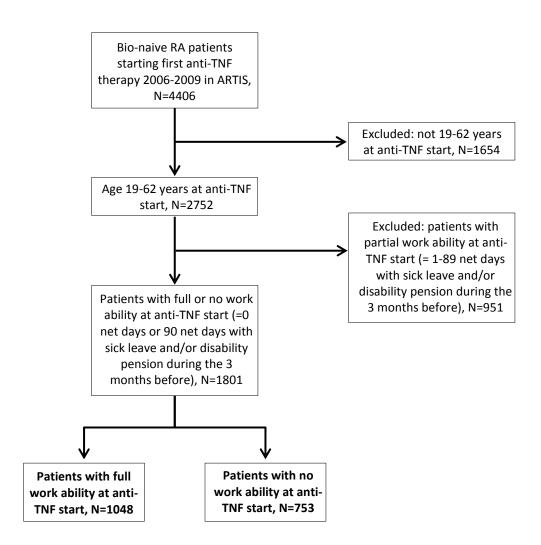
WEB APPENDIX

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Detailed data on sick leave and disability pension in Sweden

In the Swedish social insurance system, the first day of sickness ("the qualifying day") is unpaid. From day 2-14 the compensation is obtained directly from the employer ("sick pay period"). Hence, only disease periods >14 consecutive days are registered by the Social Insurance Agency. However, all days (from day 1 and on) are registered when an episode exceeds 14 days. Disability pension requires an expected duration of 1 year with at least 25% reduction in work ability. In Sweden an unemployed patient can be on sick leave but not on disability pension.



Supplementary Figure S1 Flow-chart over the process of patient inclusion in the current study

Supplementary Table S1 ICD10, ATC and Procedure codes used to identify comorbid disease via the National Patient Register (2001-2009) and the Prescribed Drug Register (2005-2009).

Disease	ICD10*, ATC** and Procedure codes ⁺
Depression/anxiety disorder	ICD10: F31-F34, F41, F43 or
	ATC: N06A, N05BA
Cardiovascular disease	ICD10: I20-I25, I50, I60-I64
Malignancy	ICD10: C00-C97, D00-D09, D37-D48
Hypertension	ATC: C02-03, C07-09
Diabetes	ATC: A10AA-A10AF, A10BA-A10BX
Hip/Knee replacement	Procedure code: NGB, NGC, NFB, NFC

* Diagnosis set within 5 years before bio-start

** Prescription within 6 months before bio-start

+ Procedure performed ever

Supplementary Table S2 Cox-regression results for disease duration as predictor of work ability gain and loss during 3 years after anti-TNF start, in working-age Swedish RA-patients starting therapy 2006-2009, shown for different cut-off points for disease duration.

	Work ability gain ≥50%						
	Univaria	te	Multivariate (n=599)				
Disease duration	HR (95%CI)	p-value	HR (95%CI)	p-value			
<1y vs ≥1y	2.73 (1.69-4.40)	<0.001	1.29 (0.73-2.28)	0.38			
<2y vs ≥2y	2.67 (1.85-3.86)	<0.001	1.76 (1.14-2.71)	0.011			
<3y vs ≥3y	2.73 (1.92-3.88)	<0.001	1.83 (1.21-2.76)	0.004			
<4y vs ≥4y	3.03 (2.13-4.30)	<0.001	2.09 (1.38-3.15)	<0.001			
<5y vs ≥5y	2.96 (2.08-4.33)	<0.001	2.13 (1.40-3.28)	<0.001			
<7y vs ≥7y	2.58 (1.79-3,72)	<0.001	1.96 (1.27-3.04)	<0.001			
	Work ability loss ≥50%						
	Univaria	te	Multivariate	(n=857)			
Disease duration	HR (95%CI)	p-value	HR (95%CI)	p-value			
<1y vs ≥1y	0.72 (0.42-1.23)	0.22	0.74 (0.53-1.03)	0.072			
<2y vs ≥2y	1.00 (0.74-1.36)	0.99	0.93 (0.67-1.30)	0.68			

