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SUPPLEMENTARY APPENDIX 1

Data assumption and methods used for calculation of resource use costs

CDI MEDICINES / OTHER MEDICINES

The 2014 BNF¹ costs were used. These prices do not reflect any hospital discount.

For patients with rCDI, the period between CDI episodes was defined as starting 72 hours after the stop date of CDI drugs given for their first CDI episode, up to and including the day prior to confirmation by positive test of the CDI recurrence. Hence any CDI medication given prior to this positive test for CDI is not included in the costs for the 28 day post-index observation period.

In the few cases where patients did not receive CDI specific treatment, had no clear stop date or were reported as on continuous antibiotics:

- For patients who were on no CDI medication, the between-episode observation period was taken from the date 14 days after the first positive CDI test (14 days = the median number of days all other patients were on CDI medication [11 days] plus 72 hours) up to the day before recurrence.
- Patients with no clear stop date for CDI medication for the initial episode were excluded from analysis of the between episode observation period.
- Patients on continuous CDI medication following the initial episode were excluded from analysis of the between episode observation period.

Dose / route

Where multiple routes were recorded as being given to the same patient e.g. oral (PO) and intravenous (IV) a mean of the PO and IV costs were used.

Where there were missing doses/routes these were replaced with a standard dose and route under the clinical guidance of a pharmacist employed by pH Associates.

Dates

If only a start date was recorded and no stop date, then the length of a usual course for a specific medication was applied as directed by a pH Associates pharmacist. If there was no stop date but a comment such as 'ongoing/continuing', 'on discharge' was provided, the end date was considered to be the date of the end of the observation period.

If there was no start date recorded but a comment such as 'pre study', 'on admission' was recorded, the start date was considered to be the date of the beginning of the observation period.

In the few cases where neither start nor stop dates were recorded and:

- the medication was considered to be one that is used on a long term basis:

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- the start date was considered to be the date of the beginning of the observation period and the stop date the date of the end of the observation period
- the medication was considered to be one that is given on a short term basis:
 - where the drug costs had a considerable impact on resource, the costs for a standard course were applied
 - where the drug costs were minimal (e.g. paracetamol) no costs were applied

IV FLUIDS

Fresenius Kabi price list 2014² was used for pricing IV fluids. These prices do not reflect any hospital discount.

Where Potassium Chloride (KCl) was recorded but no dose stated then the 20 mmol KCl in Sodium Chloride 0.9% (Saline) IV price was used.

Where 'lost drug chart', 'unable to determine', 'notes unavailable' was recorded on the IV fluids form, no costs were applied.

Where 'unknown solution' has been recorded or quantity not recorded, no costs were applied.

HOSPITAL OUTPATIENT APPOINTMENTS

Outpatient appointment costs were taken from the NHS England National Tariff prices for 2014-15.³

Assumptions:

- Assumed a 'follow-up' appointment unless otherwise stated
- Assumed single healthcare professional unless otherwise stated
- A general 'follow-up' appointment had the cost of a Gastroenterology follow-up appointment applied based on the relevance of this specialty to CDI.
- For those outpatient appointments where a cost was not identified, the median cost of all outpatient appointments was used.

| Outpatient Type | Cost per visit |
|---|-----------------------|
| Infectious Diseases | £209.00 |
| General Surgery first | £140.00 |
| General Surgery follow up | £81.00 |
| Geriatric Medicine first | £253.00 |
| Vascular Surgery follow up | £92.00 |
| Haematology Day Case | £408.00 |
| Clinical Haematology | £111.00 |
| General Medicine | £101.00 |
| General Renal Disorders with length of stay 1 day or less | £408.00 |
| Ear Nose and Throat (ENT) | £62.00 |
| Medical Oncology | £91.00 |
| Dermatology | £68.00 |

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| Outpatient Type | Cost per visit |
|---|-----------------------|
| CT 2 areas | £300.00 |
| Diabetic Medicine | £99.00 |
| Dietetics (estimate) | £75.00 |
| Echocardiograph | £100.00 |
| Gastroenterology | £101.00 |
| General Renal Disorders with length of stay 1 day or less | £408.00 |
| Hepatobiliary & Pancreatic Surgery | £101.00 |
| Geriatric Medicine | £134.00 |
| Orthopaedics | £70.00 |
| Podiatry | £99.00* |
| Clinical Oncology | £91.00 |
| Speech and Language Therapy | £99.00* |
| General Surgery | £81.00 |
| Vascular follow-up | £92.00 |

* Median of all outpatient costs used

Where 'DNA' (did not attend) was recorded against an outpatient appointment, costs were applied as for a regular outpatient appointment.

