

## Supplementary Online Content

Atalay S, van den Reek JMPA, den Broeder AA, et al. Comparison of tightly controlled dose reduction of biologics with usual care for patients with psoriasis: a randomized clinical trial. *JAMA Dermatol*. Published online February 12, 2020. doi:10.1001/jamadermatol.2019.4897

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This supplementary material has been provided by the authors to give readers additional information about their work.

## **eMethods.** Detailed Methods

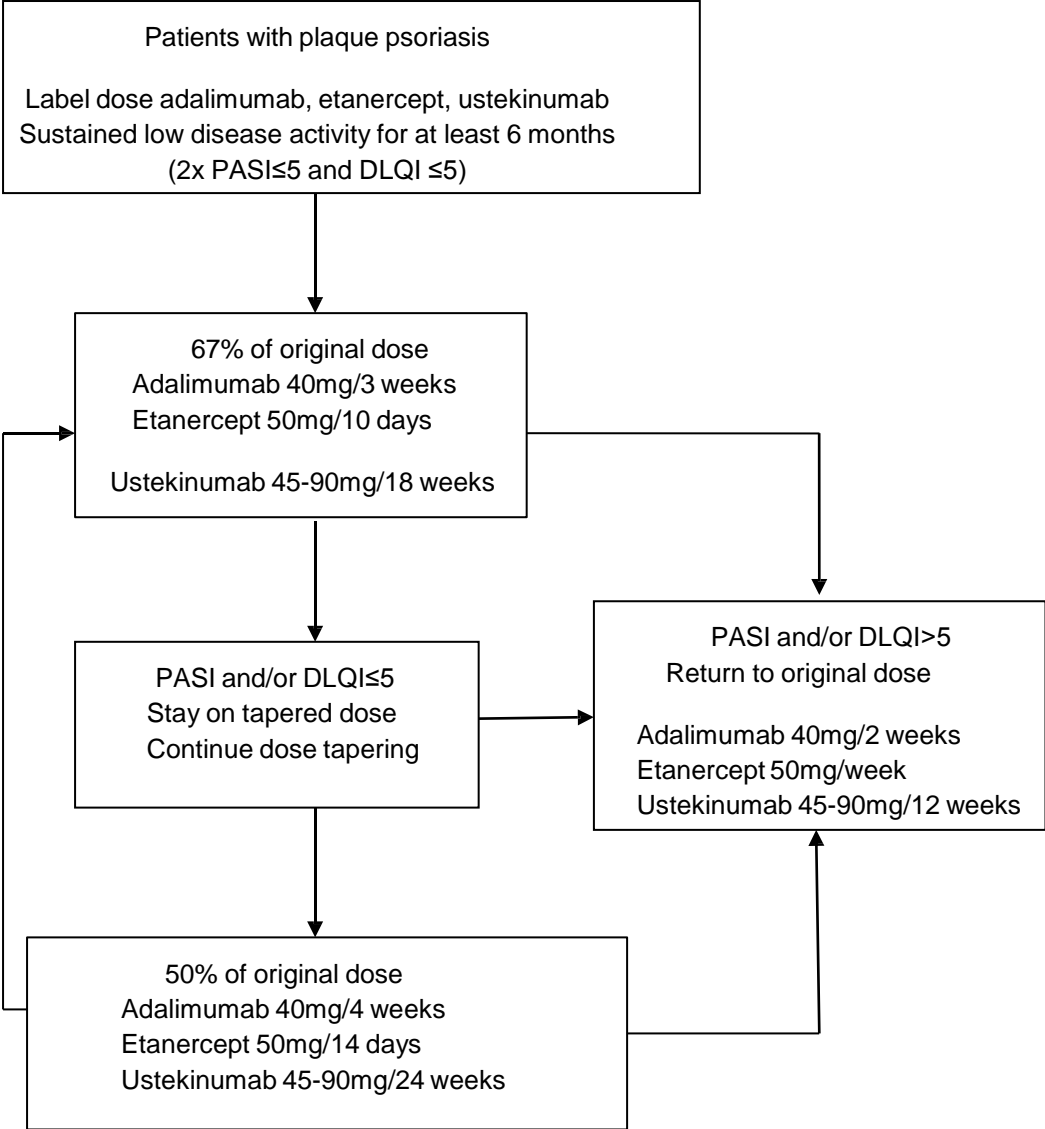
### **Dose reduction steps**

For patients allocated to DR, the time interval between biologic injections was prolonged in two steps. First, the interval was prolonged by multiplying the normal interval by 1.5. Second, the interval was doubled (normal interval multiplied by 2). The first step of interval prolongation was effectuated directly after randomization. Decision to effectuate the second step of interval prolongation was made at three months study visit, depending on disease activity. If PASI and/or DLQI were still below 5 after three months, the second interval prolongation was performed. This resulted in adalimumab administration every 21 and 28 days, etanercept every 10 and 14 days, and ustekinumab every 18 and 24 weeks, in the first and second step respectively.