0.25

0.32

0.32

0.16

0.81 (0.60-1.09)

0.89 (0.67-1.19)

0.94 (0.71-1.24)

0.88 (0.66-1.17)

0.16

0.44

0.66

0.37

<3y vs ≥3y

<4y vs ≥4y

<5y vs ≥5y

<7y vs ≥7y

0.85 (0.65-1.12)

0.88 (0.68-1.14)

0.88 (0.68-1.14)

0.83 (0.64-1.08)

			Work ability ga	in 100%		
	Univariat	te	Multivariate (n	=599)**	Multivariate + c pension sta (n=599)*	atus
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Disease duration <5y vs ≥5y	3.65 (2.33-5.73)	<0.001	2.32 (1.40-3.85)	0.001	1.08 (0.64-1.83)	0.77
Sex (men vs women)	1.74 (1.10-2.78)	0.019	1.53 (0.88-2.67)	0.14	1.31 (0.74-2.31)	0.36
Age (per 10y decrease)	2.20 (1.84-2.65)	<0.001	1.69 (1.32-2.15)	<0.001	1.46 (1.08-1.96)	0.011
Education						
>12y vs ≤9y	1.37 (0.65-2.90)	0.41	1.73 (0.75-3.99)	0.20	0.83 (0.35-1.96)	0.68
>12y vs 10-12y	0.73 (0.38-1.39)	0.33	0.94 (0.45-1.93)	0.86	0.72 (0.35-1.50)	0.38
10-12y vs ≤9y	1.89 (1.11-3.21)	0.019	1.85 (1.00-3.41)	0.050	1.15 (0.62-2.14)	0.65
HAQ						
<1 vs 1-1.49	2.10 (1.23-3.58)	0.007	1.42 (0.79-2.55)	0.24	1.27 (0.70-2.31)	0.44
<1 vs ≥1.5	1.49 (0.77-2.88)	0.24	1.12 (0.54-2.33)	0.76	0.85 (0.41-1.76)	0.66
1-1.49 vs ≥1.5	0.71 (0.39-1.29)	0.26	0.79 (0.42-1.50)	0.47	0.67 (0.35-1.29)	0.23
$DAS28^{\dagger}$						
≤3.2 vs 3.3-5.1	1.23 (0.48-3.17)	0.67	0.63 (0.21-1.83)	0.40	0.69 (0.23-2.04)	0.50
≤3.2 vs >5.1	1.54 (0.61-3.90)	0.36	0.64 (0.22-1.82)	0.40	0.75 (0.26-2.21)	0.61
3.3-5.1 vs >5.1	1.25 (0.78-2.00)	0.35	1.01 (0.61-1.66)	0.98	1.10 (0.67-1.81)	0.71
Comorbidities						
Depression/Anxiety disorder (yes vs none)	0.78 (0.46-1.31)	0.34	0.82 (0.46-1.48)	0.51	1.10 (0.60-2.03)	0.75
Hypertension (yes vs no)	0.61 (0.37-1.00)	0.050	0.83 (0.46-1.51)	0.55	0.68 (0.37-1.25)	0.215
Hip/Knee replacement (yes vs no)	0.06 (0.08-0.42)	0.005	0.16 (0.02-1.20)	0.075	0.18 (0.024- 1.33)	0.093
Work related variables						
Unemployment (any vs none) ††	5.03 (3.35-8.41)	<0.001	1.83 (1.04-3.24)	0.037	1.01 (0.62-1.94)	0.74
Disability pension status (sick leave vs disability pension) [¥]	20.2 (10.5-39.1)	<0.001	NA [§]	NA^{S}	16.9 (7.57-37.8)	<0.001

Supplementary Table S3. Predictors of work ability gain 100% for RA patients with no work ability at bio-start* assessed by Cox regression analysis during 3 years after bio-start for patients aged 18-62 years starting treatment 2006-2009 in Sweden.

