Supplementary material

Detail of the variables of the simulation dataset:

The dataset analysed contained one line per patient' treatment course, and disease activity values available after each treatment cessation were not considered since they are not representative of disease activity on the drug. CDAI at 12 months was calculated in the original dataset as the mean of available CDAI values in a 3-month centered window, whereas $CDAI_0$ is the mean of available CDAI values in a window spanning 6 weeks before treatment start and one week after. As the present simulation study focus on the imputation of missing values due to attrition, missing $CDAI_{12}$ in the original dataset for patients still on treatment after one year were imputed using the nearest CDAI value[5]. prev-bDMARD was set into 4 categories: 0, 1, 2, and 3 or more previous biological DMARD. csDMARD were classified into 4 categories: no treatment, methotrexate, other csDMARD, and methotrexate together with other csDMARD. The treatment status was set to "ongoing" for those who were still on bDMARD therapy at the time of the register extraction or 3 years after treatments start, or one of the following values if the patient stopped its treatment before 3 years: "ineffectiveness" if the treatment was stopped for ineffectiveness, "adverse event" if stopped for an adverse event, "pregnancy" if stopped for pregnancy, "remission" if stopped for remission, "other" when stopped for another reason, and "unspecified" when the reason was missing. We did not consider multiple reason for stopping. Therefore, the order of priority was the following: "adverse event", "pregnancy", "remission", "other", "ineffectiveness", "unspecified".

When used for matching, CDAI variables were divided into 10 categories containing the same amount of values.

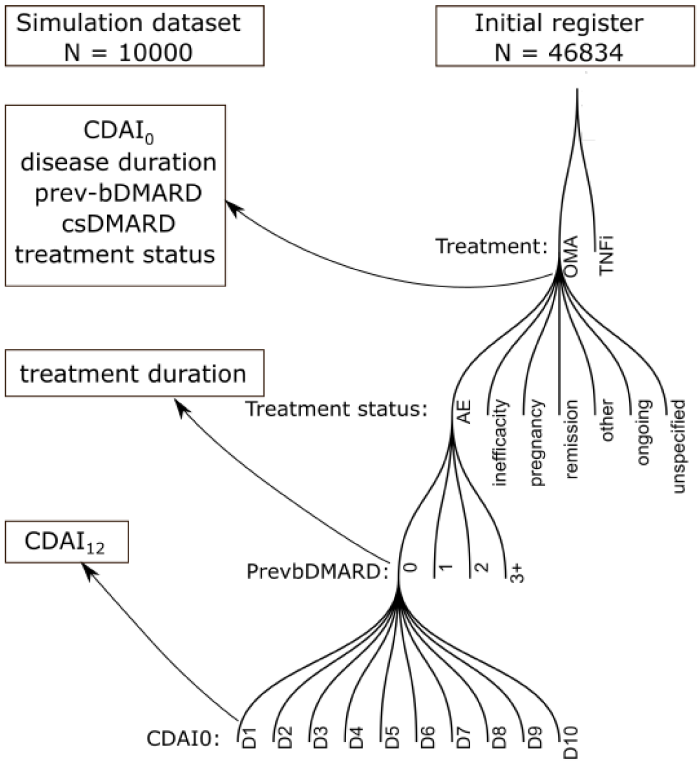

Figure S1: Schematics of the generation process of the simulation dataset: CDAI0, disease duration, prev-bDMARD, csDMARD, treatment status and treatment duration are drawn from the initial register matching the treatments; treatment duration is drawn while matching exactly the treatments, treatments status and the values of previous bDMARD (prevbDMARD); CDAI12 is drawn while matching exactly the treatments, treatments status, the values of previous bDMARD and the categories of CDAI0 (subdivided in 10 deciles: D1 to D10).