### **Linear mixed model analyses**

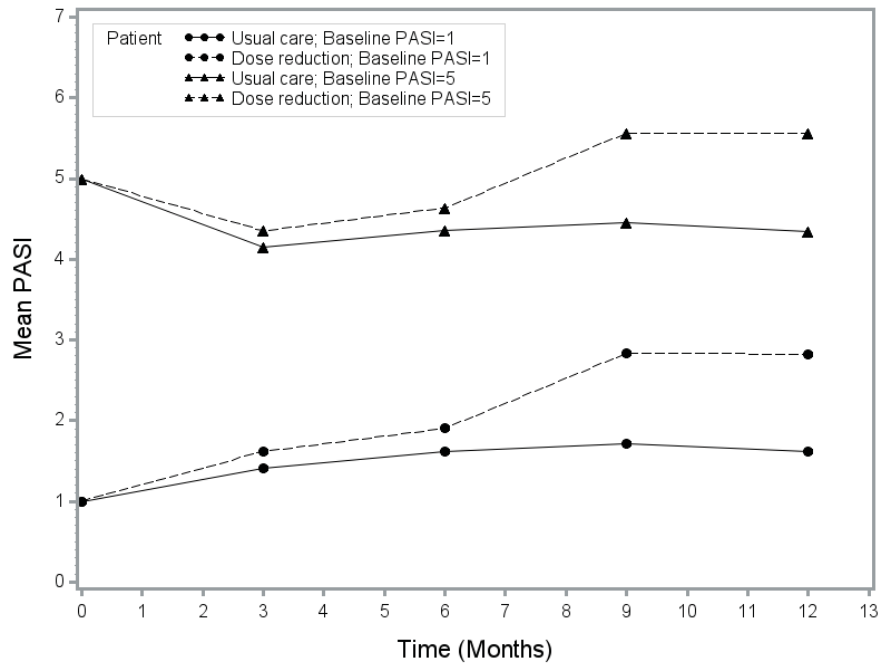
To gain insight in the differences in the course of these outcome measures between treatment arms, we performed additional linear mixed model analyses with random intercept on patient level and using variance components as covariance structure. With such a model it is allowed to use repeated correlated measurements, such as multiple PASI scores within the same patient. The following variables were used as predictors: time (3, 6, 9 and 12 months), randomization group, and baseline score. The interaction between time and randomization group was studied and shown when present. Time and randomization group were used in the model as categorical variables (factors) and score at baseline as a continuous variable.

