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Audit of voriconazole therapeutic drug monitoring (TDM) at a tertiary teaching hospital in England following the introduction of e-prescribing (Epic®)

David Enoch

Consultant Medical Microbiologist & Infection Control Doctor

PHE Cambridge – Addenbrookes Hospital

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Conflicts of interest

- Astellas
- Gilead
- Pfizer
- MSD

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Voriconazole

- Voriconazole is a triazole antifungal that is commonly used in the treatment of invasive aspergillosis
- Therapeutic drug monitoring (TDM) is key to the effective use of voriconazole:
  - non-linear pharmacokinetics
  - serum concentrations are influenced by several factors including:
    - Age
    - Weight
    - Genetic polymorphisms
    - Altered drug absorption
    - Drug interactions
  - Voriconazole trough levels greater than 6mg/L are associated with an increased likelihood of hepatotoxicity
- Evidence to support the use of TDM during voriconazole treatment is growing
- National guidelines support its use (Ashbee et al 2015)

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Audit standards

- All in-patients commencing voriconazole should be reviewed by a microbiologist
- Voriconazole pre-dose levels should be taken within 5-7 days of:
  - Commencing therapy
  - A change in dose
  - Side effects thought to be related to voriconazole
  - On request by AFS team
- All levels should be therapeutic (i.e. between 1 – 6mg/L)
  - If out of range then evidence of review and change in management instituted
- Turnaround time should be ≤3 days

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Cambridge (Addenbrooke's hospital)

- Teaching hospital (1,100 beds)
  - 70,000 inpatient admissions
  - 170,000 total admissions per annum
- Specialities include:
  - Transplantation (bone marrow, liver, kidney, pancreas, bowel)
  - Neurosciences
  - Infectious diseases
  - Plastic surgery
- Big user of antifungal drugs; the "biggest in the region"

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Methods

- Inclusion criteria: all inpatients on voriconazole
- Retrospectively analysed over the three month period (January – March 2016)
- Patients were identified using the Epic system and in-house dispensing reports
  - Report from EPIC
  - Costing report from inpatient pharmacy (Cheqs system)
  - Laboratory sendaway tests

- Exclusion criteria: outpatients
- Voriconazole pre-dose serum levels were analysed by the Mycology Reference Laboratory, Bristol, England

- Part of antifungal stewardship (AFS) programme (Micallef et al 2015)

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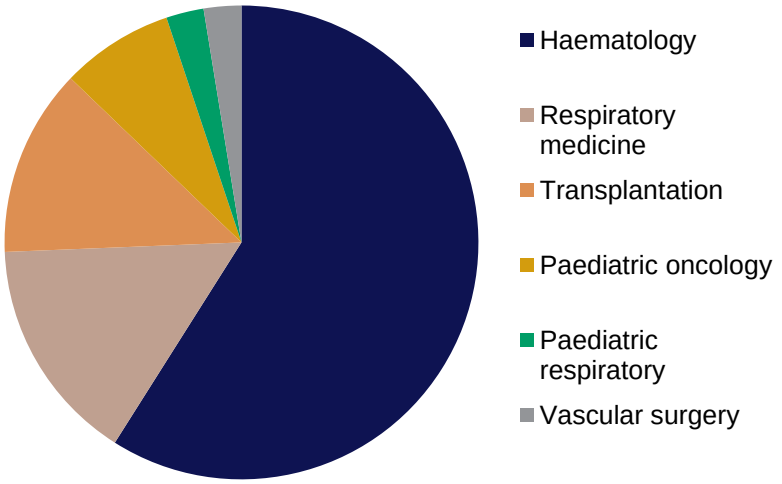
Results

- 39 patients were identified as receiving voriconazole in the study period.
- 22 (56%) male
- Age range 2 – 82 years (median 54; IQR 42 – 67 years)



Specialty

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Results

- 37/39 (95%) of patients had evidence of review by microbiology in the medical notes

- Six patients died prior to a level being taken and one patient was discharged prior to day 5 of therapy (with levels taken elsewhere)