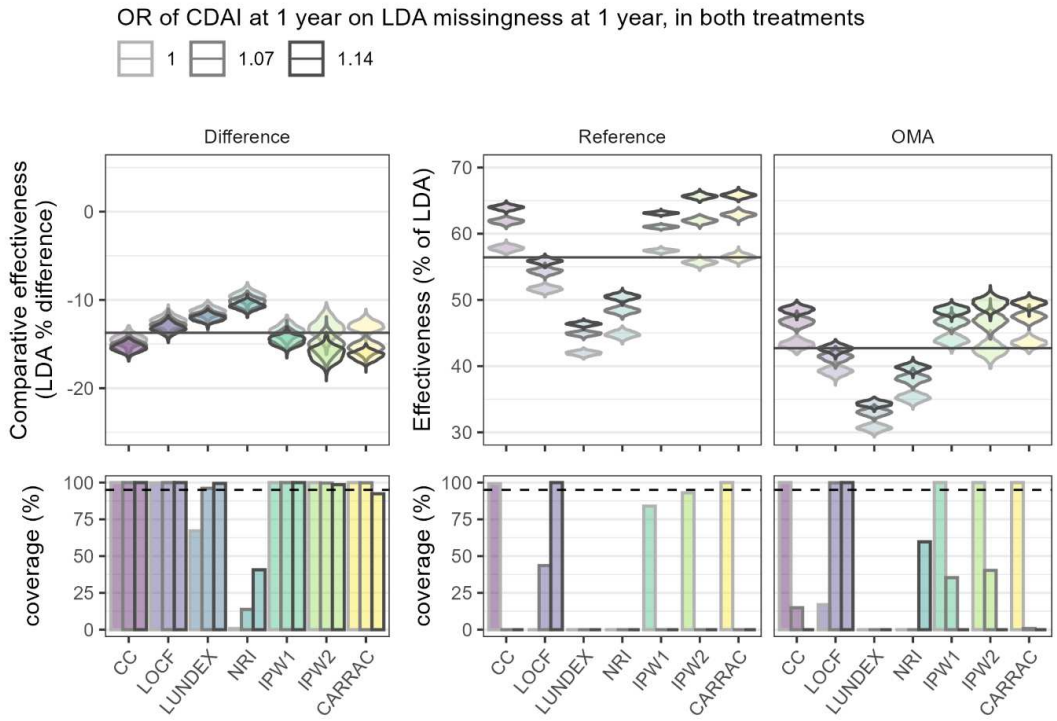

Figure S2: Distribution of the low disease activity (LDA, upper panels) and the associated coverage (lower panels) for each treatment (Reference and OMA, middle and right panels) and for the difference between the treatments (Difference, left panels) for the reference condition and when having missing not at random in both treatments. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC). The widths of the violins are fixed, so the area of the violin does not represent the number of counts. The true value is represented as a black horizontal line.