**eFigure 1. Study population and decision steps**

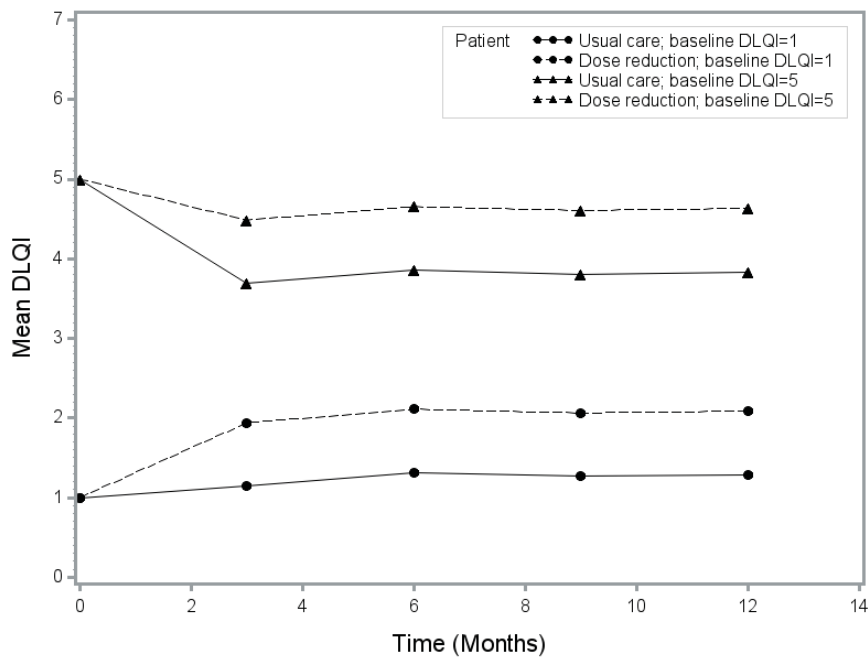


**eFigure 2. Linear mixed model analyses PASI, DLQI and SF-36**

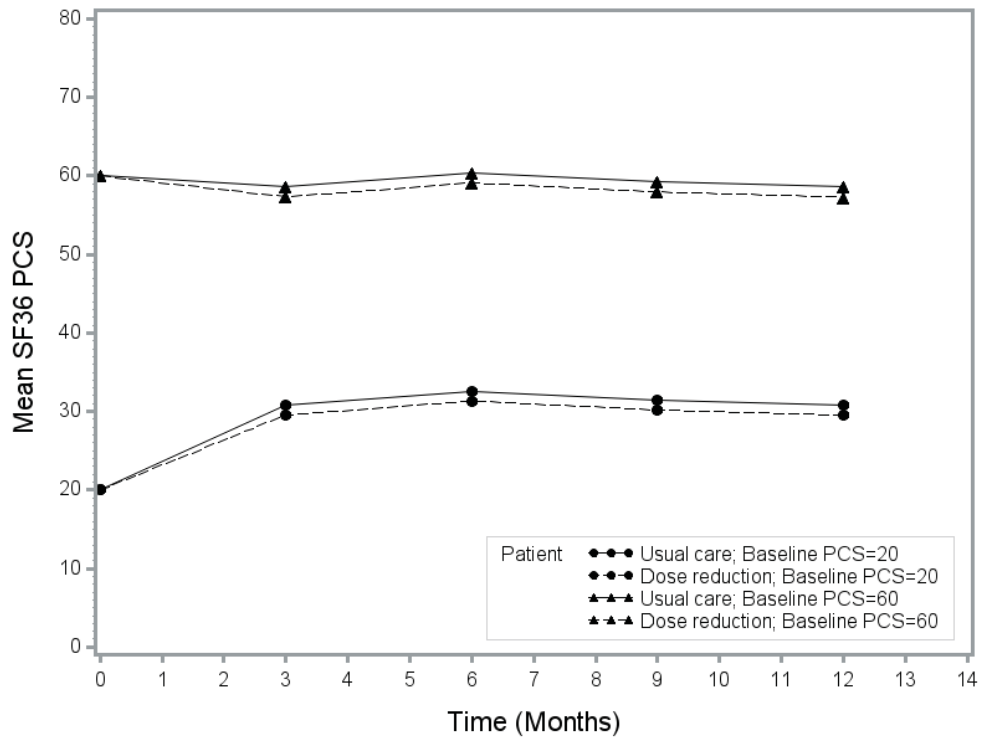
A.



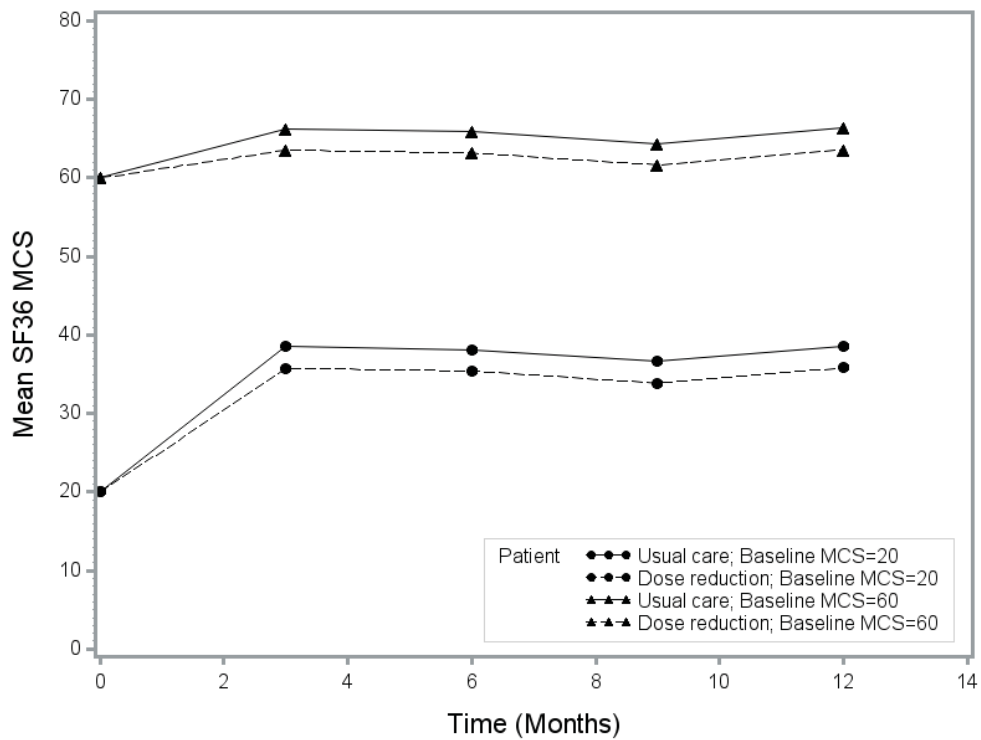
B.



C.



D.



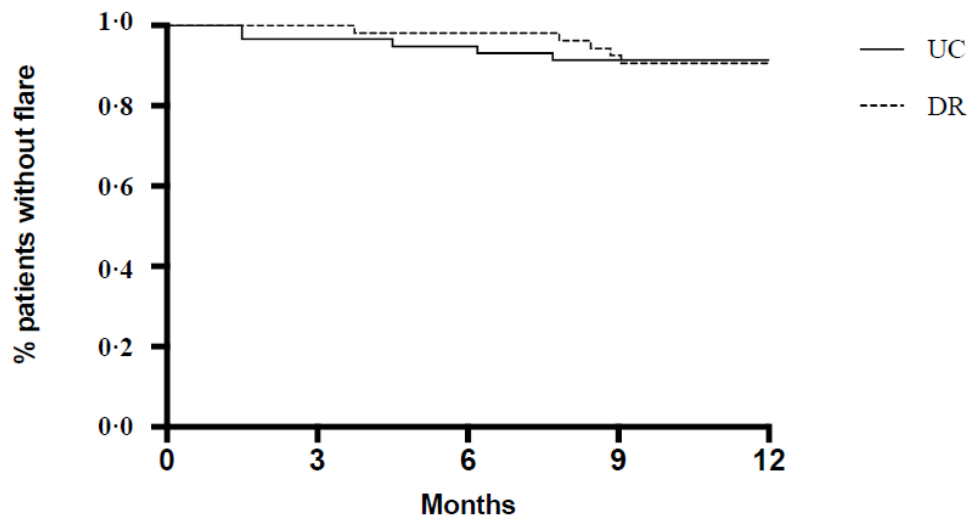
**eFigure 2.** Linear mixed model analyses PASI, DLQI and SF-36

