**Figure 1: CODIFI2 Trial design (2pages)**

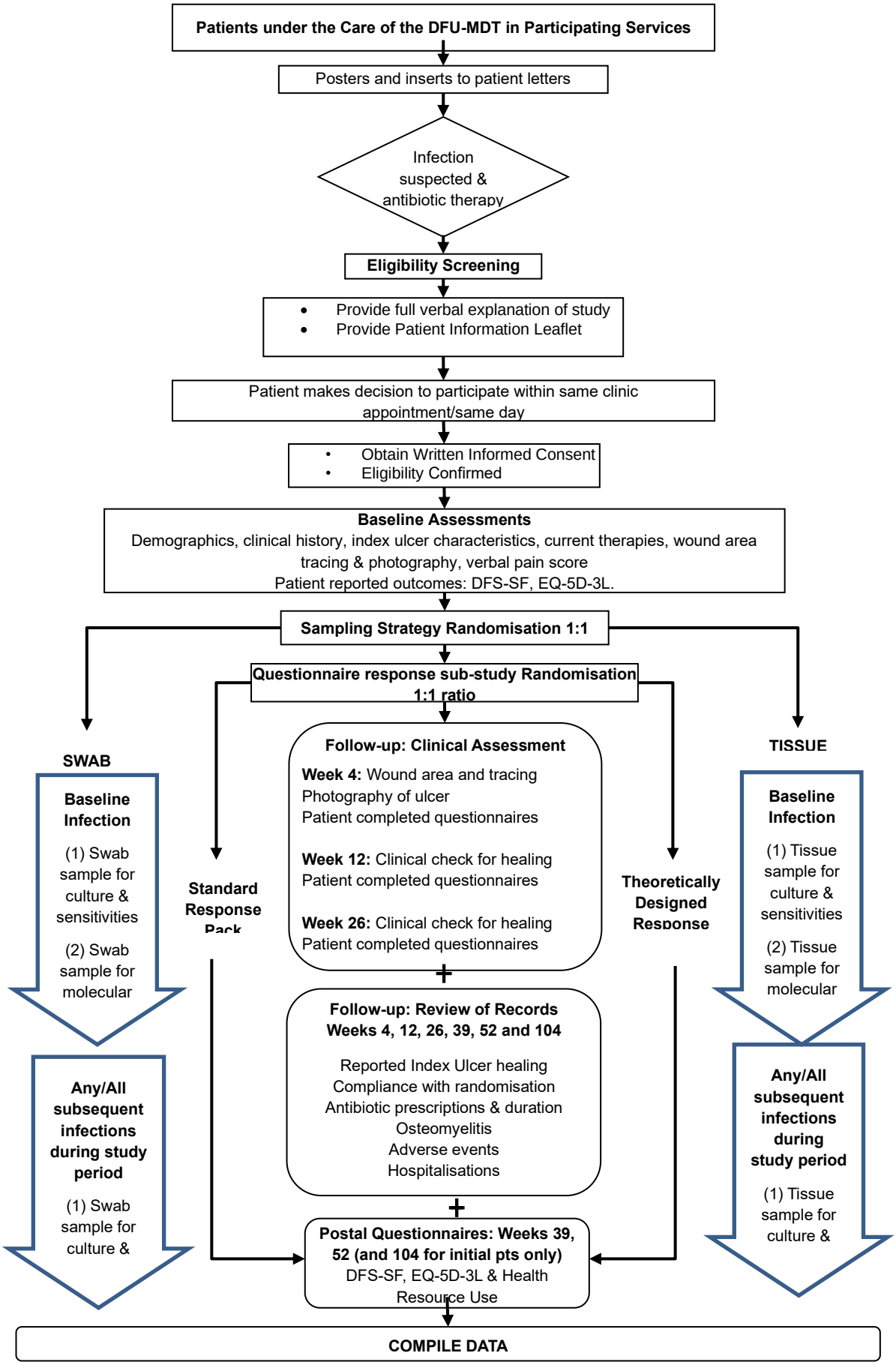

**Figure 1 (continued)**

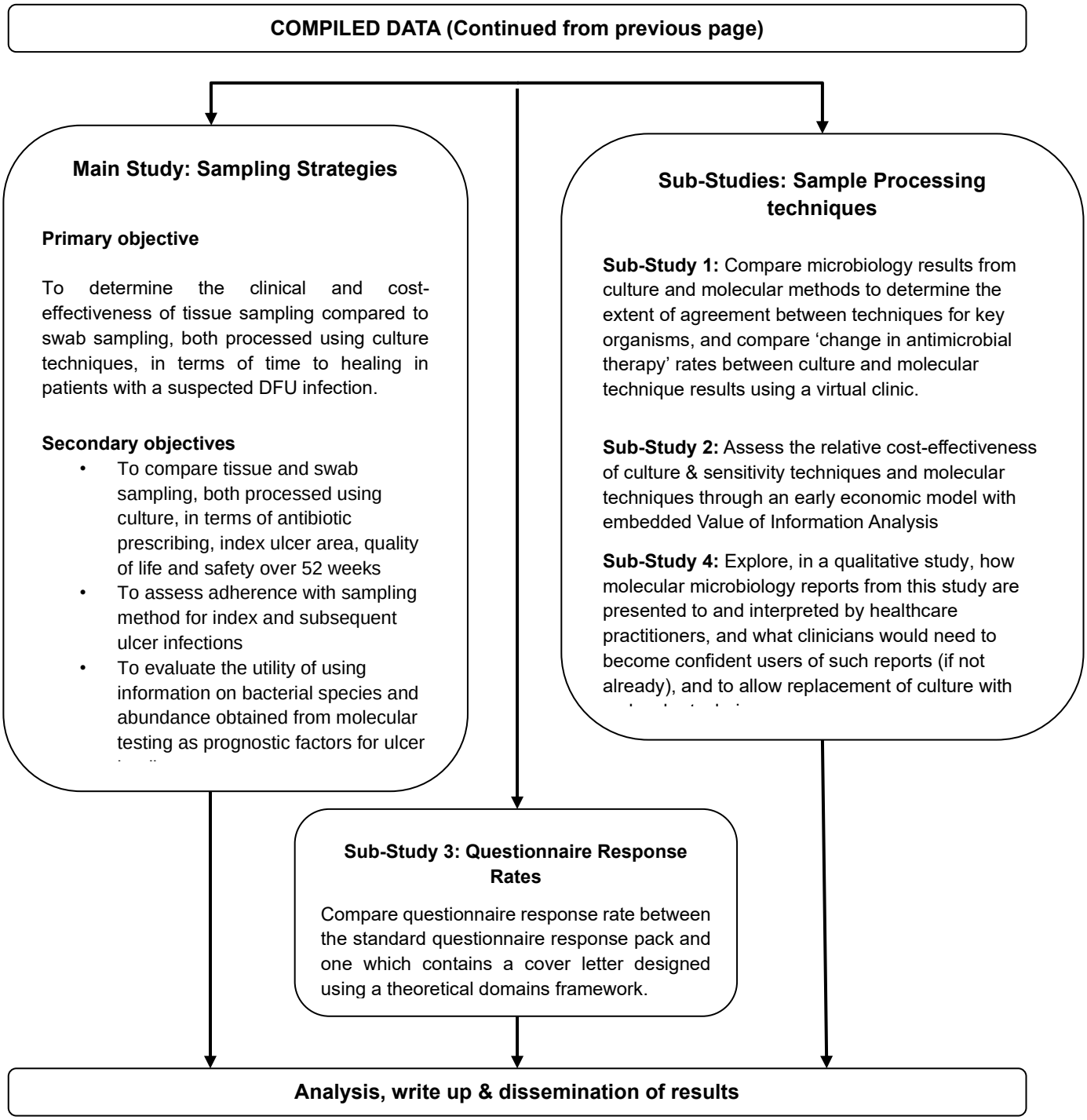

**Table 1: Baseline demographic, diabetes and diabetic foot characteristics**

| | Swab sampling (n=75) | Tissue sampling (n=74) | Total (n=149) |
|---|---|---|---|
| **Demographic characteristics** | | | |
| Age, years (Mean, (SD)) | 65.7 (11.39) | 59.7 (12.98) | 62.7 (12.54) |
| [Minimum, Maximum] | [32, 93] | [31, 86] | [31, 93] |
| Gender, male | 65 (86.7%) | 58 (78.4%) | 123 (82.6%) |
| Ethnicity, white | 72 (96.0%) | 72 (97.3%) | 144 (96.6%) |
| Current or former smoker | 41 (54.7%) | 45 (60.8%) | 86 (57.7%) |
| **Diabetes Characteristics** | | | |
