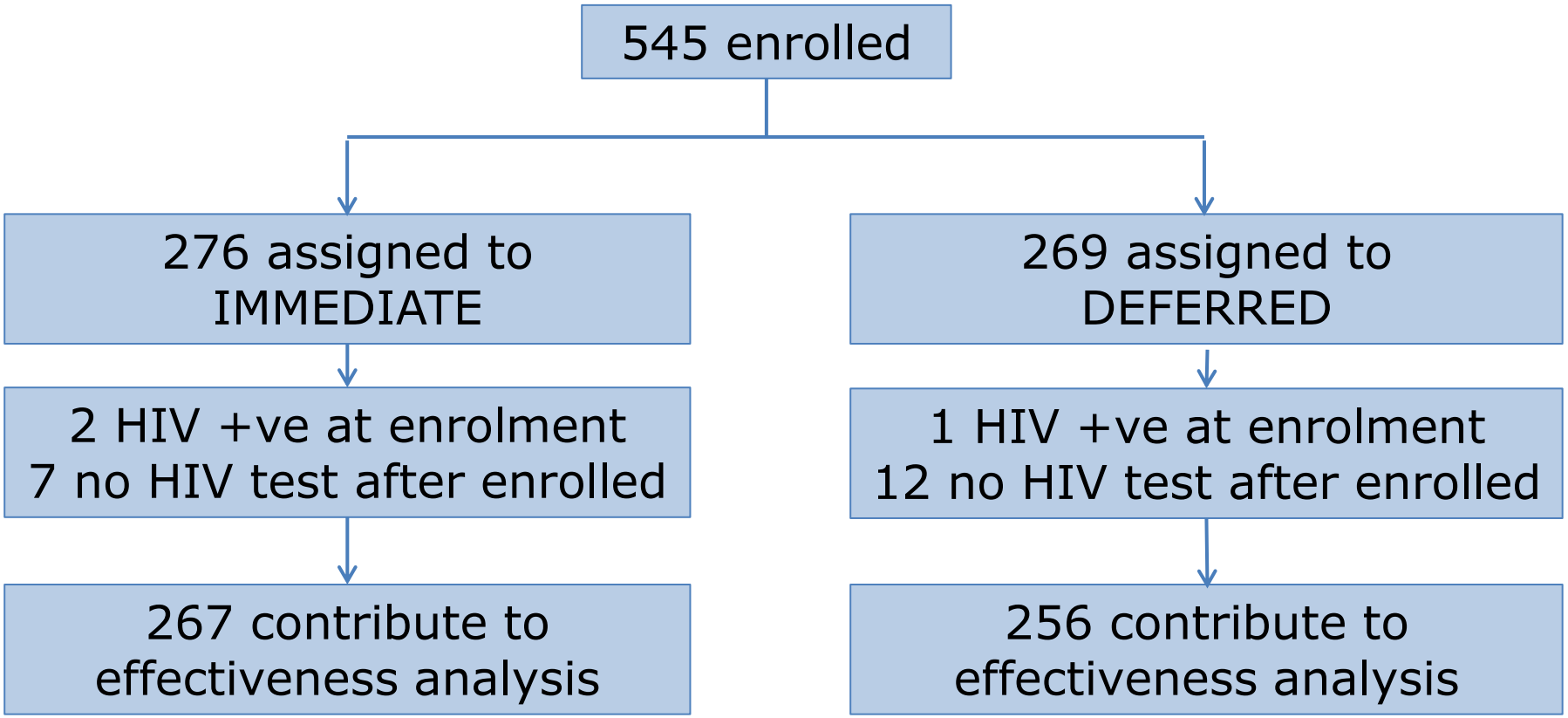
PrEP interruptions for medical event

- **PrEP interrupted** by 28 participants (**both groups**) but only **13** had events considered related to drug:
  - nausea alone or with diarrhoea/abdominal pain/aches and fatigue (n=5)
  - decline in creatinine clearance (n=2)
  - headache (n=2)
  - joint pain, with fatigue in one case (n=2)
  - sleep disturbance (n=1)
  - flu-like illness (n=1)

- **PrEP re-started** by 11 of 13 participants above

Results:

HIV endpoint



Calculation of person-years:

From enrolment to the first of the following

- HIV test at m12, or
- HIV test at the time of access to PrEP, or
- diagnosis of HIV infection