**A.** This figure presents the mean PASI scores of the biologicals as computed by the mixed model for the usual care and dose reduction group for two baseline PASI scores. PASI, Psoriasis Area and Severity Index; CI, Confidence Interval. Interaction between time and the treatment groups was present ( $P=0.0002$ ). The interaction with time was encountered by the mixed model analysis which showed that the mean PASI difference between the two groups increased in time ( $P$ -value for interaction

<0.001). At 3-month follow up the difference between both group was 0.21 (95%CI, -0.33 to 0.74), at month 6 this difference was 0.28 (95%CI, -0.26 to 0.83), at month 9 the difference was 1.12 (95%CI, -0.57 to 1.67) and at 12 month the PASI difference between both groups was 1.21 (95%CI, 0.66 to 1.76). **B**, This figure presents the mean DLQI score as computed by the mixed model analysis for the usual care and dose reduction group for two baseline DLQI scores. DLQI, Dermatology Life Quality Index; CI, Confidence Interval. In the usual care group the DLQI scores remain lower than the dose reduction group during all follow up moments. There was no interaction between time and treatment groups present. The difference in DLQI points between both groups was 0.80 (95%CI, 0.27 to 1.33) ( $P=0.0033$ ). **C**, Figure 2C presents the mean SF-36 Physical Composite Score (PCS) as computed by the mixed model analysis for the usual care and dose reduction group for two baseline PCS scores. CI, Confidence Interval. In the usual care group the PCS scores remain slightly higher than in the dose reduction group during all follow up moments. There was no interaction between time and treatment groups present. The mean difference in PCS scores between both groups was 1.29 (95%CI, -2.10 to 4.67) ( $P=0.45$ ). **D**, Figure 2D presents the mean SF-36 Mental Composite Score (MCS) as computed by the mixed model analysis for the usual care and dose reduction group for two baseline MCS scores. CI, Confidence Interval. In the usual care group the MCS scores remain slightly higher than in the dose reduction group during all follow up moments. There was no interaction between time and treatment groups present. The difference in MCS scores between both groups was 2.75 (95%CI, -0.24 to 5.74) ( $P=0.07$ ).

There was no statistically significant difference in PCS scores or MCS scores between both groups, see figure C and D.

**eFigure 3. Kaplan Meier curve presenting the time until persistent flare in the usual care and dose reduction group**



**Number at risk**

usual care	58	56	55	53	52
dose reduction	53	53	53	49	47

**eFigure 3.** The Kaplan-Meier curve shows that after 7.5 months the first persistent flare occurred in the dose reduction group and after three months in the usual care group.

**eTable 1. Subgroup analyses: outcome measures at baseline and end of study month 12**

<b>eTable 1. Subgroup analyses: outcome measures at baseline and end of study month 12</b>						
	<b>Adalimumab</b>		<b>Etanercept</b>		<b>Ustekinumab</b>	
	Usual care (n=27)	Dose reduction (n=23)	Usual care (n=14)	Dose reduction (n=13)	Usual care (n=18)	Dose reduction (n=17)
<b>PASI</b> † baseline at month 12	0.6 [0.0-1.8] 1.2 [0.4-3.6]	0.6 [0.0-2.1] 2.6 [2.0-4.2]	3.0 [1.7-4.0] 3.5 [2.3-4.3]	2.3 [1.6-3.1] 3.9 [2.6-5.3]	1.3 [0.0-2.7] 1.6 [0.5-3.2]	2.3 [1.0-3.7] 3.3 [3.0-4.7]
PASI≤5 during 12 months	27 (100)	22 (96)	8 (57)	7 (54)	16 (94)	8 (47)
<b>DLQI</b> † baseline at month 12	0.0 [0.0-1.0] 0.0 [0.0-1.0]	0.0 [0.0-1.0] 1.0 [0.0-2.0]	1.5 [0.0-4.0] 2.0 [0.8-2.5]	1.0 [0.0-1.0] 1.0 [0.0-2.5]	0.0 [0.0-1.0] 0.0 [0.0-1.0]	0.0 [0.0-1.0] 1.0 [0.5-2.5]
DLQI≤5 during 12 months	25 (93)	15 (65)	8 (57)	10 (77)	16 (94)	13 (77)
Low dose at the end of study.	0 (0)	20 (87)	0 (0)	6 (46)	0 (0)	10 (59)
Low dose at the end of study with and PASI DLQI ≤5	0 (0)	16 (70)	0 (0)	3 (23)	0 (0)	9 (53)
Abbreviations: NA, not applicable; PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index. Data are in numbers (%) or † medians [IQR]. Subgroup analyses for the effectiveness and quality of life from baseline to 12 months, split for the different types of drugs. The number of patients included at baseline was 27 and 25 for adalimumab, 14 and 14 for etanercept and 18 and 20 for adalimumab in usual care and dose reduction, respectively.						

Thirty-seven patients (70%, 95%CI 56% to 81%) in group and 51 patients (88%, 95%CI 76% to 95%) in group continuously had a PASI score ≤5 during the 12 months of follow-up (eTable 1).