- A total of 28 voriconazole levels were reported for the remaining 32 patients

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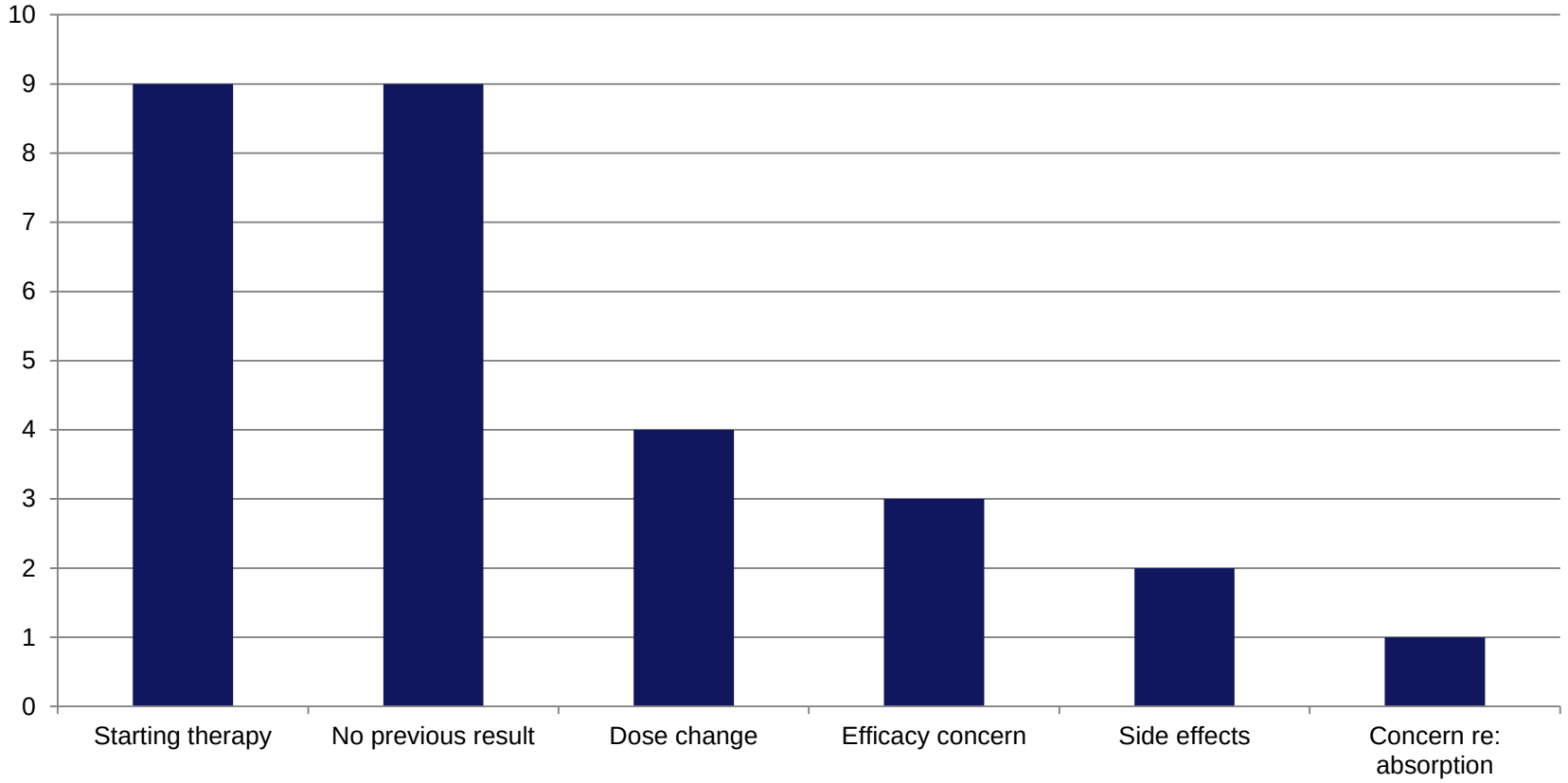
Reason for the level to be taken



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Reason for the level to be taken

Reason for taking level	Total number	Appropriate	Inappropriate	Reason
Starting therapy	9	5	4	Late
No previous result	9	0	9	Late
Dose change	4	4		
Efficacy concern	3	3		
Side effects	2	2		
Concern re: absorption	1	1		
Total	28	15	13	