| Type II Diabetes | 68 (90.7%) | 63 (85.1%) | 131 (87.9%) |
| Duration of diabetes (years) Median [IQR] | 15.0 [10.0, 24.0] | 17.0 [11.0, 21.0] | 16.0 [10.0, 22.0] |
| HbA1c, mmol/mol | 70.1 (22.97) | 73.3 (24.09) | 71.7 (23.49) |
| Current Treatment for diabetes | | | |
| -- Oral hypoglycaemic agent | 52 (69.3%) | 45 (60.8%) | 97 (65.1%) |
| -- Insulin | 37 (49.3%) | 47 (63.5%) | 84 (56.4%) |
| -- Other non-insulin injectables | 8 (10.7%) | 3 (4.1%) | 11 (7.4%) |
| -- Diet alone | 9 (12.0%) | 2 (2.7%) | 11 (7.4%) |
| **Diabetic foot characteristics** | | | |
| DFU present on both feet | 9 (12.0%) | 8 (10.8%) | 17 (11.4%) |
| More than one ulcer at baseline | 54 (72.0%) | 54 (73.0%) | 108 (72.5%) |
| Total DFU reported across both feet, Median [IQR] | 1.0 [1.0, 2.0] | 1.0 [1.0, 2.0] | 1.0 [1.0, 2.0] |
| Diabetic Foot Survey, Short Form scores, Median [IQR] (100=Best QoL) | | | |
| • Leisure | 35 [15, 80] | 50 [15, 80] | 40 [15, 80] |
| • Physical Health | 60 [35, 80] | 60 [30 , 85] | 60 [35, 85] |
| • Dependence | 50 [15, 90] | 70 [35, 95] | 65 [25 , 95] |
| • Negative Emotions | 50 [25, 83.3] | 58.3 [29.2, 83.3] | 58.3 [25, 83.3] |
| • Worried about ulcers/feet | 37.5 [18.8, 75] | 43.8 [12.5, 75] | 37.5 [12.5, 75] |
| • Bothered by ulcer care | 53.1 [31.3, 81.3] | 62.5 [37.5 , 81.3] | 56.3 [37.5, 81.3] |
| **Index DFU characteristics** | | | |
| Index DFU initial (non-recurrent) | 59 (78.7%) | 59 (79.7%) | 118 (79.2%) |
| Index DFU Aetiology | | | |