Throughout the study, the median DLQI scores remained ≤5 for both groups. Thirty-eight patients (77%, 95%CI 60% to 90%) in the dose reduction group and 49 patients (86%, 95%CI 70% to 90%) in the usual care group continuously had a DLQI score ≤5 during the 12 months of follow-up (eTable 1).



**eTable 2. Proportion of patients with dosing steps after 12 months**

<b>eTable 2. Proportion of patients with dosing steps after 12 months</b>					
<b>Successful (PASI and DLQI ≤ after 12 months)<sup>a</sup></b>				<b>Unsuccessful (returned to original dose or PASI and DLQI &gt;5 after 12 months but still on a low dose)<sup>b</sup></b>	
	<b>Total group</b>	<b>First step 67% of original dose</b>	<b>Second step 50% of original dose</b>	<b>Returned to original dose</b>	<b>PASI/DLQI &gt;5 but low dose</b>
All biological	53% (28)	19% (10)	34% (18)	32% (17)	15% (8)
<b>Biologics</b>					
Adalimumab	70% (16)	17% (4)	52% (12)	13% (3)	17% (4)
Etanercept	23% (3)	7% (1)	15% (2)	54% (7)	23% (3)
Ustekinumab	53% (9)	29% (5)	24% (4)	41% (7)	6% (1)

Abbreviations: PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index.  
<sup>a</sup> Proportion of patients with successful dose reduction and used dosages at 12 months (i.e. low dose and a PASI and DLQI ≤ 5 after 12 months) for the dose reduction group and split per biologic for this group.  
<sup>b</sup> Proportion of patients with unsuccessful dose tapering (i.e. returned to original dose or PASI and DLQI >5 after 12 months but still on a low dose).

**eTable 3. Factors associated with failure of dose tapering**

<b>eTable 3. Factors associated with failure of dose tapering</b>				
	<b>Univariable<sup>a</sup></b>		<b>Multivariable<sup>b</sup></b>	
	Relative risks (95%CI)	P-value	Relative risks (95%CI)	P-value
<b>General characteristics</b>				
Age at inclusion	1.0 (0.9 to 1.0)	0.238		
Age of onset	0.9 (0.9 to 1.0)	0.332		
Gender (men vs. women)	0.8 (0.4 to 1.4)	0.360		
Smoking		0.620		
Currently smoking vs. never smoking	1.5 (0.6 to 3.7)	0.350		
Ex-smoker vs. never smoking	1.4 (0.6 to 3.1)	0.411		
Currently smoking vs. Ex-smoker	1.1 (0.6 to 2.1)	0.793		
Weight	0.9 (0.9 to 1.0)	0.779		
Disease duration	1.0 (1.0 to 1.1)	0.052	1.0 (0.9 to 1.0)	0.62
Psoriatic arthritis yes vs. no	0.7 (0.4 to 1.4)	0.360		
DLQI baseline	1.2 (0.9 to 1.5)	0.288		
<b>Disease activity</b>				
PASI dichotomous >3.0 ≤3.0 High vs. low	2.0 (1.3 to 3.3)	0.004	1.2 (0.8 to 1.7)	0.40
CRP	1.0 (0.9 to 1.1)	0.790		
<b>Treatment</b>				
Drug		0.017		1.0
Etanercept vs. Ustekinumab	1.6 (0.8 to 2.9)	0.101	1.2 (0.8 to 1.6)	0.420
Adalimumab vs. Ustekinumab	0.7 (0.3 to 1.4)	0.280	0.9 (0.7 to 1.3)	0.711
Etanercept vs. Adalimumab	2.6 (1.3 to 5.0)	0.008	1.2 (0.9 to 1.7)	0.230
Biological naïve	0.9 (0.5 to 1.5)	0.582		
Number of previous biologics	0.9 (0.6 to 1.5)	0.288		
Methotrexate/ Acitretin baseline (yes vs. no)	1.5 (0.6 to 3.4)	0.395		
Abbreviations: PASI, Psoriasis Area and Severity Index; CI, Confidence Interval.				
<sup>a</sup> Univariable log binomial regression analysis was performed to test factors associated with successful dose tapering. The factors disease duration, baseline PASI and type of drug had p value <0.2 and were therefore included in the multivariable log binomial regression analysis.				
<sup>b</sup> In the multivariable log binomial regression analysis, variables with a p value of >0.05 were excluded (backward selection procedure); no variables were left after this selection.				

eTable 4. Cumulative dose per patient in 12 months

eTable 4. Cumulative dose per patient in 12 months					
	Normal dose per patient in 12 months (mg), according to label	Mean cumulative dose per usual care patient in 12 months (mg) <sup>a</sup>	Mean cumulative dose in dose reduction patient in 12 months (mg) <sup>b</sup>	% Reduction of cumulative dose in dose reduction versus usual care <sup>c</sup>	
<b>Adalimumab</b>	1040 (26x40 mg)	1043 (26x40 mg)	690 (17.2x40 mg)	34%	
<b>Etanercept</b>	2600 (52x50 mg)	2497 (49.9x50 mg)	1840 (36.8x50 mg)	26%	
<b>Ustekinumab 45 mg</b>	180 (4x45 mg)	189 (4.2x45 mg)	145 (3.2x45 mg)	23%	
<b>Ustekinumab 90 mg</b>	360 (4x90 mg)	391 (4.3x90 mg)	258 (2.9x90 mg)	34%	
Abbreviations: mg, milligram					
<sup>a</sup> The mean cumulative dose of the biologics over 12 months for the					
<sup>b</sup> The mean cumulative dose of the biologics over 12 months for the dose reduction group					
<sup>c</sup> The reduction of the cumulative dose relative to the dose was expressed as a proportion.					