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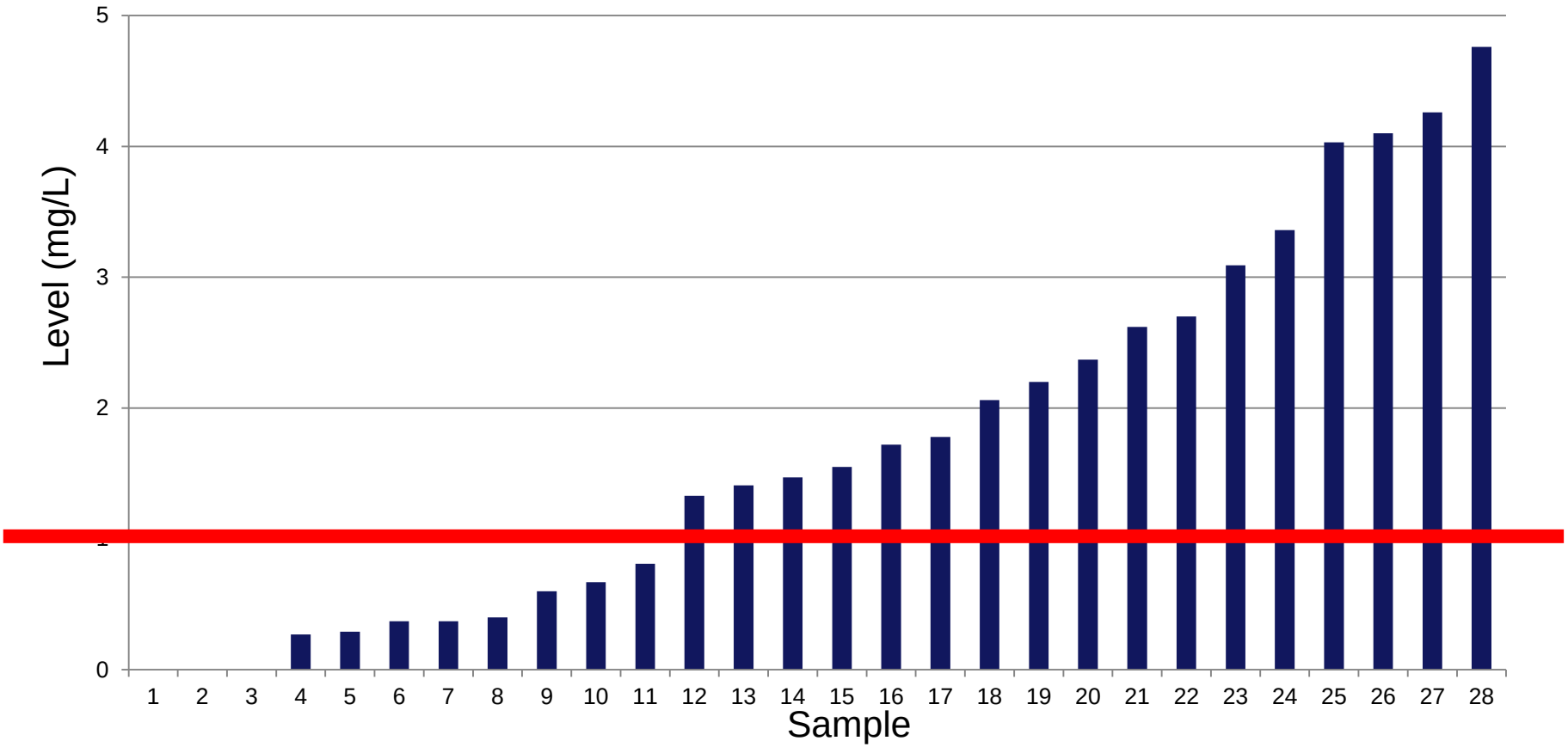
Levels



17/28 (61%) had a level >1mg/L
11/28 (39%) had a level >2mg/L
11/28 (39%) had a level <1mg/L