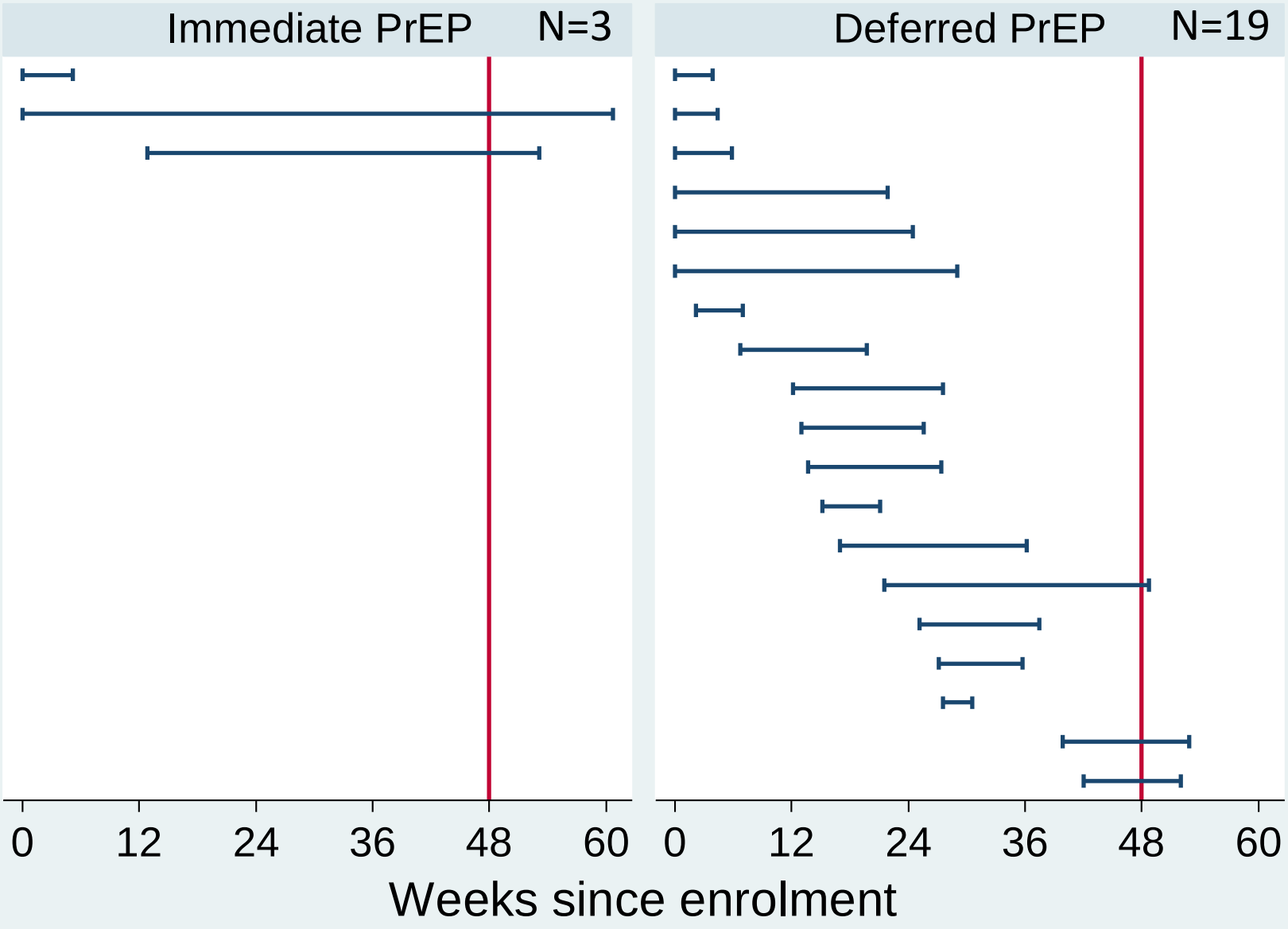
Completeness of follow-up for HIV

- **Expected** person-years calculated assuming they had precisely followed protocol schedule

Observed/expected follow-up:

- Immediate: 239/261 person years (92%)
- Deferred: 214/242 person years (88%)

Individual incident HIV infections



HIV Incidence

Group	No. of infections	Follow-up (PY)	Incidence (per 100 PY)	90% CI
Overall	22	453	4.9	3.4–6.8
Immediate	3	239	1.3	0.4–3.0
Deferred	19	214	8.9	6.0–12.7

Efficacy =86% (90% CI: 58 – 96%)
P value =0.0002

Rate Difference =7.6 (90% CI: 4.1 – 11.2)
Number Needed to Treat =13 (90% CI: 9 – 25)