EMERGENCY DEPARTMENT (ED) ATTENDANCES

ED attendance costs were taken from the NHS England National tariff prices for 2014-15.³

HOSPITAL STAYS

Where 'ICU' was recorded, this has been considered to refer to intensive care and costs for intensive therapy unit (ITU) attributed.

Where a side room was recorded, the cost of a general ward was applied.

Where a patient was recorded as attending ED the day before an in-patient admission it was assumed that the patient was admitted overnight and a ward night cost was applied in addition to the cost of ED attendance.

COST OF HOSPITAL BED NIGHTS

| Hospital bed cost per night | Cost | Reference |
|---|-------------|-------------------|
| Medical Ward | £275 | 4 |
| Surgical Ward* | £275 | 4 |
| Emergency Medical Unit (Acute Medical Unit) | £124 | 4 |
| Critical Care: Intensive Care Unit (ICU) Adults | £1,400 | 3, 5 [‡] |
| Critical Care: High Dependency Unit (HDU) Adults | £1,000 | 3, 5 [‡] |

* Cost of surgical procedure (if performed) not included.

[‡] Also personal communication (Service Level Agreement PCT:Trust 2012). Ratified by NHS Wales costs.

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INVESTIGATIONS AND PROCEDURES

The costs of procedures were sourced from the NHS England National Tariff prices for 2014-15.³ If these were unavailable the UCLH Provider-to-provider tariff⁶ was used. In the absence of costs in either of these sources, costs from private providers were used and reduced by 25%.

| Investigations/Procedures | Cost | Reference |
|---|-------------|------------------|
| Barium swallow | £84 | 6 |
| Ultrasound (US) guided central catheter insertion | £150 | 6 |
| Diagnostic bone marrow extraction | £495 | 3 |
| Cholecystectomy | £800 | 6,7 |
| Cholecystectomy open/lap with complications and comorbidities | £2,207 | 3 |
| Immunoglobulin E (IgE) specific test / coeliac serology | £27 | 8 |
| Computed tomography (CT) scan | £150 | 3,6,7 |
| CT scan with contrast | £162 | 6 |
| Bladder intermediate endoscopic procedure 19 years and over (diagnostic cystoscopy) | £438 | 3 |
| Dexascan | £62 | 3 |
| Electrocardiogram (ECG) | £80 | 6,7 |
| ECG 24 hour ambulatory tape | £265 | 6 |
| Echocardiograph | £100 | 3,6,7 |
| Electroencephalograph (EEG) | £120 | 6,7 |
| II endoscopic retrograde cholangio pancreatography (ERPC) stent | £320 | 9 |
| SP sinogram | £250 | 9 |
| Contrast fluoroscopy procedures 20-40 minutes | £118 | 6 |
| Magnetic resonance (MR) cholangiopancreatography | £500 | 9 |
| MR renal angiography | £400 | 9 |
| Magnetic resonance imaging (MRI) scan | £250 | 3,6,7 |
| MR venography | £400 | 9 |
| Nephrostomy | £468 | 10 |
| Nephrostogram | £400 | 9 |
| Nuclear medicine (NM) gallium scan whole body | £450 | 10 |
| X ray mandible | £55 | 9 |
| NM renogram | £486 | 8 |
| Lung - ventilation with Tc99m aerosol | £511 | 8 |
| Lung - perfusion and ventilation with krypton | £595 | 8 |
| Patch testing | £136 | 8 |
| Percutaneous endoscopic gastrostomy | £200 | 6 |
| Peripherally inserted central line (US guided injection) | £150 | 6 |
| Renal - static renogram | £486 | 8 |
| Radiotherapy | £449 | 8 |
| Rectal biopsy | £500 | 3 |
| Tubogram /linogram | £250 | 9 |
| Ureteric / bladder disorders with CC | £1,249 | 3 |
| II Other line insertion | £90 | 9 |

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| Investigations/Procedures | Cost | Reference |
|---|-------------|------------------|
| US aspiration of fluid | £112 | 9 |
| US guided biopsy | £127 | 6 |
| US guided drainage | £258 | 6 |
| US guided nephrostomy with CC | £4,014 | 3 |
| Ultrasound scan | £60 | 3,6 |
| Ultrasound scan (venous) | £200 | 9 |
| Vascular duplex scan (NM) | £92 | 6 |
| Water soluble contrast swallow | £81 | 6 |
| Water soluble contrast swallow and meal | £223 | 8 |
| X-ray (abdomen/chest/mandible) | £45 | 6,7 |
| X-ray (spine) | £50 | 6,7 |

LABORATORY COSTS

Laboratory costs were sourced through personal communication with the Principal Investigators at Leeds Teaching Hospitals NHS Trust and NHS Greater Glasgow and Clyde.

