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Sensitivity analyses varying carry-over period for the comparisons between RA patients initiating bDMARDs and those continuing on csDMARDs

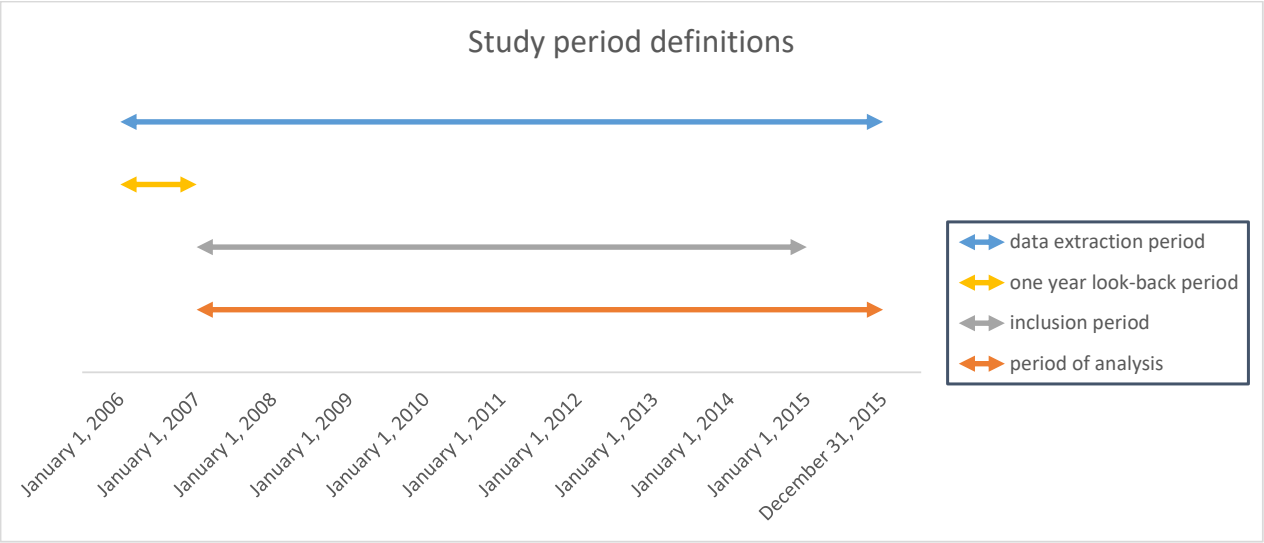
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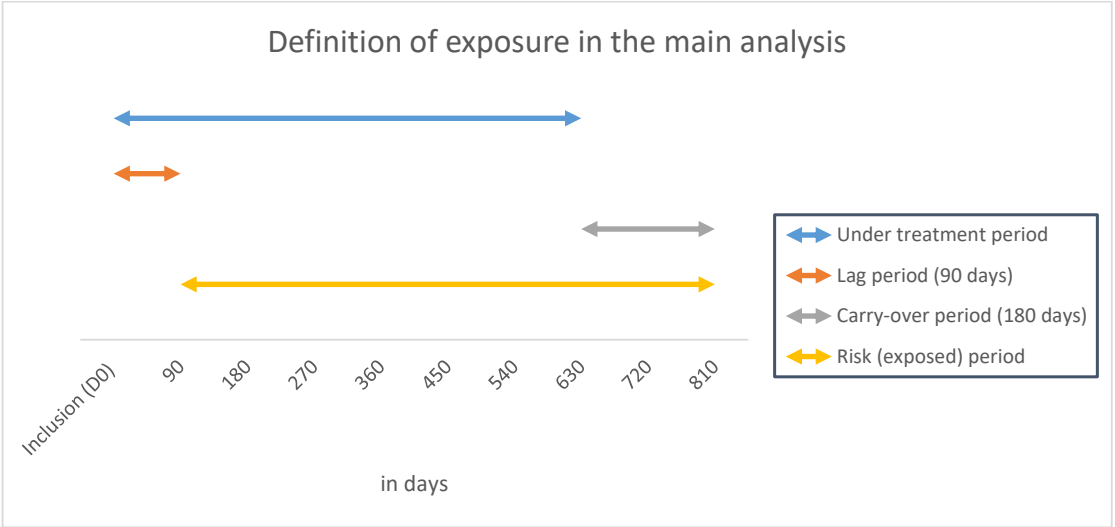
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METHODS