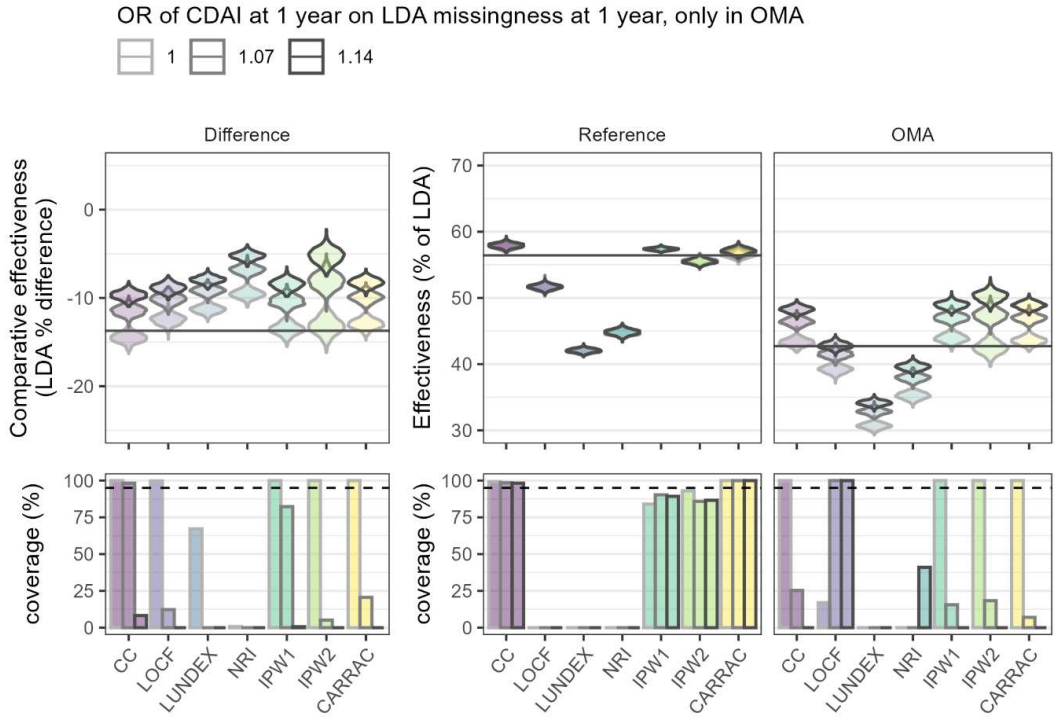

Figure S3: Distribution of the low disease activity (LDA, upper panels) and the associated coverage (percentage of confidence intervals in the simulation samples which include the true value, lower panels) for each treatment (Reference and OMA – other modes of action-, middle and right panels) and for the difference between the treatments (Difference, left panels) for the reference condition and when having missing not at random in OMA. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC). The widths of the violins are fixed, so the area of the violin does not represent the number of counts. The true value is represented as a black horizontal line.

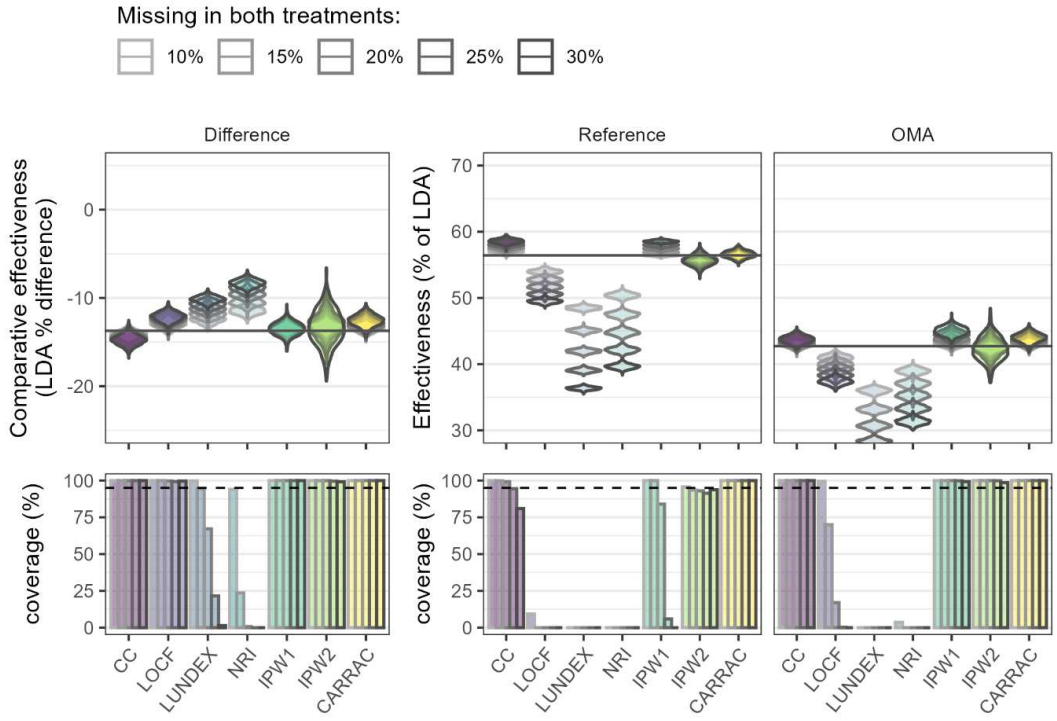

Figure S4: Distribution of the low disease activity (LDA, upper panels) and the associated coverage (percentage of confidence intervals in the simulation samples which include the true value, lower panels) for each treatment (Reference and OMA- other modes of action-, middle and right panels) and for the difference between the treatments (Difference, left panels) for the reference condition (20%) and when changing the attrition in both treatments. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC). The widths of the violins are fixed, so the area of the violin does not represent the number of counts. The true value is represented as a black horizontal line.