Adjustment for year of bio-start was performed in all regressions.

* No work ability at bio-start=90 days with sick leave and disability pension during 3 months before bio-start.

** Missingness 154/753=20%

⁺ Analysed in separate regression model not including HAQ.

++ Any days with unemployment benefit the calendar year prior to the year of bio-start

¥ Full sick leave or a combination of partial sick leave and partial disability pension vs. full disability pension.

§ Not applicable

Supplementary Table S4 Variables associated with full-time disability pension at anti-TNF start in RA patients (18-62 years) with no work ability* when starting treatment 2006-2009.

	Full-time disability pension at bio-start (yes vs. no)			
	OR (95%CI)	p-value		
Disease duration (≥5y vs <5y)	4.85 (3.16-7.43)	<0.001		
Sex (women vs men)	1.33 (0.79-2.24)	0.291		
Age (per 10y increase)	1.60 (1.23-2.06)	<0.001		
Education				
≤9y vs >12y	3.85 (1.94-7.64)	<0.001		
10-12y vs >12y	1.54 (0.85-2.77)	0.16		
≤9y vs 10-12y	2.51 (1.52-4.13)	<0.001		
HAQ				
≥1.5 vs <1	2.39 (1.20-4.76)	0.013		
1-1.49 vs <1	2.01 (1.22-3.50)	0.007		
≥1.5 vs 1-1.49	1.16 (0.65-2.06)	0.62		
Comorbidities				
Depression/anxiety disorder (yes vs no)	1.51 (0.92-2.46)	0.10		
Hypertension (yes vs no)	0.91 (0.59-1.42)	0.91		
Hip/knee replacement (yes vs no)	1.35 (0.70-2.60)	0.37		
Work-related variables				
Unemployment (any vs none)**				

 \ast 90 days with sick leave or disability pension during the 3 months prior to anti-TNF start

 $\ast\ast$ Any days with unemployment benefit the calendar year prior to the year of biostart

Supplementary Table S5. Predictors of work ability loss 100% for RA patients with full work ability at bio-start* assessed by Cox regression analysis during 3 years after bio-start for patients aged 18-62 years starting treatment 2006-2009 in Sweden.

	Work ability loss 100%				
	Univariat	te	Multivariate (n=857)**		
	HR (95%CI)	p-value	HR (95%CI)	p-value	
Disease duration <5y vs ≥5y	1.31 (0.84-2.05)	0.24	1.47 (0.88-2.44)	0.14	
Sex (men vs women)	1.20 (0.76-1.92)	0.44	1.14 (0.66-1.97)	0.65	
Age (per 10y increase)	1.00 (0.99-1.02	0.69	1.01 (0.99-1.03)	0.47	
Education					
>12y vs ≤9y	0.59 (0.29-1.18)	0.13	1.03 (0.45-2.36)	0.94	
>12y vs 10-12y	0.48 (0.29-0.79)	0.004	0.57 (0.33-0.99)	0.045	
10-12y vs ≤9y	1.22 (0.65-2.32)	0.54	1.82 (0.83-3.98)	0.14	
HAQ					
<1 vs 1-1.49	0.55 (0.33-0.94)	0.028	0.66 (0.38-1.5)	0.14	
<1 vs ≥1.5	0.56 (0.29-1.09)	0.086	0.64 (0.31-1.29)	0.21	
1-1.49 vs ≥1.5	1.01 (0.50-2.00)	0.99	0.96 (0.47-1.99)	0.92	
DAS28 [†]					
≤3.2 vs 3.3-5.1	0.44 (0.19-2.08)	0.62	0.73 (0.22-2.48)	0.61	
≤3.2 vs >5.1	0.28 (0.09-0.90)	0.033	0.34 (0.10-1.13)	0.078	
3.3-5.1 vs >5.1	0.45 (0.27-0.76)	0.003	0.47 (0.27-0.81)	0.006	
Comorbidities					
Depression/Anxiety disorder (any vs none	2.09 (1.11-3.95)	0.023	2.25 (1.13-4.50)	0.021	
Hypertension (yes vs no)	1.10 (0.60-2.03)	0.76	1.33 (0.67-2.64)	0.42	
Hip/Knee replacement (yes vs no)	2.69 (1.34-5.37)	0.005	3.66 (1.51-8.87)	0.004	
Work related variables					
Unemployment (any vs none) ††	3.53 (2.11-5.91)	<0.001	4.12 (2.25-7.54)	<0.001	

Adjustment for year of bio-start was performed in all regressions.