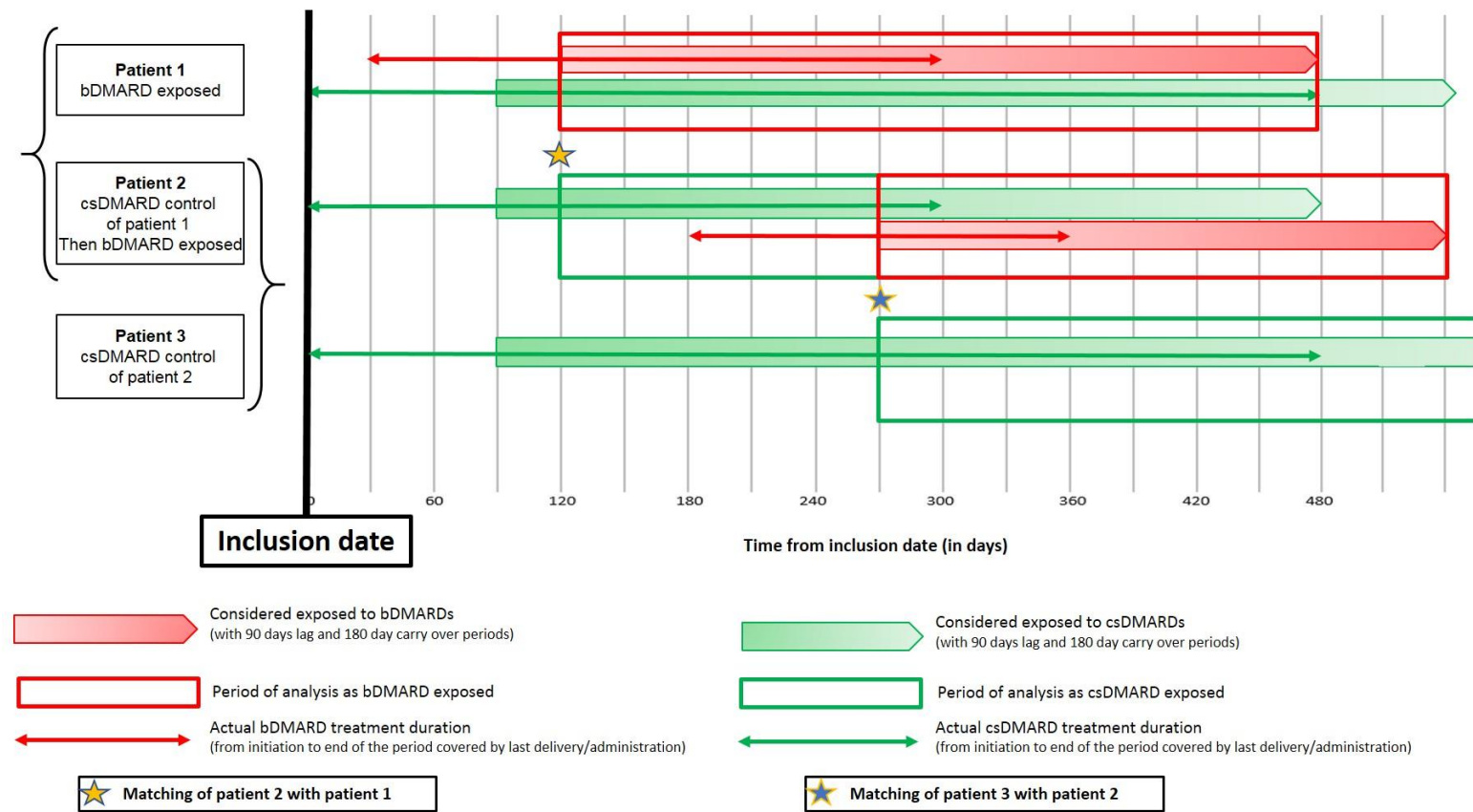
1) Supplemental figure 1 : Study period definitions



1) Supplemental figure 2 : Definition of exposure in the main analysis



Supplemental figure 3. Exposure periods and group of analysis for comparing RA patients initiating bDMARDs and matched RA patients continuing on csDMARDs alone



Supplemental table 1: Time covered by a delivery for each csDMARD and bDMARD not taking into account lag or carry over period.