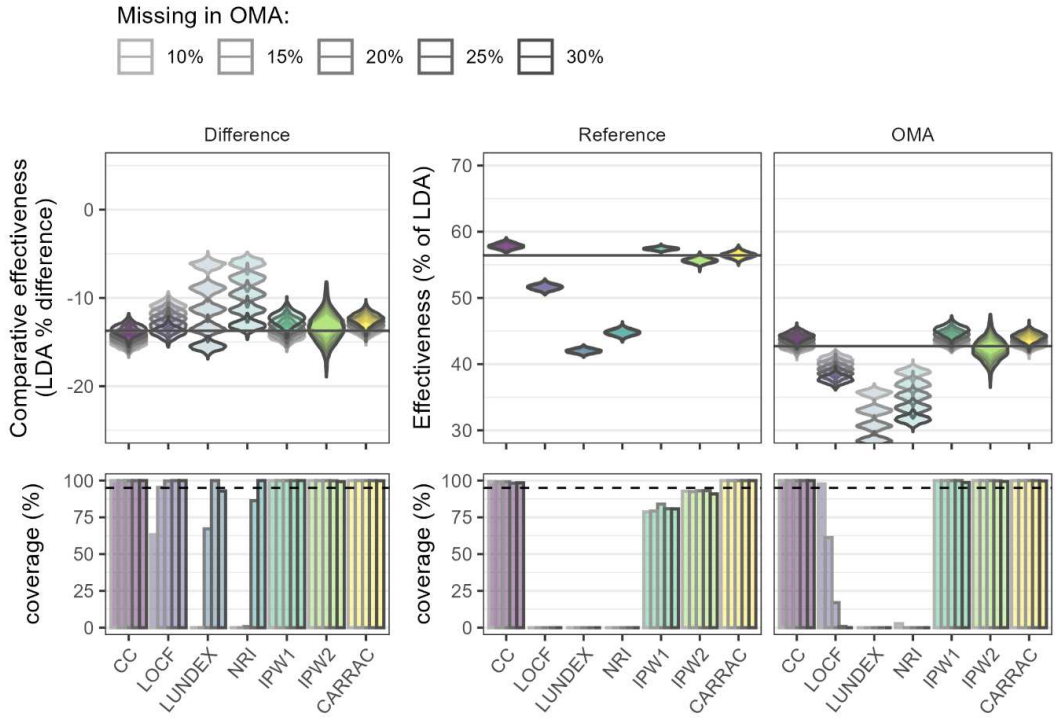

figure S5: Distribution of the low disease activity (LDA, upper panels) and the associated coverage (percentage of confidence intervals in the simulation samples which include the true value, lower panels) for each treatment (Reference and OMA – other modes of action-, middle and right panels) and for the difference between the treatments (Difference, left panels) for the reference condition (20%) and when changing the attrition in OMA. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC). The widths of the violins are fixed, so the area of the violin does

table S1: Median [IQR] of the difference between the estimated LDA difference and the true LDA difference and coverage (cov) of the estimated LDA difference, for each parameter condition and method. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC).

parameter	CC		LOCF		LUNDEX		NRI	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	-0.8 [-1.2, -0.4]	100	1.3 [0.9, 1.7]	99.8	2.4 [2.1, 2.7]	67.1	4.1 [3.9, 4.5]	0.7
2	-1.5 [-1.8, -1.2]	100	2.8 [2.5, 3.1]	63.2	7.5 [7.2, 7.7]	0.0	7.7 [7.4, 8.0]	0.0
3	-1.2 [-1.5, -0.8]	100	2.0 [1.7, 2.4]	95.3	4.8 [4.5, 5.1]	0.0	5.9 [5.6, 6.2]	0.0
4	-0.4 [-0.8, 0.0]	100	0.5 [0.1, 0.9]	100	0.2 [-0.1, 0.5]	100	2.4 [2.1, 2.7]	86.4
5	0.1 [-0.3, 0.5]	100	-0.2 [-0.5, 0.2]	100	-1.8 [-2.1, -1.5]	92.9	0.6 [0.3, 0.9]	100
6	-0.4 [-0.7, -0.1]	100	0.7 [0.4, 1.1]	100	1.3 [1.0, 1.5]	99.8	2.3 [2.0, 2.6]	94.0
7	-0.6 [-1.0, -0.3]	100	1.0 [0.6, 1.4]	100	1.8 [1.5, 2.1]	94.4	3.2 [2.9, 3.6]	23.6
8	-1.0 [-1.3, -0.6]	100	1.5 [1.1, 1.9]	99.3	3.0 [2.7, 3.3]	21.6	4.9 [4.6, 5.2]	0.0
9	-1.1 [-1.5, -0.7]	100	1.6 [1.2, 2.0]	99.7	3.6 [3.3, 3.8]	1.4	5.4 [5.1, 5.7]	0.0
10	2.3 [1.9, 2.6]	98.2	3.6 [3.2, 4.0]	12.3	4.6 [4.3, 4.8]	0.0	6.9 [6.6, 7.2]	0.0
11	4.0 [3.7, 4.4]	8.3	4.9 [4.5, 5.2]	0.0	5.8 [5.5, 6.0]	0.0	8.5 [8.2, 8.7]	0.0
12	-1.5 [-1.9, -1.1]	100	0.8 [0.4, 1.1]	100	1.8 [1.5, 2.1]	96.1	3.4 [3.1, 3.8]	13.8
13	-1.7 [-2.0, -1.4]	100	0.5 [0.2, 0.8]	100	1.7 [1.4, 1.9]	99.4	3.0 [2.8, 3.3]	40.7