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Results

- <u>Actions performed for those with levels <1mg/L</u>

• Increase dose	2
• Switch drug / formulation	4
• Stop	2
• Nothing	3

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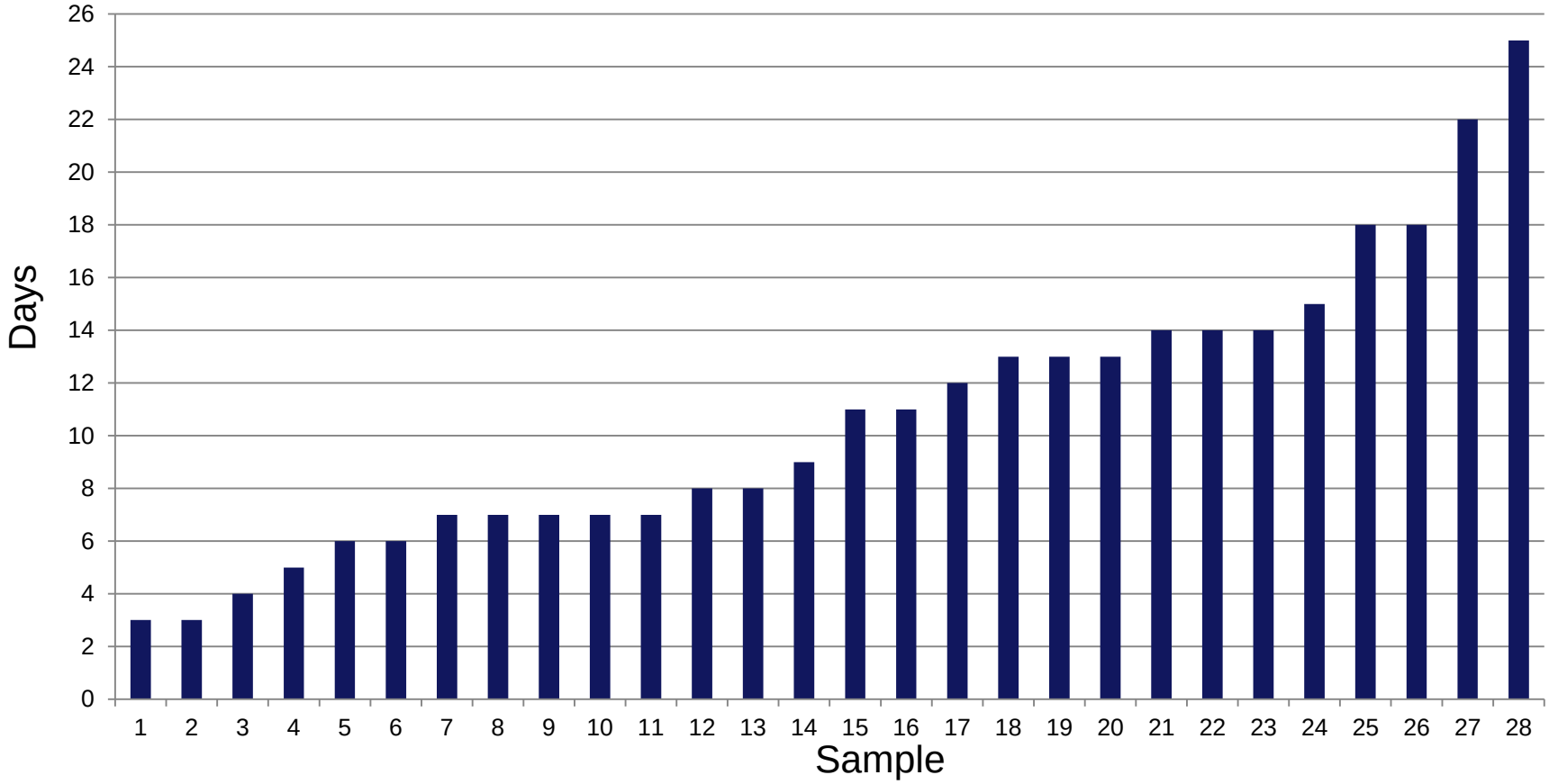
Turnaround time



Range 3 – 25 days (median 8 days)
2 (7%) had a TAT of ≤3 days
11 (39%) had a TAT of ≤7 days

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Summary of results

- Microbiology approval obtained 37/39 (95%) of the time
- 28 levels taken from 32 eligible patients
- 15/28 (54%) levels appropriate
  - Room for improvement re: appropriateness of taking levels (especially timing after starting therapy
- 9/12 (75%) low levels actioned
  - Room for improvement re: action after receiving low levels
- 2/28 (7%) had acceptable turnaround time
  - Dramatic room for improvement re: turnaround times

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Limitations

- Look into reasons why:
  - levels weren’t taken
  - low levels weren’t actioned
  - The turnaround times are so long

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Plan

- Education of clinical teams (especially haematology and respiratory medicine) and pharmacy

- Recommence AFS programme
  - This needs to be adequately resourced

- Look into laboratory working patterns
  - In-house testing has been refused…

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Questions