Treatment	Time period covered by one delivery (days)
csDMARDs	
methotrexate	30
leflunomide	30
sulfasalazine	30
azathioprine	30
hydroxychloroquine	30
bDMARDs	
infliximab	60
adalimumab	30
certolizumab	30
golimumab	30
etanercept	30
rituximab	180
abatacept	30
tocilizumab	30
ustekinumab	90
anakinra	30

DMARD: disease modifying anti-rheumatic agent; csDMARD: conventional synthetic DMARD; bDMARD: biologic DMARD.

Supplemental table 2. Malignancy definitions according to ICD-10 codes

Malignancy	ICD-10 Codes
All malignancy, except non-melanoma skin cancer	C01-C97
All solid cancer, except non-melanoma skin cancer	C01-C75
Hematologic malignancy	C81-C96
Hematologic malignancy (excluding lymphoma)	C90-C96
Invasive melanoma	C43
Invasive cancer of the cervix	C53
Breast cancer	C50
Lung cancer	C33-C34
Colorectal cancer	C18-C21
Prostate cancer	C61
Kidney cancer	C64-C66 ; C68
Hepatic cancer	C22
Pancreatic cancer	C25
Lymphoma	C81-C86 ; C88
Hodgkin lymphoma	C81
Non-Hodgkin lymphoma	C82-C86 ; C88
Diffuse large B-cell Lymphoma	C83.3
Follicular lymphoma	C82
Non-follicular lymphoma	C83

Results

Sensitivity analyses varying carry-over period for the comparisons between RA patients initiating bDMARDs and those continuing on csDMARDs alone

Supplemental table 3. Risk of malignancy associated with bDMARDs initiation compared to continuing csDMARDs alone in RA patients: analysis with a 2 years carry-over period.

Type of malignancy	Sex	No. of bDMARD exposed/ csDMARD matched RA	No. of cancer in bDMARD exposed patients	No. of cancer in csDMARD matched patients	HR	CI 95%(HR)	P-value
All malignancies excluding non-melanoma skin cancer		19764-19764	592	420	1.07	[0.94;1.21]	0.293
All solid malignancies excluding non-melanoma skin cancer		19764-19764	502	373	1.02	[0.89;1.17]	0.777
Hematologic malignancies		19764-19764	69	34	1.53	[1.02;2.31]	0.035
Malignant lymphoma		19764-19764	39	17	1.70	[0.97;3.00]	0.052
Hodgkin lymphoma		19764-19764	2	0	NE	NE	NE
Non-Hodgkin lymphoma		19764-19764	37	17	1.61	[0.90;2.87]	0.092
Hematologic malignancies (excluding lymphoma)		19764-19764	30	17	1.36	[0.74;2.49]	0.307
Invasive melanoma		19764-19764	27	19	1.07	[0.60;1.91]	0.807
Invasive cancer of the cervix	Women	14749-14749	8	11	0.60	[0.24;1.49]	0.277
Breast cancer	Women	14749-14749	107	88	0.91	[0.69;1.21]	0.531
Lung cancer		19764-19764	77	54	1.09	[0.77;1.54]	0.628
Colo-rectal cancer		19764-19764	54	37	1.09	[0.72;1.67]	0.680
Prostate cancer	Men	5015-5015	35	34	0.78	[0.49;1.24]	0.296
Kidney cancer		19764-19764	15	19	0.62	[0.31;1.24]	0.182
Liver cancer		19764-19764	9	2	3.43	[0.79;14.96]	0.059
Pancreas cancer		19764-19764	16	8	1.44	[0.62;3.36]	0.376

DMARD: disease modifying anti-rheumatic agent; csDMARD: conventional synthetic DMARD; bDMARD: biologic DMARD.