parameter	IPW1		IPW2		CARRAC	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	0.2 [-0.2, 0.6]	100	0.5 [-0.1, 1.2]	100	0.8 [0.4, 1.2]	100
2	-0.7 [-1.0, -0.3]	100	0.6 [0.1, 1.0]	100	0.1 [-0.2, 0.4]	100
3	-0.3 [-0.7, 0.1]	100	0.6 [0.0, 1.2]	100	0.4 [0.0, 0.7]	100
4	0.7 [0.3, 1.2]	100	0.5 [-0.4, 1.3]	99.9	1.1 [0.7, 1.5]	100
5	1.4 [0.9, 1.9]	100	0.3 [-0.7, 1.4]	99.3	1.4 [1.0, 1.9]	99.9
6	0.3 [-0.1, 0.6]	100	0.5 [0.1, 0.9]	100	0.3 [0.0, 0.7]	100
7	0.2 [-0.2, 0.6]	100	0.5 [-0.1, 1.0]	100	0.5 [0.2, 0.9]	100
8	0.2 [-0.3, 0.7]	100	0.5 [-0.4, 1.4]	99.6	0.9 [0.6, 1.3]	100
9	0.2 [-0.3, 0.7]	100	0.3 [-0.9, 1.7]	99.2	1.2 [0.7, 1.6]	100
10	3.4 [3.0, 3.8]	82.3	5.6 [5.0, 6.3]	5.2	3.8 [3.4, 4.1]	20.6
11	5.3 [4.9, 5.7]	0.6	8.5 [7.9, 9.1]	0.0	5.5 [5.1, 5.8]	0.0
12	-0.6 [-1.0, -0.2]	100	-1.4 [-2.1, -0.8]	99.7	-1.7 [-2.1, -1.3]	99.9
13	-0.9 [-1.3, -0.5]	100	-2.4 [-3.1, -1.9]	98.6	-2.6 [-2.9, -2.3]	92.4

table S2: Median [IQR] of the difference between the estimated LDA and the true LDA in the reference treatment, and coverage (cov) of the estimated LDA in the reference treatment, for each parameter condition and method. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC).

