University of BRISTOL

Peer review intervention for monitoring and evaluating sites (PRIME) that improved trial conduct and performance

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MRC Hubs for Trials Methodology Research

ConDuCT Hub

Bristol Randomised Trials Collaboration

NHS National Institute for Health Research

Trial monitoring: ICH-GCP

- Monitoring aims to verify that:
  - The rights of participants are protected
  - Trial data is accurate, complete and verifiable
  - Trial conduct adheres to the protocol and to GCP
- “Generally there is a need for on-site monitoring, before, during and after the trial”

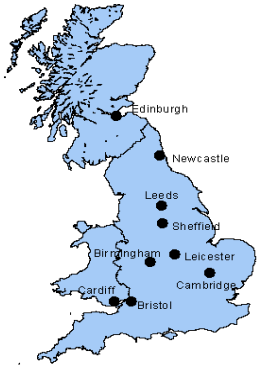
On-site trial monitoring systems

- Systematic review of on-site monitoring literature (2010)
- Little consistency of processes
- Poor evaluation of costs/benefits
- Mostly US non-commercial trials & groups (e.g. NCI & VA)

Research aims

- Design on-site monitoring system utilising best evidence
- Focus on pragmatic phase III trials
- Evaluation, process evaluation and costs

PRIME structure



Peer reviewers
TM & 2 site nurses (from 5)

Annual PRIME visits to all sites
(1-2 d)

SOP & report template

Exit meeting & problem solving

Report to CIs & local PI

PRIME intervention

Component	Objective	PRIME activity	Hours
Training	Training	Site staff training discussion	0.5
Orientation	Training	Orientation & trial progress meeting	0.5
Site performance	Performance	Site recruitment and attrition rates	
Site organisation	Performance	Coordinating centre communication	0.5
Protocol adherence	GCP	Observation, feedback & meetings	6
Data collection	GCP	Observation of CRF completion	1
Safety monitoring	GCP	Review process & documentation	0.5
Documentation	GCP	Site file review	1