* Full work ability at bio-start=0 days with sick leave and disability pension during 3 months before bio-start.

** Missingness 191/1048=18%

⁺ Analysed in separate regression model not including HAQ.

++ Any days with unemployment benefit the calendar year prior to the year of bio-start

Supplementary Table S6. Predictors of work ability gain ≥50% for RA patients with no work ability at bio-start* assessed by Cox regression analysis during 3 years after bio-start for patients aged 18-62 years starting treatment 2006-2009 in Sweden. Missing values are replaced through multiple imputation. This table corresponds to Table 2 in the main article.

	Work ability gain ≥50%					
	Univariate**		Multivariate**		Multivariate + disability pension status**	
	HR (95%CI)	p-value	HR (95%CI)	p-value	HR (95%CI)	p-value
Disease duration <5y vs ≥5y	2.90 (2.04-4.13)	<0.001	2.01 (1.38-2.92)	< 0.001	1.05 (0.69-1.50)	0.93
Sex (men vs women)	1.54 (1.04-2.28)	0.037	1.58 (1.06-2.37)	0.026	1.25 (0.82-1.90)	0.30
Age (per 10y decrease)	2.08 (1.78-2.44)	<0.001	1.77 (1.47-2.13)	< 0.001	1.52 (1.27-1.82)	<0.001
Education						
>12y vs ≤9y	1.46 (0.81-2.65)	0.21	1.32 (0.72-2.43)	0.37	0.76 (0.41-1.42)	0.40
>12y vs 10-12y	0.82 (0.49-1.36)	0.44	0.93 (0.55-1.57)	0.78	0.76 (0.45-1.30)	0.32
10-12y vs ≤9y	1.79 (1.17-2.74)	0.008	1.43 (0.92-2.22)	0.11	1.00 (0.64-1.57	0.99
HAQ						
<1 vs 1-1.49	1.92 (1.28-2.88)	0.002	1.37 (0.87-2.16)	0.18	1.11 (0.70-1.77)	0.65
<1 vs ≥1.5	1.67 (0.96-2.89)	0.069	1.25 (0.68-2.28)	0.47	1.04 (0.57-1.90)	0.89
1-1.49 vs ≥1.5	0.87 (0.53-1.44)	0.59	0.91 (0.54-1.54)	0.73	0.94 (0.54-1.63)	0.81
DAS28 ⁺						
≤3.2 vs 3.3-5.1	1.13 (0.50-2.56)	0.78	0.68 (0.28-1.68)	0.40	0.63 (0.25-1.60)	0.32
≤3.2 vs >5.1	1.30 (0.57-2.96)	0.52	0.65 (0.26-1.63)	0.36	0.62 (0.24-1.62)	0.40
3.3-5.1 vs >5.1	1.16 (0.78-1.72)	0.46	0.95 (0.65-1.40)	0.80	0.98 (0.68-1.47)	0.99
Comorbidities						
Depression/Anxiety disorder (any vs none)	0.66 (0.43-1.03)	0.068	0.54 (0.34-0.87)	0.011	0.68 (0.42-1.10)	0.12
Hypertension (yes vs no)	0.66 (0.45-0.98)	0.037	1.01 (0.66-1.53)	0.97	0.95 (0.62-1.45)	0.81
Hip/Knee replacement (yes vs no)	0.24 (0.10-0.54)	0.001	0.48 (0.21-1.11)	0.086	0.55 (0.23-1.28)	0.16
Work related variables						
Unemployment (any vs none) **	4.97 (3.37-7.34)	<0.001	2.06 (1.34-3.17)	<0.001	1.16 (0.77-1.78)	0.47
Disability pension status (sick leave vs disability pension) [¥]	18.4 (11.2-30.2)	<0.001	NA [§]	NA [§]	15.0 (8.72-25.7)	<0.001

Adjustment for year of bio-start was performed in all regressions.