Drug Resistance

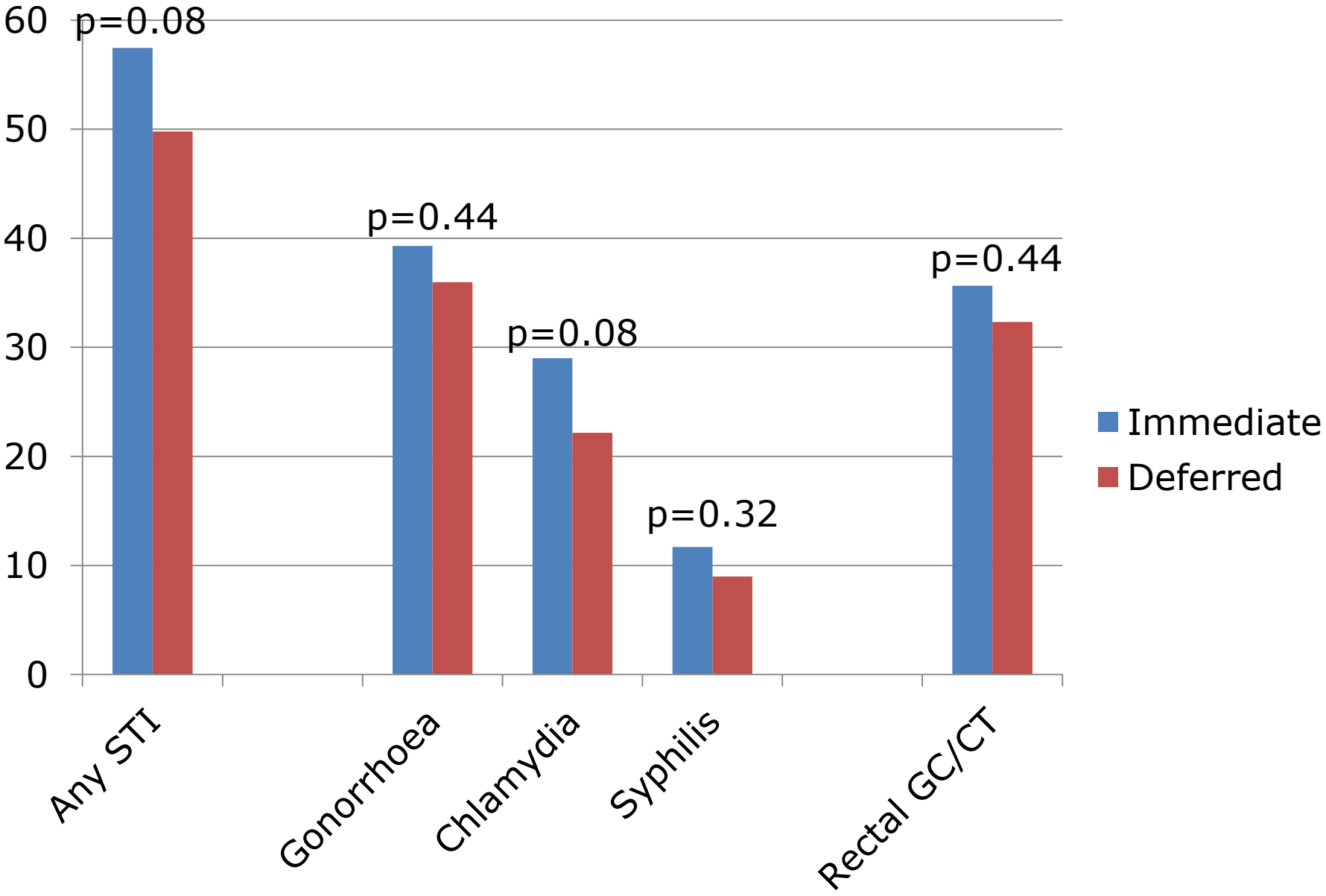
- **3** of **6** individuals who were seroconverting around baseline (immediate group) or month 12 (deferred group) developed **M184V/I** mutations (as a mixture with wild type)