| Laboratory test | Cost | Also includes tests recorded as: |
|---|-------------|--|
| Acid-Fast Bacilli (AFB) culture | £31.10 | |
| Alpha-fetoprotein (AFP) | £5.83 | |
| Amikacin | £8.75 | |
| Amiodarone | £37.51 | |
| Amylase | £3.95 | |
| Anti-factor XA level | £37.91 | |
| Anti-myeloperoxidase | £11.66 | |
| Anti-Nuclear Antibody (ANA) | £7.78 | |
| Anti-proteinase 3 antibody | £11.66 | |
| Anti-Neutrophil Cytoplasmic Antibody (ANCA) | £11.66 | |
| Beta natriuretic peptide (BNP) | £10.00 | |
| Beta-2-microglobulin | £8.75 | |
| Blood cross match | £7.78 | Blood typing / antibodies, HLA typing, CAM |
| Bone profile | £3.50 | Bone profile inc phosphate |
| C Diff | £8.88 | CDT |
| C Diff +ve | £13.32 | INFC CDCU |
| CA125 | £11.66 | |
| CA15.3 | £22.36 | |
| CA19.9 | £16.53 | |
| Calcium | £3.95 | inc Adjusted calcium, phosphate and serum phosphate, P |
| Carcinoembryonic antigen (CEA) | £15.00 | |
| Cholesterol | £2.92 | TCHOLS |
| Chlamydia | £8.75 | Chlamydia ELISA |

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| Laboratory test | Cost | Also includes tests recorded as: |
|--|-------------|--|
| Cytomegalovirus (CMV) / Immunoglobulin G (IgG) Qualitative | £8.75 | CMV viral load, CMV/DNA qualitative, CMV/DNA quantitative copies, Viral serology – Toxoplasma IgG |
| Cortisol | £3.50 | |
| Creatine kinase | £1.50 | |
| C-Reactive protein (CRP) | £8.88 | |
| Ciclosporin | £27.23 | |
| D Dimer | £11.66 | |
| Digoxin | £11.66 | DIG |
| Extractable nuclear antigen (ENA) antibody | £16.53 | |
| Epstein Barr virus polymerase chain reaction (PCR) | £11.66 | Galactomannan |
| Erythrocyte sedimentation rate (ESR) | £5.83 | Plasma viscosity (plus 3.89) |
| Faeces | £16.78 | Campylobacter/Shigella/Salmonella/E. coli0157 / Norwalk rotavirus / Helicobacter pylori, Cryptosporidium, MID Specimen – faeces PCR- Norovirus, Rotavirus, Sapovirus, Astrovirus, Adenovirus PCR, STC |
| Full blood count (FBC) | £5.92 | MCV, neutrophils, basophils, monocytes, lymphocytes, MCH, WBC, nucleated red cells, NRB, Hb, HCT, platelet count, blood, reticulocyte count, RETICS, fluid cell count, PLT, RBC, eosinophils, full blood group |
| FK506 | £27.23 | |
| Fluid Protein | £2.92 | Protein S, Protein C |
| Factor VIII assay | £18.47 | FVII inhibitor screen |
| Gentamicin level | £2.00 | |
| Glucose | £1.50 | Serum glucose, G |
| Glycated Haemoglobin | £5.83 | Hemoglobin A1c, HbA1c, A1C, or Hb1c, |
| Herpes simplex type I & II PCR | £11.66 | |
| Human immunodeficiency virus (HIV) screen | £8.75 | Viral serology (Hep B,C and HIV screen), Hepatitis screen, Hep C screen |
| I Complement C3+C4 | £8.75 | Serum complement |
| Immunoglobulins | £4.50 | IgA; IgG; IgM; IgE 7 IgD, |
| International normalised ratio (INR) | £5.92 | Coagulation screen / clotting / Fibrinogen level / Oral anticoagulant control /APTT / PT / Heparin control (including INR), APTT ratio, ATTP ratio, standard COAG profile, heparin assay |
| Lactate dehydrogenase (LDH) | £2.92 | |
| Legionella | £16.53 | Legionella sample, Legionella culture |
| Liver function test (LFT) | £3.95 | ALB and ALK phos, ASL , ALT, GGT, serum protein, globulin, bilirubin, total protein, albumin |
| Luteinizing hormone (LH) + follicle stimulating hormone | £8.75 | |

