

**Title:** Cost-effectiveness of multicomponent interventions in type 2 diabetes mellitus in a cluster randomized controlled trial: the INDICA Study

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## Appendix 2. Description of mechanism for imputation of missed data.

Multiple imputation was performed by means of *mi impute chained* using the software Stata 15.0. Imputations were performed in a differentiated way for each of the four treatment groups. The following variables were considered regular and used as predictors to perform imputations: age of onset of the study, sex, baseline smoker status and baseline diabetes treatment. A total of 79 variables were imputed. Each variable was imputed in chronological order: baseline first and afterwards 3, 6, 12, 18 and 24 months. As a general rule, the latest available information of the variable to impute was used. When information from other variables was used the information from the same time moment was used. The imputation was not performed using secondary variables as random effects without fixed effects being used. A total of 90 imputations was performed for every missed data. For some imputations, predictor variables were omitted due to convergence problems.

The following table shows the order of imputation of the variables, the variables used in the imputation, the prediction model and the number of lost data for this variable.

	Imputed variable	Variables used in the imputation	Imputation Model	N missed
1	Mobility EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Duration of Diabetes	mlogit	21
2	Mobility EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L baseline	mlogit	573
3	Mobility EQ-5D-5L, 12 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L 6 months	mlogit	670
4	Mobility EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L 12 months	mlogit	745
5	Mobility EQ-5D-5L, 24 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L 18 months	mlogit	671
6	Self-care EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L baseline	mlogit	27
7	Self-care EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L 6 months	mlogit	577
8	Self-care EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Duration of Diabetes, Mobility EQ-5D-5L 18 months	mlogit	743
9	Usual activities EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L baseline	mlogit	25
10	Usual activities EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 6 months	mlogit	578
11	Usual activities EQ-5D-5L, 12 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 12 months	mlogit	671
12	Usual activities EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 18 months	mlogit	750
13	Usual activities EQ-5D-5L, 24 months	Age, Sex, Diabetes treatment baseline	mlogit	677
14	Pain/Discomfort EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L baseline	mlogit	22
15	Pain/Discomfort EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L baseline	mlogit	575

	<b>Imputed variable</b>	<b>Variables used in the imputation</b>	<b>Imputation Model</b>	<b>N missed</b>
16	Pain/Discomfort EQ-5D-5L, 12 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 6 months	mlogit	670
17	Pain/Discomfort EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 12 months	mlogit	743
18	Pain/Discomfort EQ-5D-5L, 24 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 18 months	mlogit	672
19	Anxiety/Depression EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L Baseline, Usual activities EQ-5D-5L Baseline, Pain/Discomfort EQ-5D-5L baseline	mlogit	32
20	Anxiety/Depression EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 6 months, Usual activities EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, Anxiety/Depression EQ-5D-5L baseline	mlogit	575
21	Anxiety/Depression EQ-5D-5L, 12 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 6 months	mlogit	670
22	Anxiety/Depression EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 18 months, Usual activities EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, Anxiety/Depression EQ-5D-5L 12 months	mlogit	745
23	Anxiety/Depression EQ-5D-5L, 24 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 24 months, Usual activities EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 18 months	mlogit	671
24	VAS EQ-5D-5L, baseline	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline	poisson	47
25	VAS EQ-5D-5L, 6 months	Age, Sex, Diabetes treatment baseline, Mobility EQ-5D-5L 6 months, Self-care EQ-5D-5L 6 months, Usual activities EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, Anxiety/Depression EQ-5D-5L 6 months, VAS EQ-5D-5L baseline	poisson	584
26	VAS EQ-5D-5L, 12 months	Age, Smoking status baseline, Mobility EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, VAS EQ-5D-5L 6 months	poisson	686
27	VAS EQ-5D-5L, 18 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Mobility EQ-5D-5L 18 months, Self-care EQ-5D-5L 18 months, Usual activities EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, Anxiety/Depression EQ-5D-5L 18 months, VAS EQ-5D-5L 12 months	poisson	746
28	VAS EQ-5D-5L, 24 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Mobility EQ-5D-5L 24 months, Usual activities EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 24 months, VAS EQ-5D-5L 18 months	poisson	679
29	Lab tests by general practitioner, baseline	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Pain/Discomfort EQ-5D-5L baseline, VAS EQ-5D-5L baseline	poisson	70
30	Lab tests by general practitioner, 3 months	Age, Sex, Smoking status baseline, Comorbidity baseline, Pain/Discomfort EQ-5D-5L 6 months, VAS		490