* No work ability at bio-start=90 days with sick leave and disability pension during 3 months before bio-start.

** Missing values replaced through multiple imputation. Number of replacements: disease duration=22, HAQ=129, DAS28=145, Education level=4.

⁺ Analysed in separate regression model not including HAQ.

++ Any days with unemployment benefit the calendar year prior to the year of bio-start

¥ Full sick leave or a combination of partial sick leave and partial disability pension vs. full disability pension.

§ Not applicable

Supplementary Table S7. Predictors of work ability loss ≥50% for RA patients with full work ability at bio-start* assessed by Cox regression analysis during 3 years after bio-start for patients aged 18-62 years starting treatment 2006-2009 in Sweden. Missing values are replaced through multiple imputation. This table corresponds to Table 3 in the main article.

	Work ability loss ≥50%				
	Univariate	**	Multivariate**		
	HR (95%CI)	p-value	HR (95%CI)	p-value	
Disease duration <5y vs ≥5y	0.87 (0.67-1.12)	0.28	0.95 (0.73-1.24)	0.70	
Sex (men vs women)	0.84 (0.63-1.13)	0.24	0.79 (0.58-1.05)	0.10	
Age (per 10y increase)	1.13 (1.01-1.27)	0.034	1.08 (0.95-1.22)	0.23	
Education					
>12y vs ≤9y	0.71 (0.47-1.05)	0.088	0.78 (0.52-1.18)	0.24	
>12y vs 10-12y	0.59 (0.45-0.78)	<0.001	0.56 (0.42-0.74)	<0.001	
10-12y vs ≤9y	1.20 (0.82-1.76)	0.34	1.39 (0.94-2.06)	0.097	
HAQ					
<1 vs 1-1.49	0.60 (0.45-0.80)	0.001	0.68 (0.51-0.92)	0.012	
<1 vs ≥1.5	0.61 (0.42-0.90)	0.014	0.66 (0.45-0.98)	0.038	
1-1.49 vs ≥1.5	1.02 (0.68-1.55)	0.90	0.97 (0.64-1.46)	0.88	
$DAS28^{\dagger}$					
≤3.2 vs 3.3-5.1	0.93 (0.56-1.53)	0.77	0.95 (0.57-1.59)	0.85	
≤3.2 vs >5.1	0.60 (0.36-0.98)	0.041	0.64 (0.38-1.07)	0.09	
3.3-5.1 vs >5.1	0.64 (0.48-0.86)	0.003	0.67 (0.50-0.90)	0.008	
Comorbidities					
Depression/Anxiety disorder (any vs none)	1.47 (0.97-2.24)	0.073	1.37 (0.90-2.11)	0.15	
Hypertension (yes vs no)	1.62 (1.18-2.28)	0.003	1.46 (1.04-2.07)	0.030	
Hip/Knee replacement (yes vs no)	1.93 (1.21-3.09)	0.006	1.93 (1.18-3.16)	0.008	
Work related variables					
Unemployment (any vs none) $^{^{++}}$	1.80 (1.24-2.61)	0.002	1.79 (1.21-2.65)	0.003	

Adjustment for year of bio-start was performed in all regressions.

* Full work ability at bio-start=0 days with sick leave and disability pension during 3 months before bio-start.

** Missing values replaced through multiple imputation. Number of replacements: disease

duration= 12, HAQ=169. DAS28=186, Education level=13.

+ Analysed in separate regression model not including HAQ.

++ Any days with unemployment benefit the calendar year prior to the year of bio-start