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| Laboratory test | Cost | Also includes tests recorded as: |
|---|--------|---|
| (FSH) | | |
| Lipid profile | £4.50 | Fluid triglycerides |
| Magnesium | £5.92 | MG |
| Mast cell tryptase | £22.36 | |
| Methicillin-resistant staphylococcus aureus (MRSA) screen | £15.79 | MRSA MRPC |
| Mycoplasma serology | £46.67 | Mycoplasma culture, Mycoplasma PCR |
| Paraprotein | £16.00 | IgS and paraproteins |
| Parathyroid hormone | £16.53 | |
| Phenytoin level | £5.83 | |
| Procalcitonin | £15.55 | |
| Prothrombin gene variant (PGV) | £5.83 | Prothrombin time |
| Prostate specific antigen (PSA) | £8.75 | |
| Rheumatoid factor | £8.75 | |
| Serum copper | £13.61 | |
| Serum ferritin | £5.92 | Ferritin, Ferritin assay, Iron/Transferrin, iron, serum iron, (I)Iron + iron saturation, |
| Serum haptoglobin | £8.75 | |
| Serum osmolality | £1.50 | Blood - osmolality |
| Serum selenium | £13.61 | |
| Serum zinc | £13.61 | |
| Sex hormone binding globulin (SHBG) | £16.53 | |
| Sickle cell / thalassemia screen + FBC | £15.00 | |
| Sodium | £3.95 | Serum sodium |
| Specimen for acid alcohol fast bacilli (AAFB) | £24.31 | AAFB culture |
| Swabs for microscopy, culture and sensitivity (MC&S) | £15.55 | (Per swab) Abdo wound swab, Abdo pus drain culture, Stomach / pus culture, Abdo aspirate culture, Swab (MC), Penile swab MCS, Ascitic fluid, Pleural fluid MC+S, Ascitic fluid (MCS), Synovial fluid MC+S, Sputum, Wound swab, MC+S, synovial fluid MC+S, Throat swab, Pus MC+S, Sputum MC+S, TIP MC+S, Arterial line, Wound swab, Wound swab - MC&S, Endotracheal swab - MC&S, Pus swab, Tissue MC+S, Sputum, Extended Culture fluid, Ascitic Fluid Small Volume, Extended Culture PUS, Extended Culture SWAB, Throat, Ascitic fluid culture, Throat swab, R+L eye swab, Pus culture, Sputum, microbiology, Eye swabs, Sputum culture, blood culture, general pathology, MID Specimen – throat gargle PCR, MID Specimen – plasma adenovirus, CMV, EBV PCR, Respiratory virus PCR, catheter tip, Specimen for PCR, blood film microscopy, Miscellaneous fluids, Respiratory multiplex RT-PCR, TIP |

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| Laboratory test | Cost | Also includes tests recorded as: |
|--|--------|---|
| Syphilis enzyme immunoassay (EIA) | £13.61 | |
| Testosterone + SHBG | £11.66 | |
| Thyroid function test | £7.00 | Free thyroxine, free T4 plasma, thyroid stimulating hormone, TFT, endocrine tests |
| Total human chorionic gonadotropin (HCG) | £5.83 | |
| Troponin | £3.50 | Cardiac markers |
| Urine microalbumin | £8.75 | |
| Urate | £2.92 | |
| Urea & Electrolytes (U&E) | £3.95 | Chloride, bicarbonate, fluid U&E, routine biochemistry, potassium, serum creatinine, urine electrolytes, GFR, renal, eGFR, routine urine biochemistry, urine creatinine |
| Urine (MC&S) | £8.88 | Catheter specimen of urine, MSU, CSU |
| Urine electrophoresis | £11.66 | Protein electrophoresis, Bence-Jones protein - urine |
| Urine osmolality | £2.00 | Protein / creatinine ratio in urine / fluid protein |
| Vancomycin level | £2.00 | |
| Vitamin B 12 | £11.84 | Serum folate, haematinics |
| Vitamin D | £15.00 | |

The laboratory data at one of the participating centres was incomplete; all laboratory data from this centre was excluded from analysis of laboratory costs.

A market forces factor index was applied to costs at each centre as below:

MARKET FORCES FACTOR INDEX (MFFI)

| Centre | Centre name | MFFI | Reference |
|--------|---|---------|-----------|
| 1 | Leeds Teaching Hospitals, NHS Trust | 1.04610 | 11,12 |
| 2 | Royal Free London, NHS Trust | 1.24648 | 11,12 |
| 4 | Multiplier for Scotland | 1.20000 | 11 |
| 5 | Brighton and Sussex University Hospitals NHS Trust | 1.07439 | 11,12 |
| 6 | City Hospitals Sunderland, NHS Foundation Trust | 1.02633 | 11,12 |
| 7 | Central Manchester University Hospitals, NHS Foundation Trust | 1.05737 | 11,12 |

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