parameter	CC		LOCF		LUNDEX		NRI	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	1.4 [1.1, 1.6]	99.2	-4.8 [-5.1, -4.5]	0.0	-14.5 [-14.7, -14.3]	0	-11.7 [-11.9, -11.3]	0
2	1.3 [1.1, 1.5]	99.3	-4.8 [-5.0, -4.5]	0.0	-14.5 [-14.7, -14.3]	0	-11.6 [-11.9, -11.3]	0
3	1.4 [1.1, 1.6]	99.1	-4.8 [-5.1, -4.5]	0.0	-14.5 [-14.7, -14.3]	0	-11.6 [-11.9, -11.3]	0
4	1.4 [1.1, 1.7]	98.2	-4.8 [-5.1, -4.5]	0.0	-14.5 [-14.7, -14.3]	0	-11.7 [-12.0, -11.4]	0
5	1.4 [1.2, 1.7]	98.4	-4.8 [-5.1, -4.6]	0.0	-14.4 [-14.6, -14.2]	0	-11.6 [-12.0, -11.4]	0
6	0.6 [0.4, 0.9]	100	-2.5 [-2.7, -2.3]	9.4	-7.9 [-8.1, -7.7]	0	-6.0 [-6.3, -5.8]	0
7	1.0 [0.7, 1.2]	99.9	-3.7 [-3.9, -3.4]	0.0	-11.4 [-11.5, -11.2]	0	-8.9 [-9.2, -8.7]	0
8	1.7 [1.5, 2.0]	94.5	-5.9 [-6.1, -5.6]	0.0	-17.4 [-17.5, -17.2]	0	-14.3 [-14.6, -14.0]	0
9	2.1 [1.9, 2.4]	81.0	-6.9 [-7.1, -6.7]	0.0	-20.1 [-20.2, -19.9]	0	-16.8 [-17.0, -16.6]	0
10	1.4 [1.2, 1.7]	98.5	-4.8 [-5.1, -4.5]	0.0	-14.4 [-14.6, -14.2]	0	-11.7 [-11.9, -11.4]	0
11	1.5 [1.3, 1.8]	98.2	-4.8 [-5.0, -4.5]	0.0	-14.4 [-14.6, -14.2]	0	-11.6 [-11.9, -11.3]	0
12	5.5 [5.2, 5.7]	0.0	-2.1 [-2.4, -1.9]	43.6	-11.5 [-11.7, -11.4]	0	-8.0 [-8.3, -7.8]	0
13	7.5 [7.3, 7.7]	0.0	-0.5 [-0.8, -0.3]	100	-10.0 [-10.2, -9.9]	0	-5.9 [-6.2, -5.7]	0

parameter	IPW1		IPW2		CARRAC	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	1.0 [0.9, 1.1]	84.0	-0.8 [-1.0, -0.6]	93.0	0.0 [-0.2, 0.3]	100
2	1.0 [0.9, 1.2]	78.7	-0.8 [-1.0, -0.5]	92.8	0.0 [-0.3, 0.3]	100
3	1.0 [0.9, 1.1]	79.3	-0.8 [-1.0, -0.5]	92.5	0.0 [-0.2, 0.3]	100
4	1.0 [0.9, 1.1]	80.8	-0.8 [-1.1, -0.5]	93.1	0.1 [-0.2, 0.4]	100
5	1.0 [0.9, 1.1]	80.7	-0.8 [-1.0, -0.5]	90.9	0.1 [-0.2, 0.4]	100
6	0.0 [-0.1, 0.2]	100	-0.8 [-0.9, -0.6]	95.7	0.0 [-0.2, 0.3]	100
7	0.5 [0.4, 0.6]	100	-0.8 [-1.0, -0.6]	93.6	0.0 [-0.2, 0.3]	100
8	1.5 [1.4, 1.7]	5.9	-0.8 [-1.1, -0.4]	91.4	0.1 [-0.2, 0.4]	100
9	2.1 [2.0, 2.2]	0.0	-0.8 [-1.3, -0.3]	93.8	0.1 [-0.3, 0.5]	100
10	0.9 [0.8, 1.1]	90.3	-0.9 [-1.2, -0.7]	85.8	0.5 [0.2, 0.8]	100
11	0.9 [0.8, 1.1]	89.3	-0.9 [-1.2, -0.7]	86.6	0.7 [0.4, 1.0]	100
12	4.6 [4.5, 4.7]	0.0	5.5 [5.3, 5.8]	0.0	6.4 [6.2, 6.7]	0
13	6.7 [6.6, 6.8]	0.0	9.2 [9.0, 9.4]	0.0	9.4 [9.2, 9.6]	0

table S3: Median [IQR] of the difference between the estimated LDA and the true LDA in the OMA treatment, and coverage (cov) of the estimated LDA in the OMA treatment, for each parameter condition and method. The methods analysed are complete case analysis (CC), last observation carried forward (LOCF), LUNDEX, non-responder imputation (NRI), Inverse Probability Weighting accounting for the reasons for treatment cessation in the attrition weights (IPW2) or not (IPW1), and Confounder-Adjusted Response Rate with Attrition Correction by reason for drug cessation (CARRAC).