| | | | |
|---|---|---|---|
| --- Neuro-ischaemic | 10 (13.3%) | 7 (9.5%) | 17 (11.4%) |
| --- Ischaemic | - | 2 (2.7%) | 2 (1.3%) |
| --- Neuropathic | 64 (85.3%) | 65 (87.8%) | 129 (86.6%) |
| --- Normal (Unusual Presentation) | 1 (1.3%) | - | 1 (0.7%) |
| Index DFU Located on forefoot (+/- digits) | 63 (84.0%) | 61 (82.4%) | 124 (83.2%) |
| Duration of index DFU (months) Median [IQR] | 1.0 [0.5 to 3.0] | 2.0 [0.5 to 4.0] | 1.0 [0.5 to 4.0] |
| Index Ulcer Grade | | | |
| --- Grade 1 - Superficial full-thickness | 46 (61.3%) | 52 (70.3%) | 98 (65.8%) |
| --- Grade 2 - Deep ulcer, penetrating to below dermis | 26 (34.7%) | 15 (20.3%) | 41 (27.5%) |
| --- Grade 3 - Affecting all layers, including bone and/or joint | 3 (4.0%) | 7 (9.5%) | 10 (6.7%) |
| Index DFU area ($cm^2$) Median [IQR] | 2.2 [0.7 to 4.7] | 1.1 [0.5 to 3.1] | 1.3 [0.6 to 3.8] |
| **Infection characteristics** | | | |
| Infection Classification | | | |
| --- Grade 2 | 53 (70.7%) | 46 (62.2%) | 99 (66.4%) |
| --- Grade 3 | 22 (29.3%) | 27 (36.5%) | 49 (32.9%) |
| --- Grade 4 | - | 1 (1.4%) | 1 (0.7%) |
| Prior treatments | | | |
| --- Both Antimicrobial / antiseptic dressings and Antibiotics (any indication) | 9 (12.0%) | 9 (12.2%) | 18 (12.1%) |
| --- Antibiotics (any indication) only | 12 (16.0%) | 10 (13.5%) | 22 (14.8%) |
| --- Antimicrobial / antiseptic dressings only | 17 (22.7%) | 15 (20.3%) | 32 (21.5%) |
| --- Neither | 37 (49.3%) | 40 (54.1%) | 77 (51.7%) |

Table 2: Primary Outcome – Estimated cumulative incidence of confirmed healing and competing events at end of follow-up

| First event | Time point (Weeks) | SWAB Cumulative Incidence (95% Confidence interval) | TISSUE Cumulative Incidence (95% Confidence interval) | ALL Cumulative Incidence (95% Confidence interval) |
|---|---|---|---|---|
| Healed (Primary, blinded confirmation of healing required) | 52 | 45.3% (33.5% to 56.4%) | 44.6% (33.0% to 55.6%) | 44.9% (36.7% to 52.8%) |
| | 104 | 45.3% (33.5% to 56.4%) | 44.6% (33.0% to 55.6%) | 44.9% (36.7% to 52.8%) |
| Amputation involving index DFU | 52 | 12.2% (6.0% to 20.9%) | 13.5% (6.9% to 22.4%) | 12.9% (8.1% to 18.9%) |
| | 104 | 13.9% (7.1% to 23.1%) | 13.5% (6.9% to 22.4%) | 13.8% (8.7% to 20.0%) |
| Died, any causes | 52 | 8.2% (3.3% to 16.0%) | 4.1% (1.1% to 10.5%) | 6.1% (3.0% to 10.8%) |
| | 104 | 15.4% (7.7% to 25.4%) | 7.8% (2.8% to 16.2%) | 11.6% (6.7% to 17.9%) |

Table 3: Safety: Reportable AEs and Serious AEs

| | Swab Sampling | Tissue Sampling | Total |
|---|---|---|---|
| Related and Expected Adverse Events (AE) | | | |
| Participants experiencing at least 1 AE | 47/75 (62.7%) | 59/74 (79.7%) | 106/149 (71.1%) |
| Number of such AEs | (n=129) | (n=195) | (n=324) |
| Related and Expected Serious Adverse Events (SAE) | | | |
| Participants experiencing at least 1 SAE | 21/75 (28.0%) | 25/74 (33.8%) | 46/149 (30.9%) |
| Number of such SAEs | (n=43) | (n=54) | (n=97) |
| Unrelated and Expected Serious Adverse Events (SAE) | | | |
| Participants experiencing at least 1 SAE | 34 (45.3%) | 20 (27.0%) | 54 (36.2%) |
| Number of such SAEs | (n=59) | (n=38) | (n=97) |
| Death | 17 | 7 | 24 |