## eResults. Adverse Events

### Usual Care

110008	vertigo	
110008	vertebrobasilar transient ischemic attack	<b>Cardiovascular event</b>
110008	hospitalization due to gastroenteritis/orthostasis	<b>Infectious event</b>
110008	belching and vomiting	
110008	cystitis	<b>Infectious event</b>
110010	common cold	<b>Infectious event</b>
110010	herpes labialis	<b>Infectious event</b>
110010	herpes labialis	<b>Infectious event</b>
110010	worsening headache	
110010	common cold	<b>Infectious event</b>
110012	pneumonia	<b>Infectious event</b>
110015	bursitis right shoulder	<b>Musculoskeletal disorder</b>
110015	rhinitis	
110015	flu	<b>Infectious event</b>
110015	flu	<b>Infectious event</b>
110018	flu	<b>Infectious event</b>
110020	ear infection	<b>Infectious event</b>
110020	ear infection	<b>Infectious event</b>
110020	bronchitis	<b>Infectious event</b>
110020	increase of back pain due to foramen stenose	
110021	excision pigmentated seborrhoic keratoses right hand	<b>Skin diseases</b>
110021	hip and back pain	<b>Musculoskeletal disorder</b>
110025	common cold	<b>Infectious event</b>
110025	arthritis due to arthritis psoriatica left shoulder	<b>Musculoskeletal disorder</b>
110025	worsening (pre-existent) delusional disorder	
110026	pain of scar on shoulder	
110026	hypercholesterolaemia	
110026	hyperventilation	
110026	diarrhea, nausea, abdominal cramps	
110026	superficial basal cell carcinoma	<b>Non melanoma skin cancer</b>

110026	pain due to chronic venous insufficiency	
110028	flu	<b>Infectious event</b>
110030	actinic keratosis forehead	<b>Skin diseases</b>
110030	bruised rib	
110031	diabetes mellitus type 2	
110031	common cold	<b>Infectious event</b>
110034	coughing	
110034	flu	<b>Infectious event</b>
110036	tooth extraction	
110036	common cold	<b>Infectious event</b>
110036	restless legs	
110036	stung by wasp	
110036	paronychia	<b>Infectious event</b>
110036	flu	<b>Infectious event</b>
110041	worsening of preexistent angina pectoris	<b>Cardiovascular disorder</b>
110041	furuncle	<b>Infectious</b>
110041	COPD, disturbed lung diffusion capacity	
110043	Postoperative infection after gastric bypass surgery	<b>Infectious event</b>
110043	flu	<b>Infectious event</b>
110043	hair loss	
110043	flu	<b>Infectious event</b>
110044	cystitis	<b>Infectious event</b>
110044	coughing	
110044	cystitis	<b>Infectious event</b>
110044	diarrhea	
110047	erysipelas left leg	<b>Infectious event</b>
110047	erysipelas left leg	
110047	erysipelas left leg	<b>Infectious event</b>
110047	erysipelas left leg	
110051	vitamin D deficiency	
110052	flu	<b>Infectious event</b>
110052	bruising of left foot	
110052	onychomycosis	<b>Infectious event</b>

110056	increase of joint pain	<b>Musculoskeletal disorder</b>
110056	gastroenteritis	<b>Infectious event</b>
110056	surmenage	
110058	pneumonia	<b>Infectious event</b>
110061	sinusitis	<b>Infectious event</b>
110061	common cold	<b>Infectious event</b>
110061	common cold	<b>Infectious event</b>
110063	coughing	
110063	gastroenteritis	<b>Infectious event</b>
110063	bronchitis	<b>Infectious event</b>
110063	infection parotid gland	<b>Infectious event</b>
110065	gastroenteritis	<b>Infectious event</b>
110065	recurrent urinary tract infections	<b>Infectious event</b>
110067	respiratory tract infection (bacterial)	<b>Infectious event</b>
110067	common cold	<b>Infectious event</b>
110067	surgery of right hip fracture	<b>Elective surgery</b>
110067	respiratory tract infection	<b>Infectious event</b>
110067	conjunctivitis	<b>Infectious event</b>
110067	neck and shoulders complaints	<b>Musculoskeletal disorder</b>
110069	back pain	<b>Musculoskeletal disorder</b>
110074	common cold	<b>Infectious event</b>
110077	gastroenteritis	<b>Infectious event</b>
110077	common cold	<b>Infectious event</b>
110077	coughing	<b>Infectious event</b>
110079	flu	<b>Infectious event</b>
110079	vitamin B12 deficiency	
110079	more bruising	
110079	common cold	<b>Infectious event</b>
110079	herpes simplex	<b>Infectious event</b>
110079	increase of fatigue complaints after discontinuation vitamin B12 administration	
110079	herpes simplex	<b>Infectious event</b>