parameter	CC		LOCF		LUNDEX		NRI	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	0.6 [0.2, 1.0]	100	-3.5 [-3.9, -3.1]	17.0	-12.0 [-12.3, -11.7]	0	-7.5 [-7.8, -7.1]	0.0
2	-0.2 [-0.5, 0.1]	100	-2.0 [-2.3, -1.6]	97.7	-7.0 [-7.3, -6.8]	0	-3.9 [-4.2, -3.6]	2.7
3	0.1 [-0.2, 0.5]	100	-2.8 [-3.2, -2.4]	61.3	-9.7 [-10.0, -9.4]	0	-5.8 [-6.1, -5.4]	0.0
4	1.0 [0.6, 1.4]	100	-4.3 [-4.7, -3.9]	0.8	-14.3 [-14.5, -14.0]	0	-9.3 [-9.7, -9.0]	0.0
5	1.6 [1.2, 2.0]	100	-5.0 [-5.4, -4.6]	0.0	-16.2 [-16.5, -16.0]	0	-11.1 [-11.4, -10.7]	0.0
6	0.2 [-0.1, 0.5]	100	-1.8 [-2.1, -1.4]	99.4	-6.7 [-7.0, -6.4]	0	-3.8 [-4.1, -3.5]	3.6
7	0.3 [0.0, 0.7]	100	-2.7 [-3.1, -2.3]	70.0	-9.5 [-9.9, -9.3]	0	-5.7 [-6.0, -5.3]	0.0
8	0.8 [0.5, 1.2]	100	-4.4 [-4.8, -4.0]	0.2	-14.4 [-14.7, -14.1]	0	-9.4 [-9.7, -9.0]	0.0
9	1.1 [0.6, 1.4]	100	-5.3 [-5.7, -5.0]	0.0	-16.5 [-16.8, -16.3]	0	-11.4 [-11.7, -11.1]	0.0
10	3.7 [3.3, 4.1]	25.3	-1.2 [-1.6, -0.9]	100	-9.9 [-10.1, -9.6]	0	-4.7 [-5.1, -4.4]	0.0
11	5.6 [5.2, 5.9]	0.0	0.1 [-0.2, 0.5]	100	-8.6 [-8.8, -8.3]	0	-3.1 [-3.4, -2.8]	41.0
12	4.0 [3.6, 4.3]	14.9	-1.3 [-1.7, -1.0]	99.9	-9.7 [-10.0, -9.4]	0	-4.6 [-4.9, -4.2]	0.0
13	5.8 [5.5, 6.2]	0.0	0.0 [-0.4, 0.3]	100	-8.4 [-8.6, -8.1]	0	-2.9 [-3.2, -2.6]	59.7

parameter	IPW1		IPW2		CARRAC	
	LDA – true LDA	cov	LDA – true LDA	cov	LDA – true LDA	cov
1	1.2 [0.8, 1.6]	100	-0.3 [-0.9, 0.4]	100	0.8 [0.4, 1.2]	100
2	0.4 [0.1, 0.7]	100	-0.2 [-0.6, 0.2]	100	0.1 [-0.2, 0.4]	100
3	0.8 [0.4, 1.1]	100	-0.2 [-0.7, 0.3]	100	0.4 [0.0, 0.8]	100
4	1.7 [1.3, 2.2]	100	-0.3 [-1.2, 0.5]	99.9	1.1 [0.7, 1.5]	100
5	2.4 [1.9, 2.9]	98.7	-0.4 [-1.5, 0.6]	99.4	1.5 [1.1, 1.9]	99.8
6	0.3 [0.0, 0.6]	100	-0.3 [-0.7, 0.1]	100	0.4 [0.1, 0.7]	100
7	0.7 [0.4, 1.1]	100	-0.3 [-0.8, 0.2]	100	0.5 [0.2, 0.9]	100
8	1.7 [1.3, 2.2]	99.9	-0.2 [-1.0, 0.5]	99.9	1.0 [0.6, 1.4]	100
9	2.3 [1.8, 2.8]	99.3	-0.4 [-1.6, 0.8]	98.6	1.3 [0.9, 1.8]	100
10	4.3 [3.9, 4.7]	15.6	4.7 [4.1, 5.3]	18.3	4.3 [3.9, 4.6]	7.0
11	6.2 [5.9, 6.6]	0.0	7.6 [7.0, 8.1]	0.0	6.2 [5.8, 6.5]	0.0
12	4.0 [3.6, 4.4]	35.4	4.1 [3.5, 4.8]	40.3	4.7 [4.3, 5.1]	0.8
13	5.8 [5.4, 6.1]	0.0	6.8 [6.2, 7.3]	0.0	6.8 [6.5, 7.1]	0.0