Concordance in Diabetic Foot Infection (CODIFI)

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CODIFI
Comparing sampling methods in diabetic foot infections

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Background

- Diabetic foot ulcers are highly prevalent and cause considerable morbidity at individual and population level
- Accurate identification of pathogens, rather than colonising bacteria is a prerequisite for targeted antibiotic therapy to ensure optimal patient outcome
- Wound swabs are the most commonly used sampling technique but some experts recommend removal of a tissue sample
- Previous systematic literature review has highlighted that there is no evidence based 'gold standard' for identifying organisms [1]

Aim

To assess agreement between culture results from swab and tissue samples taken from infected diabetic foot ulcers.

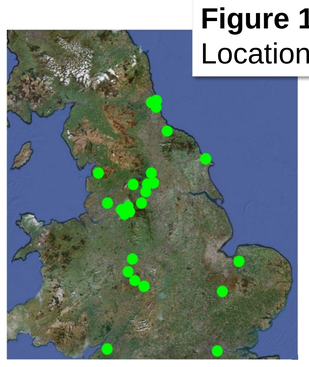


Figure 1: Location of sites

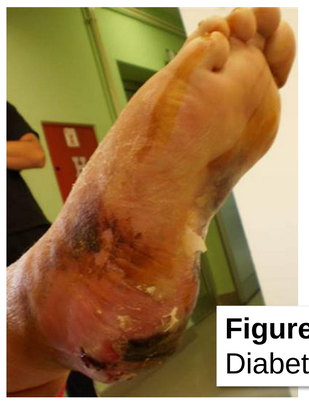
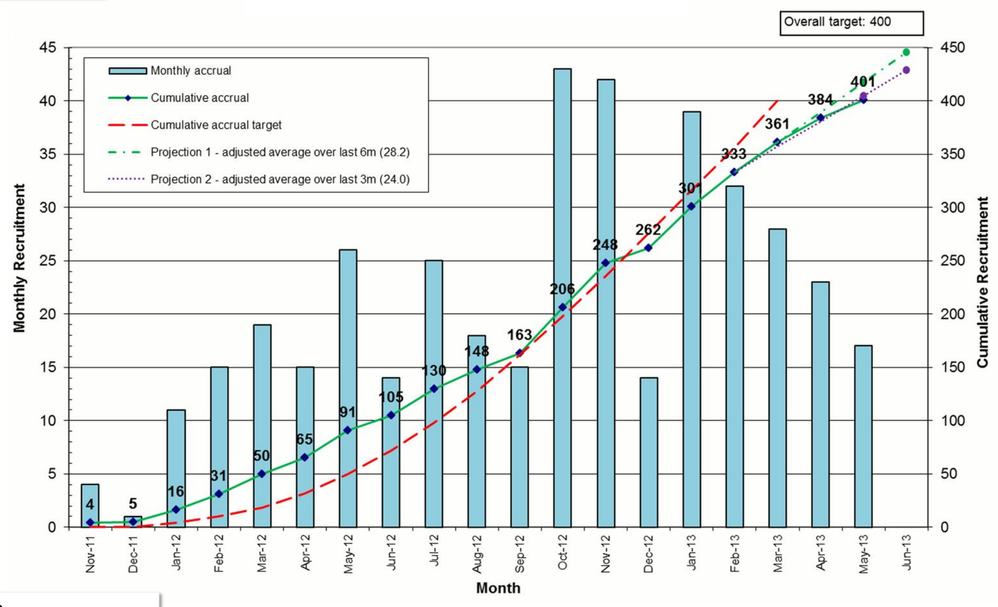


Figure 2: Diabetic foot ulcer

Overall recruitment chart



Study Summary

- Multicentre cross-sectional study involving 400 patients recruited from 25 sites across England *(See Figure 1)*
- Patient population: Patients with a diabetic foot ulcer with suspected infection requiring antibiotic therapy *(See Figure 2)*
- Patients recruited from multidisciplinary primary and secondary care based foot ulcer / diabetic clinics and hospital wards
- Consenting patients have both a swab and tissue sample taken from the diabetic foot ulcer
- Planned sub-study in 20 patients: second swab sample and half of tissue sample processed using molecular techniques

Sample size calculation

- 400 patients provides 80% power for detecting a difference of 3% in the primary outcome
- Overall prevalence of 10% (e.g. pseudomonas)
- Discordance of 5%
- Difference in discordance of 3%
- 2-sided 5% significance level
- Acceptable agreement defined a priori as Kappa larger than 0.6 [4]

Swab sample	Tissue sample		
	Isolate reported	Isolate not reported	Total
Isolate reported	0.075	**0.01**	0.085
Isolate not reported	**0.04**	0.875	0.915
Total	0.115	0.885	1

Study Endpoints & Methodology

Co-primary endpoints

Assess agreement between <u>swab & tissue</u> sampling for the microbiological parameters:

- Reported presence of key pathogens
  - Cross-tabulations on the extent of growth and presence of **likely** isolates
  - An overall summary and comparison of **all** isolates reported via each method will be generated.

Level of growth for Isolate					
	Tissue results				
Swab results	Not reported	+	++	+++	Total
Not reported					
+					
++					
+++					
Total					

- Identification of antimicrobial resistance
- Number of isolates reported per specimen

Secondary endpoints

- Compare conventional plating against molecular (PCR) techniques
- Evaluate clinical relevance of differences in bacterial profile between sampling techniques through clinical review
- Report adverse events

Statistical methods

- Agreement – Kappa statistic
- Pattern of disagreement – McNemar's
- Influence of baseline factors on agreement – Multinomial Logistic & Ordinal Regression

Clinical review & significance

- Evaluation of the appropriateness of empirical antibiotic therapy to assess the clinical significance of differences in swab and tissue results

E.g. Tissue sample but not swab indicates a change in therapy

Review involves:

- 16 clinical review members with prescribing rights
- 250 pairs of samples to compare swab and tissue results
- 30 pairs of random selected validation samples to assess both inter-rater and intra-rater reliability

E.g. Reviewers agree on change in therapy for both swab and tissue sample

Discussion

- CODIFI will produce robust evidence to evaluate the two most commonly used wound sampling techniques
- In terms of both reported pathogens and the clinical impact on antibiotic prescribing
- This holds immediate relevance for clinicians working with diabetic foot ulcers

Acknowledgements

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References **1**. O'Meara S.M., *et al*. (2006) A series of systematic reviews to inform a decision analysis for sampling and treating infected diabetic foot ulcers. *Health Technology Assessment* 10(12). **2**. Health Protection Agency 2009. Investigation of skin, superficial and non-surgical wound swabs. www.hpa-standardmethods.org.uk/documents/bsop/pdf/bsop11.pdf. **3**. Health Protection Agency 2009. Investigation of abscesses and deep seated infections. www.hpa-standardmethods.org.uk/documents/ bsop/pdf/bsop14.pdf. **4**. Landis J.R., Koch G. (1977) The measurement of observer agreement for categorical data. *Biometrics* 33:159 - 174

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