	Imputed variable	Variables used in the imputation	Imputation Model	N missed
		EQ-5D-5L 6 months, Lab tests by general practitioner baseline		
31	Lab tests by general practitioner, 6 months	Age, Sex, Smoking status baseline, Comorbidity baseline, Pain/Discomfort EQ-5D-5L 6 months, VAS EQ-5D-5L 6 months, Lab tests by general practitioner 3 months	poisson	593
32	Lab tests by general practitioner, 12 months	Age, Comorbidity 12 months, Pain/Discomfort EQ-5D-5L 12 months, Lab tests by general practitioner 6 months	poisson	670
33	Lab tests by general practitioner, 18 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Pain/Discomfort EQ-5D-5L 18 months, VAS EQ-5D-5L 18 months, Lab tests by general practitioner 12 months	poisson	746
34	Lab tests by general practitioner, 24 months	Age, Sex, Comorbidity 24 months, Lab tests by general practitioner 18 months	poisson	676
35	Lab tests by specialist, baseline	Age, Diabetes treatment baseline, Comorbidity baseline	poisson	83
36	Lab tests by specialist, 3 months	Age, Sex, Comorbidity baseline, Lab tests by specialist baseline		539
37	Lab tests by specialist, 6 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Lab tests by specialist 3 months	poisson	597
38	Lab tests by specialist, 12 months	Sex, Smoking status baseline, Comorbidity 12 months, Lab tests by specialist 6 months	poisson	676
39	Lab tests by specialist, 18 months	Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Lab tests by specialist 12 months	poisson	748
40	Lab tests by specialist, 24 months	Age, Sex, Diabetes treatment baseline, Comorbidity 24 months, Lab tests by specialist 18 months	poisson	677
41	Retinography, baseline	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline	poisson	78
42	Retinography, 3 months	Sex, Smoking status baseline, Comorbidity baseline, Retinography baseline	poisson	497
43	Retinography, 6 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Retinography 3 months	poisson	593
44	Retinography, 12 months	Age, Smoking status baseline, Comorbidity 12 months	poisson	669
45	Retinography, 18 months	Age, Smoking status baseline, Comorbidity 12 months	poisson	745
46	Retinography, 24 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 24 months, Retinography 18 months	poisson	676
47	Visits to general practitioner, baseline	Age, Sex, Diabetes treatment baseline, Comorbidity baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline	poisson	147

	Imputed variable	Variables used in the imputation	Imputation Model	N missed
48	Visits to general practitioner, 3 months	Age, Sex, Smoking status baseline, Comorbidity baseline, Mobility EQ-5D-5L Baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline, Visits to general practitioner baseline	poisson	505
49	Visits to general practitioner, 6 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Mobility EQ-5D-5L 6 months, Usual activities EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, Anxiety/Depression EQ-5D-5L 6 months, VAS EQ-5D-5L 6 months, Visits to general practitioner 3 months	poisson	615
50	Visits to general practitioner, 12 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, Visits to general practitioner 6 months	poisson	667
51	Visits to general practitioner, 18 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, Visits to general practitioner 12 months	poisson	746
52	Visits to general practitioner, 24 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 24 months, Mobility EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 24 months, VAS EQ-5D-5L 24 months, Visits to general practitioner 18 months	poisson	672
53	Visits to nurse at primary care, baseline	Age, Sex, Smoking status baseline, Comorbidity baseline, Mobility EQ-5D-5L baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline	poisson	202
54	Visits to nurse at primary care, 3 months	Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, VAS EQ-5D-5L baseline, Visits to nurse at primary care baseline	poisson	511
55	Visits to nurse at primary care, 6 months	Age, Sex, Smoking status baseline, Comorbidity baseline, Mobility EQ-5D-5L 6 months, Usual activities EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, Anxiety/Depression EQ-5D-5L 6 months, VAS EQ-5D-5L 6 months, Visits to nurse at primary care 3 months	poisson	626
56	Visits to nurse at primary care, 12 months	Age, Sex, Smoking status baseline, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, VAS EQ-5D-5L 12 months, Visits to nurse at primary care 6 months	poisson	668
57	Visits to nurse at primary care, 18 months	Sex, Comorbidity 12 months, Usual activities EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, Anxiety/Depression EQ-5D-5L 18 months, Visits to nurse at primary care 12 months	poisson	747
58	Visits to nurse at primary care, 24 months	Age, Sex, Comorbidity 24 months, Mobility EQ-5D-5L 24 months, Usual activities EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 24 months, VAS EQ-5D-5L 24 months, Visits to nurse at primary care 18 months	poisson	670