- **K65R** was not detected

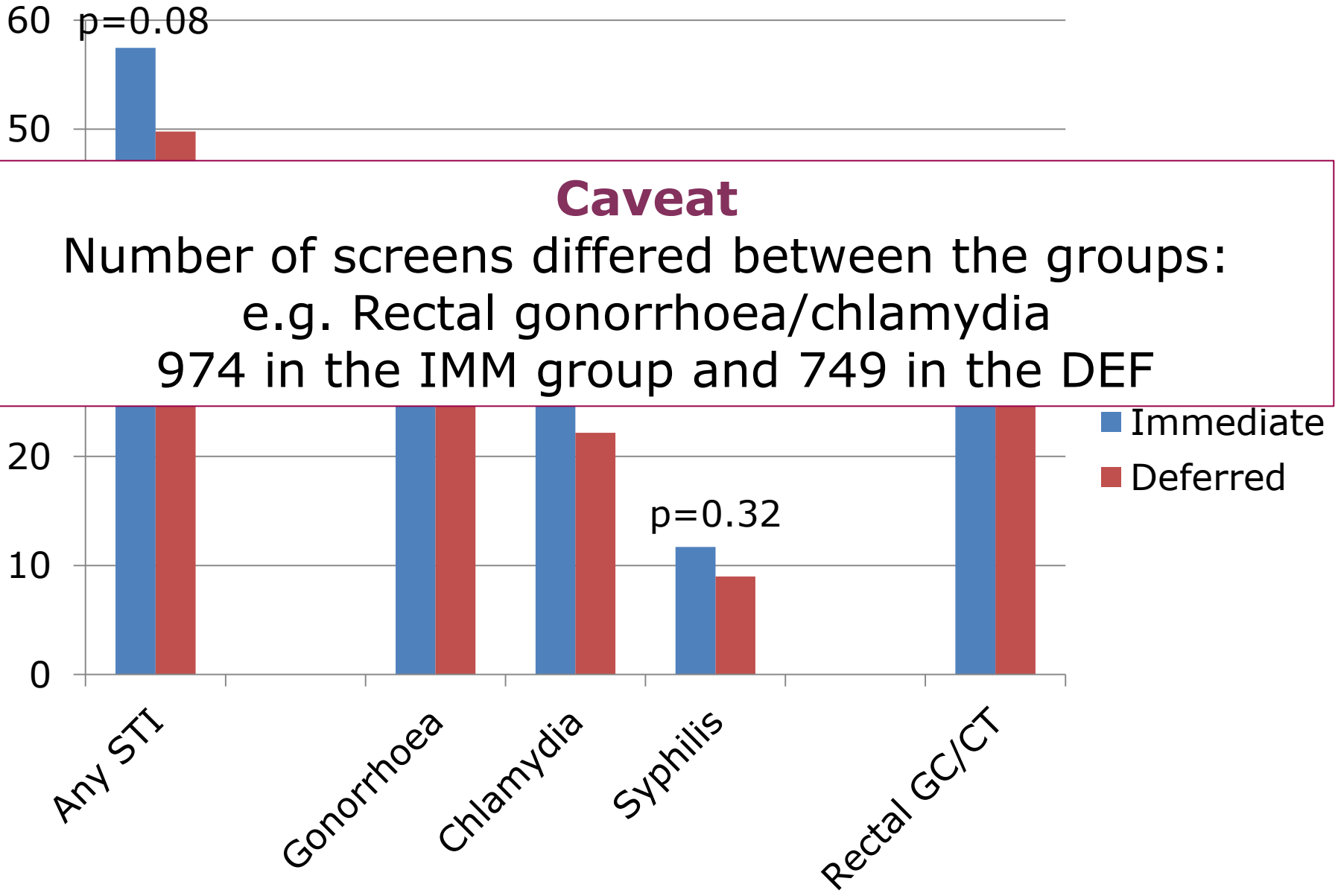
Results:

STI endpoints

STIs


60
50
40
30
20
10
0
p=0.08
p=0.44
p=0.08
p=0.32
p=0.44
Any STI
Gonorrhoea
Chlamydia
Syphilis
Rectal GC/CT
Immediate
Deferred

STIs



Caveat

Number of screens differed between the groups:
e.g. Rectal gonorrhoea/chlamydia
974 in the IMM group and 749 in the DEF

Results:

Sexual behaviour

Reported sexual behaviour (preliminary)

Anal sex partners in last 90 days **BASELINE n=539**	**Immediate** Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10.5 (5-20)	10 (4-20)
Condomless partners, participant receptive	3 (1-5)	2 (1-5)
Condomless partners, participant insertive	2.5 (1-6)	3 (1-7)

Anal sex partners in last 90 days **MONTH 12 n=349**	**Immediate** Median (IQR)	**Deferred** Median (IQR)
Total number of partners	10 (3-24)	8 (3-15)
Condomless partners, participant receptive	3 (1-8)	2 (1-5)
Condomless partners, participant insertive	3 (1-8)	3 (1-6)

Conclusions

- HIV incidence in the population who came forward to access PrEP was much higher than predicted based on all MSM attending sexual health clinics
- Despite extensive use of PEP in the deferred period
- Our concerns about PrEP being less effective in the real world were unfounded

- MSM incorporated PrEP into existing risk reduction strategies which continued to include condom use
- There was no difference in STIs, which were common in both groups

- Clinics were able to adapt routine practice to incorporate PrEP

Acknowledgements (1)

Study participants

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Acknowledgements (2)

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