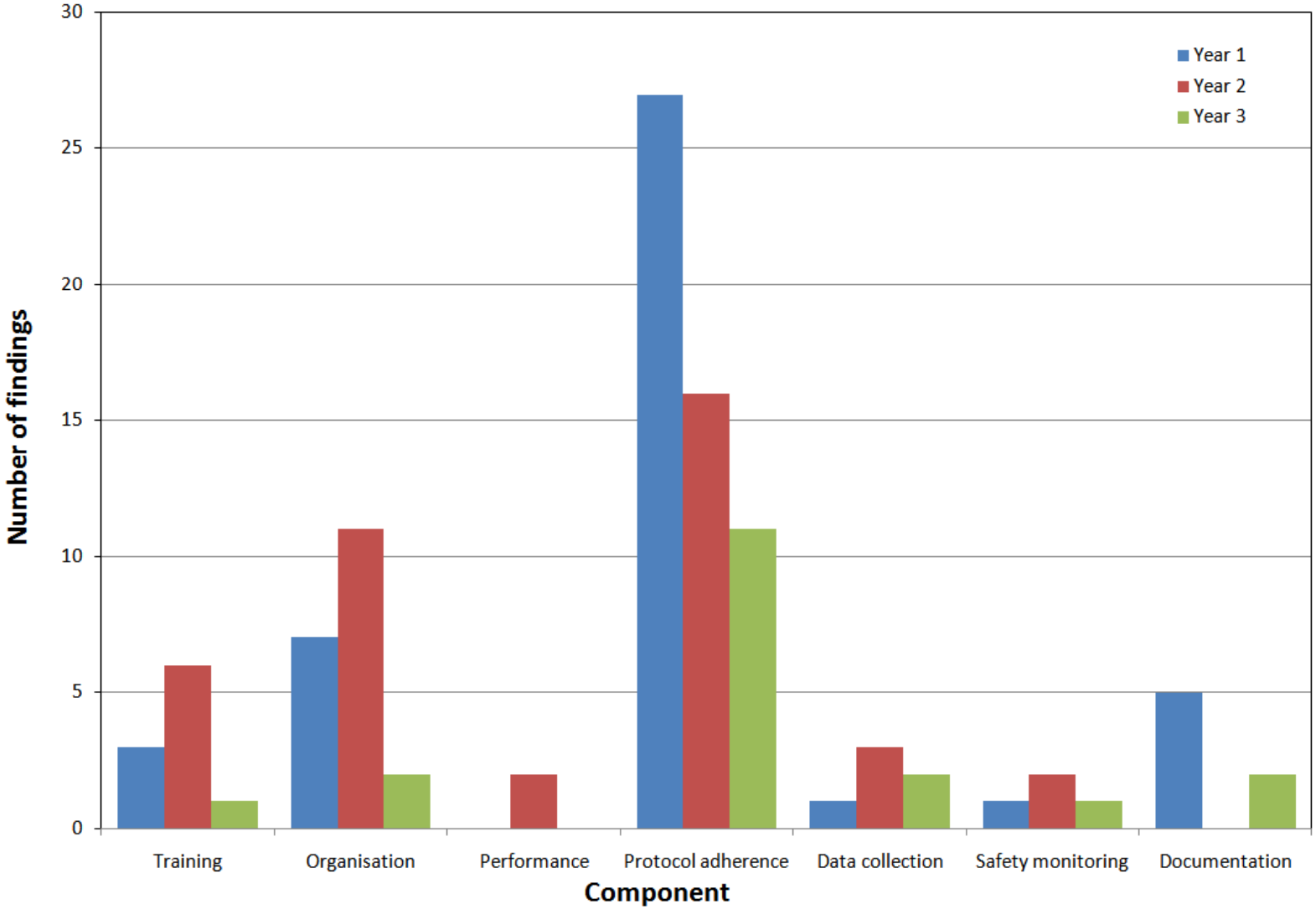
Trial conduct observation

- Recruitment & follow-up appointments
- Individual feedback given to site staff
- Errors difficult to identify otherwise
  - Local exclusion criteria
  - Weight taken with shoes on

Evaluation of PRIME

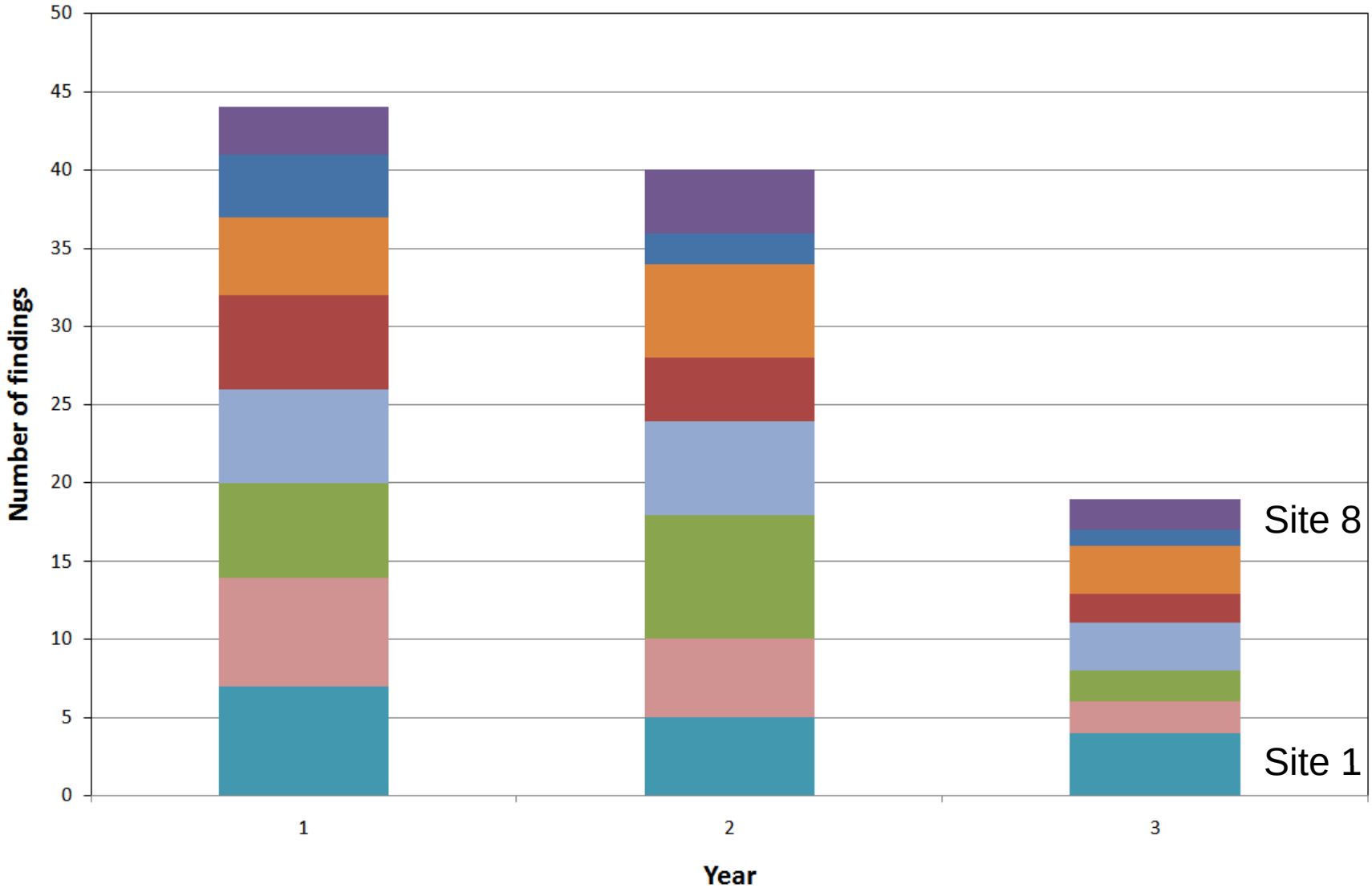
- ProtecT: pragmatic phase III trial of prostate cancer treatments (NIHR HTA) (ISRCTN20141297)
- Site monitoring reports analysed:
  - Findings by PRIME component and objective
  - Findings over three years and by site
  - Resolution of findings
- Resource use