110079	increase of fatigue complaints after adalimumab injection	
110081	cataract	
110081	Boucharde's nodes	
110082	respiratory infection	<b>Infectious event</b>
110084	tonsillitis	<b>Infectious event</b>
110085	actinic keratosis right eyelid	<b>Skin diseases</b>
110085	actinic keratosis	<b>Skin diseases</b>
110085	renal function disorder	
110088	gastroenteritis	<b>Infectious event</b>
110088	common cold	<b>Infectious event</b>
110088	hand eczema (orthoergic)	<b>Skin diseases</b>
110088	gastroenteritis	<b>Infectious event</b>
110091	common cold	<b>Infectious event</b>
110092	flu	<b>Infectious event</b>
110092	flu	<b>Infectious event</b>
110095	obstructive sleep apnea syndrome	
110099	allergy (hay fever/ dogs)	
110099	cystitis	<b>Infectious event</b>
110100	common cold	<b>Infectious event</b>
110100	verruca vulgaris	<b>Skin diseases</b>
110100	flu	<b>Infectious event</b>
110102	common cold	<b>Infectious event</b>
110103	flu	<b>Infectious event</b>
110103	contusion intercostal muscles	
110103	warm feeling of skin	
110103	contusion right foot (digit 2)	
110103	flu	<b>Infectious event</b>
110105	total knee prosthesis due to gonartrosis	<b>Elective surgery</b>
110108	hyperhidrosis	
110116	carotis desobstruction	<b>Elective surgery</b>

110116	ischemic cerebrovascular accident	<b>Cardiovascular event</b>
110119	inflammation left tooth (molar)	<b>Infectious event</b>
110119	tooth inflammation	<b>Infectious event</b>
110119	trichilemmal cyst/ pilar cyst	<b>Skin diseases</b>
110119	common cold	<b>Infectious event</b>
110119	cat bite	
110119	inflammation digit 4 (right side feet)	<b>Infectious event</b>
110119	common cold	<b>Infectious event</b>
110119	filliformic wart left eyelid	<b>Skin diseases</b>
110119	pigmentated hyperkeratotic seborrheic keratosis	<b>Skin diseases</b>
110119	ballondilatation distal anastomosis femoral-femoral crossover	<b>Elective surgery</b>
110119	pain left groin	
110121	flu	<b>Infectious event</b>
110122	flu	<b>Infectious event</b>
110126	actinic keratosis nose	<b>Skin diseases</b>

**Dose reduction**

110009	back pain	<b>Musculoskeletal disorder</b>
110009	supraspinatus tendinosis left shoulder	<b>Musculoskeletal disorder</b>
110009	common cold	<b>Infectious event</b>
110011	stomachache	
110011	pneumonia	<b>Infectious event</b>
110011	submammary mycosis	<b>Infectious event</b>
110014	flu	<b>Infectious event</b>
110014	headache	
110014	gonarthrosis left	<b>Musculoskeletal disorder</b>
110016	tendovaginitis stenosaurs	<b>Musculoskeletal disorder</b>
110017	diarrhea	
110017	common cold	<b>Infectious event</b>
110017	common cold	<b>Infectious event</b>



110019	common cold	<b>Infectious event</b>
110019	flu	<b>Infectious event</b>
110019	otitis externa media	<b>Infectious event</b>
110022	common cold	<b>Infectious event</b>
110022	gastroenteritis	<b>Infectious event</b>
110022	palpitations due to preexistent paroxysmal artrial tachycardia	<b>Cardiovascular disorder</b>
110023	common cold	<b>Infectious event</b>
110024	diabetes mellitus type 2	
110024	common cold	<b>Infectious event</b>
110024	common cold	<b>Infectious event</b>
110024	common cold	<b>Infectious event</b>
110024	increased pain of flexor tendinopathy	<b>Musculoskeletal disorder</b>
110024	intestinal polyp removed (2x)	
110027	eczema	<b>Skin diseases</b>
110027	flu	<b>Infectious event</b>
110029	actinic keratoses	<b>Skin diseases</b>
110029	common cold	<b>Infectious event</b>
110029	ankle fracture	
110029	decreased bone reformation after ankle fracture	<b>Musculoskeletal disorder</b>
110029	flu	<b>Infectious event</b>
110033	flu	<b>Infectious event</b>
110035	common cold	<b>Infectious event</b>
110035	otitis	<b>Infectious event</b>
110035	excision scar tissue	
110035	common cold	<b>Infectious event</b>
110037	cystitis	<b>Infectious event</b>
110037	common cold	<b>Infectious event</b>
110037	pain left foot (digit 3)	<b>Musculoskeletal disorder</b>
110038	common cold	<b>Infectious event</b>
110039	seborrheic keratosis	<b>Skin diseases</b>
110039	common cold	<b>Infectious event</b>
110039	cystitis	<b>Infectious event</b>