	<b>Imputed variable</b>	<b>Variables used in the imputation</b>	<b>Imputation Model</b>	<b>N missed</b>
59	Visits to endocrinologist, baseline	Age, Sex, Smoking status baseline, Comorbidity baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, VAS EQ-5D-5L 12 months	poisson	227
60	Visits to endocrinologist, 3 months	Age, Sex, Comorbidity baseline, Mobility EQ-5D-5L baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline, Visits to endocrinologist baseline	poisson	524
61	Visits to endocrinologist, 6 months	Age, Sex, Comorbidity baseline, Mobility EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, VAS EQ-5D-5L 6 months, Visits to endocrinologist 3 months	poisson	630
62	Visits to endocrinologist, 12 months	Age, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, Visits to endocrinologist 6 months	poisson	668
63	Visits to endocrinologist, 18 months	Sex, Comorbidity 12 months, Usual activities EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, VAS EQ-5D-5L 18 months, Visits to endocrinologist 12 months	poisson	744
64	Visits to endocrinologist, 24 months	Age, Sex, Smoking status baseline, Comorbidity 12 months, Usual activities EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 24 months, VAS EQ-5D-5L 24 months, Visits to endocrinologist 18 months	poisson	671
65	Visit to accident & emergency (outpatient centre), baseline	Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Usual activities EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline, VAS EQ-5D-5L baseline	poisson	229
66	Visit to accident & emergency (outpatient centre), 3 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline, Visit to accident & emergency (outpatient centre) baseline	poisson	535
67	Visit to accident & emergency (outpatient centre), 6 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Mobility EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, Anxiety/Depression EQ-5D-5L 6 months, Visit to accident & emergency (outpatient centre) 3 months	poisson	632
68	Visit to accident & emergency (outpatient centre), 12 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, VAS EQ-5D-5L 12 months, Visit to accident & emergency (outpatient centre) 6 months	poisson	671
69	Visit to accident & emergency (outpatient centre), 18 months	Sex, Comorbidity 12 months, Mobility EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, Anxiety/Depression EQ-5D-5L 18 months, Visit to accident & emergency (outpatient centre) 12 months	poisson	748
70	Visit to accident & emergency (outpatient centre), 24 months	Age, Sex, Diabetes treatment baseline, Comorbidity 24 months, Usual activities EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Anxiety/Depression EQ-5D-5L 24 months, VAS EQ-5D-5L 24 months, Visit to accident & emergency (outpatient centre) 18 months	poisson	672

	<b>Imputed variable</b>	<b>Variables used in the imputation</b>	<b>Imputation Model</b>	<b>N missed</b>
71	Visit to accident & emergency (hospital), baseline	Comorbidity baseline, Mobility EQ-5D-5L baseline, Pain/Discomfort EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline	poisson	243
72	Visit to accident & emergency (hospital), 3 months	Comorbidity baseline, Mobility EQ-5D-5L baseline, Usual activities EQ-5D-5L baseline, Anxiety/Depression EQ-5D-5L baseline, VAS EQ-5D-5L baseline	poisson	532
73	Visit to accident & emergency (hospital), 6 months	Age, Comorbidity baseline, Mobility EQ-5D-5L 6 months, Pain/Discomfort EQ-5D-5L 6 months, VAS EQ-5D-5L 6 months	poisson	630
74	Visit to accident & emergency (hospital), 12 months	Age, Sex, Diabetes treatment baseline, Smoking status baseline, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, VAS EQ-5D-5L 12 months, Visit to accident & emergency (hospital) 6 months	poisson	670
75	Visit to accident & emergency (hospital), 18 months	Age, Sex, Comorbidity 12 months, Mobility EQ-5D-5L 18 months, Usual activities EQ-5D-5L 18 months, Pain/Discomfort EQ-5D-5L 18 months, VAS EQ-5D-5L 18 months	poisson	748
76	Visit to accident & emergency (hospital), 24 months	Sex, Diabetes treatment baseline, Comorbidity 24 months, Mobility EQ-5D-5L 24 months, Pain/Discomfort EQ-5D-5L 24 months, Visit to accident & emergency (hospital) 18 months	poisson	672
77	Hospital stays, Baseline	Age, Diabetes treatment baseline, Smoking status baseline, Comorbidity baseline, Pain/Discomfort EQ-5D-5L baseline, VAS EQ-5D-5L baseline, Visit to accident & emergency (hospital) baseline	poisson	11
78	Hospital stays, 12 months	Age, Comorbidity 12 months, Mobility EQ-5D-5L 12 months, Usual activities EQ-5D-5L 12 months, Pain/Discomfort EQ-5D-5L 12 months, Anxiety/Depression EQ-5D-5L 12 months, VAS EQ-5D-5L 12 months, Visit to accident & emergency (hospital) 12 months	poisson	664
79	Hospital stays, 24 months	Age, Mobility EQ-5D-5L 24 months	poisson	670
VAS, Visual Analogue Scale.				