Findings by component and year

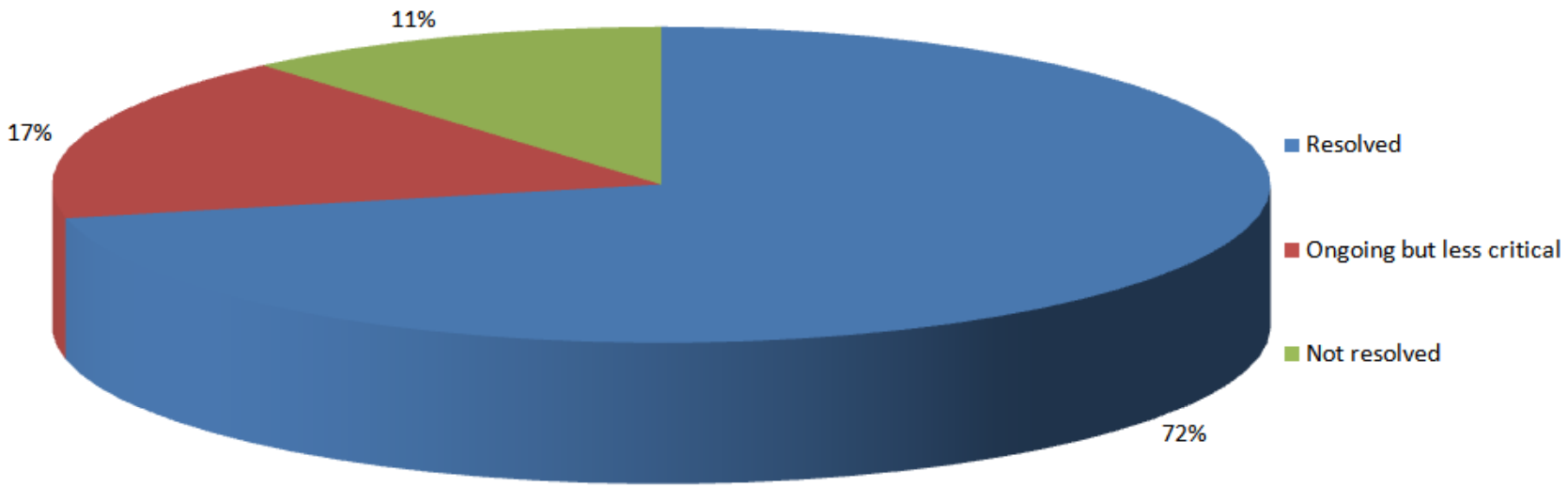


Training Performance ← GCP adherence →

Findings by year for eight sites



Resolution of findings



Percentage of findings resolved by subsequent PRIME visit

PRIME benefits and costs

- Benefits: site performance gains, e.g.
  - Increased radiotherapy CRF return (65%)
- Study cohesion & communication
- Identifies individual and study training needs
- “Useful for ensuring everything is in order! Good for sharing good practice” (staff survey)
- Annual costs: staff time (32-56 d) & $7,337 direct costs

Summary

- PRIME visits annually to all trial sites
- Standardises trial conduct & good practice
- Site staff focus including as peer reviewers
- Improves GCP compliance
- Performance gains
- Adapting for other trials currently
- PRIME : J Clin Epi 2011 64: 628-36: Lane JA