110039	common cold	<b>Infectious event</b>
110040	idiopathic hypomelanosis gutata	<b>Skin diseases</b>
110040	common cold	<b>Infectious event</b>
110042	sore throat	
110042	flu	<b>Infectious event</b>
110048	more pain feet due to (preexistent) peripheral arterial disease	
110048	fasciotomy left leg (clinically suspected for compartment syndrome)	
110048	common cold	<b>Infectious event</b>
110048	percutaneous intentional extraluminal recanalization left superficial femoral artery	<b>Elective Surgery</b>
110048	delirium	
110048	percutaneous transluminal angioplasty with stent in right a. iliaca externa	<b>Elective Surgery</b>
110048	percutaneous transluminal angioplasty with stent in right a. iliaca	<b>Elective Surgery</b>
110048	apathy	
110048	ischemic CVA left hemisphere	<b>Cardiovascular event</b>
110048	retrograde percutaneous intentional extraluminal recanalization left superficial femoral artery	<b>Elective Surgery</b>
110048	open wound left leg	
110049	tooth extraction	
110049	flu	<b>Infectious Event</b>
110049	nycturia	
110050	common cold	<b>Infectious event</b>
110053	flu	<b>Infectious event</b>
110054	sore throat	
110054	headache	
110054	hypertension due to stress	
110054	flu	<b>Infectious event</b>
110054	flu 1	<b>Infectious event</b>
110054	common cold	<b>Infectious event</b>
110055	bursitis left shoulder	<b>Musculoskeletal disorder</b>
110059	bruised ankle	
110059	night sweats	
110060	common cold	<b>Infectious event</b>

110060	back pain	<b>Musculoskeletal disorder</b>
110060	gastroenteritis	<b>Infectious event</b>
110060	flu 1	<b>Infectious event</b>
110062	grawitz tumor right kidney	<b>Malignancy</b>
110062	back pain	<b>Musculoskeletal disorder</b>
110064	common cold	<b>Infectious event</b>
110064	swollen right knee	<b>Musculoskeletal disorder</b>
110066	coughing	
110068	diarrhea	
110068	gout right foot (metatarsophalangeal 2)	<b>Musculoskeletal disorder</b>
110068	gout	<b>Musculoskeletal disorder</b>
110068	common cold	<b>Infectious event</b>
110068	gout right foot (metatarsophalangeal 1)	<b>Musculoskeletal disorder</b>
110068	gout right foot (metatarsophalangeal 1) and lower knuckle (left feet)	<b>Musculoskeletal disorder</b>
110070	diarrhea	
110070	papillotomy due to cholangitis	<b>Elective surgery</b>
110070	diverticulitis	<b>Infectious event</b>
110072	more pain left knee and both hips	<b>Musculoskeletal disorder</b>
110072	pain left arm and elbow	<b>Musculoskeletal disorder</b>
110072	hoarseness	
110076	depression	
110076	migraine	
110076	more pain (preexistent) hernia nuclei pulposi	<b>Musculoskeletal disorder</b>
110076	increased frequency migraine attacks	
110076	common cold	<b>Infectious event</b>
110076	wound left knee due to chain saw	
110080	gout (lateral side right foot)	<b>Musculoskeletal disorder</b>
110080	gout	<b>Musculoskeletal disorder</b>
110080	onychomycosis	<b>Infectious event</b>
110080	flu	<b>Infectious event</b>
110080	night sweats	
110087	more joint pain	<b>Musculoskeletal disorder</b>

110086	viral infection	<b>Infectious event</b>
110086	more joint complaints	<b>Musculoskeletal disorder</b>
110089	more complaints (preexistent) irritable bowel syndrome	
110089	tonsillitis	<b>Infectious event</b>
110089	flu	<b>Infectious event</b>
110089	shoulder tendinopathy	<b>Musculoskeletal disorder</b>
110089	coughing	
110090	cystitis	<b>Infectious event</b>
110090	common cold	<b>Infectious event</b>
110090	cystitis	<b>Infectious event</b>
110096	partial medial meniscectomy (left)	<b>Elective surgery</b>
110097	common cold	<b>Infectious event</b>
110097	common cold	<b>Infectious event</b>
110098	sore throat	
110098	night sweats	
110098	onychomycosis	<b>Infectious event</b>
110101	common cold	<b>Infectious event</b>
110101	onychomycosis	<b>Infectious event</b>
110104	cystitis	<b>Infectious event</b>
110104	microdular and nodular basalcellcarcinoma (nose)	<b>Non melanoma skin cancer</b>
110104	infection left foot	<b>Infectious event</b>
110104	infection left foot	<b>Infectious event</b>
110104	hordeolum (stye) left eye	<b>Infectious event</b>
110104	bursitis right shoulder	<b>Musculoskeletal disorder</b>
110104	hordeolum (stye)	<b>Infectious event</b>
110106	back pain	<b>Musculoskeletal disorder</b>
110106	more joint pain	<b>Musculoskeletal disorder</b>
110109	mycosis	<b>Infectious event</b>
110111	cystitis	<b>Infectious event</b>
110112	bursitis	<b>Musculoskeletal disorder</b>

110113	cerebrovascular accident (brainstem)	<b>Cardiovascular event</b>
110117	migraine	
110117	migraine	
110117	migraine	
110123	flu	<b>Infectious event</b>
110123	flu	<b>Infectious event</b>
110123	migraine	
110123	migraine	
110123	hay fever	
110123	eye infection	<b>Infectious event</b>
110123	hay fever	
110123	laryngitis	<b>Infectious event</b>
110124	common cold	<b>Infectious event</b>
110124	more muscle and joint pain	<b>Musculoskeletal disorder</b>
110125	flu	<b>Infectious event</b>
110125	wound left hand (digit 2)	