Supplemental table 4. Risk of malignancy associated with bDMARDs initiation compared to continuing csDMARDs alone in RA patients: analysis with 5 years carry-over period.

Type of malignancy	Sex	No. of bDMARD exposed/ csDMARD matched RA	No. of cancer in bDMARD exposed patients	No. of cancer in csDMARD matched patients	HR	CI 95%(HR)	P-value
All malignancies excluding non-melanoma skin cancer		19790-19790	663	501	1.07	[0.96;1.21]	0.221
All solid malignancies excluding non-melanoma skin cancer		19790-19790	563	440	1.04	[0.92;1.18]	0.547
Hematologic malignancies		19790-19790	76	52	1.19	[0.83;1.69]	0.335
Malignant lymphoma		19790-19790	42	27	1.26	[0.78;2.03]	0.334
Hodgkin lymphoma		19790-19790	2	5	0.36	[0.07;1.85]	0.213
Non-Hodgkin lymphoma		19790-19790	40	22	1.46	[0.87;2.45]	0.146
Hematologic malignancies (excluding lymphoma)		19790-19790	34	25	1.11	[0.66;1.88]	0.698
Invasive melanoma		19790-19790	31	22	1.14	[0.66;1.95]	0.639
Invasive cancer of the cervix	Women	14758-14758	9	5	1.51	[0.50;4.58]	0.457
Breast cancer	Women	14758-14758	118	105	0.92	[0.71;1.19]	0.533
Lung cancer		19790-19790	92	59	1.25	[0.90;1.73]	0.174
Colo-rectal cancer		19790-19790	60	40	1.22	[0.82;1.82]	0.319
Prostate cancer	Men	5032-5032	39	44	0.71	[0.47;1.09]	0.120
Kidney cancer		19790-19790	16	24	0.56	[0.29;1.06]	0.076
Liver cancer		19790-19790	9	3	2.43	[0.67;8.75]	0.143
Pancreas cancer		19790-19790	17	10	1.36	[0.63;2.94]	0.429

DMARD: disease modifying anti-rheumatic agent; csDMARD: conventional synthetic DMARD; bDMARD: biologic DMARD.

Supplemental table 5. Risk of malignancy associated with bDMARDs initiation compared to continuing csDMARDs alone in RA men ≥65 years: analysis with a 90-days lag period and a 180 days carry-over period.

Type of malignancy	No. of bDMARD exposed/ csDMARD matched RA	No. of cancer in bDMARD exposed patients	No. of cancer in csDMARD matched patients	HR	CI 95%(HR)	P-value
All malignancies excluding non-melanoma skin cancer	843-843	48	40	1.04	[0.68;1.59]	0.866
All solid malignancies excluding non-melanoma skin cancer	843-843	40	32	1.08	[0.67;1.73]	0.753
Hematologic malignancies	843-843	6	5	1.04	[0.32;3.40]	0.948
Malignant lymphoma	843-843	5	3	1.44	[0.34;6.01]	0.610

Supplemental table 6. Risk of malignancy associated with bDMARDs initiation compared to continuing csDMARDs alone in RA women ≥65 years: analysis with a 90-days lag period and a 180 days carry-over period.

Type of malignancy	No. of bDMARD exposed/ csDMARD matched RA	No. of cancer in bDMARD exposed patients	No. of cancer in csDMARD matched patients	HR	CI 95%(HR)	P-value
All malignancies excluding non-melanoma skin cancer	2541-2541	69	61	0.96	[0.68;1.36]	0.819
All solid malignancies excluding non-melanoma skin cancer	2541-2541	61	54	0.95	[0.66;1.38]	0.801
Hematologic malignancies	2541-2541	5	6	0.74	[0.22;2.47]	0.624
Malignant lymphoma	2541-2541	3	4	0.67	[0.15;3.05]	0.610