Response to 'Missing pebble in the mosaic of rheumatic diseases and mental health: younger does not always mean happier' by Alunno *et al*

In their letter 'A missing pebble in the mosaic of rheumatic diseases and mental health: younger does not always mean happier',[1] Alunno *et al* commented on our recent publication[2] and raised the issue of determinants of psychological well-being in different age groups of persons with axial spondyloarthritis (axSpA). We very much appreciate their interest in our study and valuable comments made and would like to address the raised issues here in more details.

In our study, we investigated determinants of psychological well-being in persons with axSpA using the five-item WHO Well-Being Index (WHO-5), a sensitive and specific screening tool for depression. We found that among 1736 persons with axSpA aged 18–79 years only 42% had a good well-being, whereas 28% had mild depressive symptoms and 31% even had moderate-to-severe depressive symptoms.[2] In the linear regression model, we found a negative association between age and the odds of having moderate-to-severe depressive symptoms. Interestingly, a closer look at the association between age and WHO-5 showed a non-linear trend. In fact, the prevalence of moderate-to-severe depressive symptoms increased from 15% for patients aged 18–29 years to almost 40% for patients aged 40–59 years and then decreased to 24% for patients aged 70–79 years (figure 1).

Importantly, on the group level, persons aged 30–49 years had higher levels of stress (self-reported) compared with younger and older age groups but also reported the highest level of income (table 1). A self-reported lack of exercise was highest in persons aged between 18 and 49 and decreased thereafter. Disease activity and functional impairment (Bath Ankylosing Spondylitis Disease Activity Index and Bath Ankylosing Spondylitis Functional Index, respectively) were lowest in the youngest group (18–29 years) and rather comparable in all other age groups.

Data from the Consortium of Rheumatology Researchers of North America registry revealed that among persons with rheumatoid arthritis (RA), the overall prevalence of comorbidities is higher in older patients.[3] In our study, we found that among persons with axSpA, the prevalence of cardiovascular diseases, neurological disorders, metabolic and endocrine disorders, osteoarthritis, spondylosis and disorders of bone density was also increasing with age (table 2). However, mental disorders (according to the claims data) were more common in middle-aged persons compared with younger and older persons mirroring the distribution of the prevalence of depressive symptoms according to the WHO-5.

In addition, we conducted a multivariable regression analysis for each age group. In all models, we included sex plus all parameters which were found to be associated with depressive symptoms in the original analysis conducted in the entire group (table 3). Age groups 18–29 years and 30–39 years were analysed as one group in order to achieve convergence of the procedure that was not possible otherwise due to a relatively small number of patients in the youngest age group. Higher disease activity and a higher level of functional impairment were associated with moderate-to-severe depressive symptoms in almost all age groups (table 3). At the same time, suffering from stress and lack of exercise showed the strongest association with depressive symptoms in the youngest group, while lower income played a role only in the young and mid-aged groups.

In conclusion, we found the highest prevalence of both, depressive symptoms derived from the WHO-5 score and mental

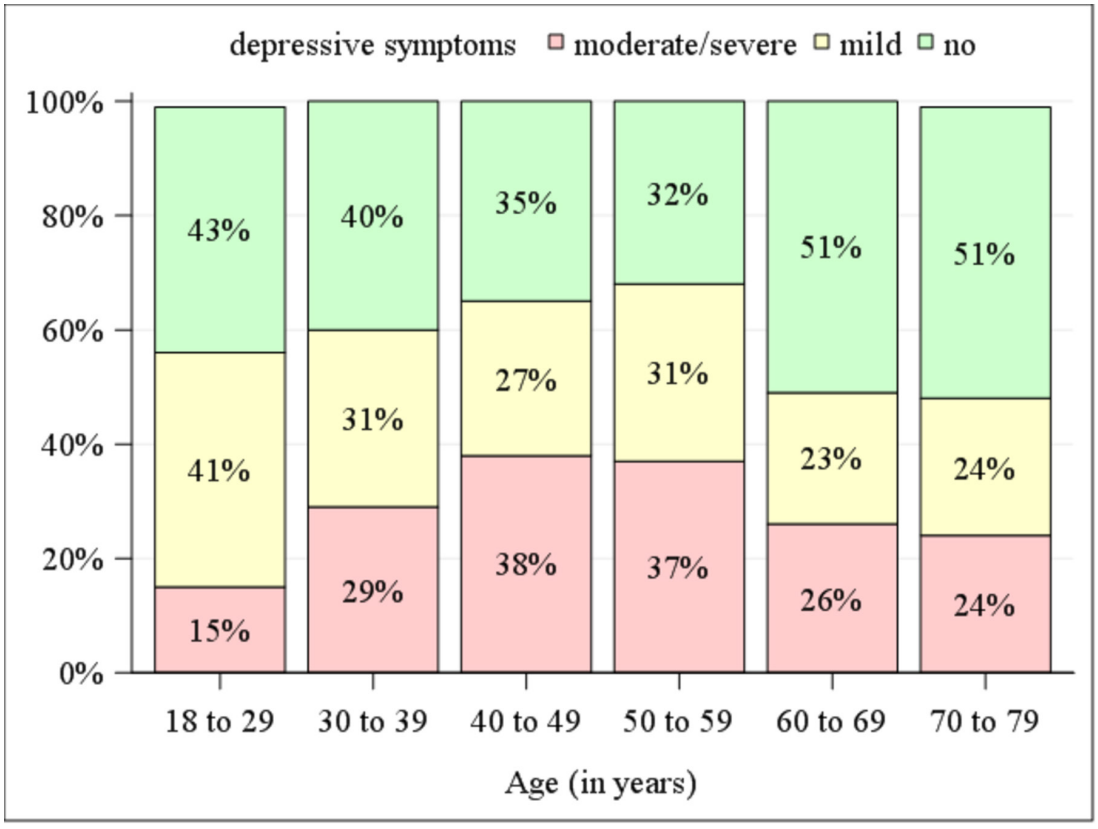

Figure 1 Prevalence of depressive symptoms (according to the five-item WHO Well-Being Index (WHO-5)) in different age groups.

Table 1 Main demographic, disease related, lifestyle and socioeconomic characteristics of patients with axial spondyloarthritis in different age groups

	Age (years)					
	18–29, n=80	30–39, n=207	40–49, n=361	50–59, n=376	60–69, n=372	70–79, n=340
Sex, female	41.1	47.9	54.7	50.3	45.0	35.7
BASDAI, 0–10	3.5±0.2	4.0±0.1	4.6±0.1	4.8±0.1	4.5±0.1	4.6±0.1
BASFI, 0–10	2.1±0.2	2.6±0.1	3.6±0.1	4.3±0.1	4.6±0.1	5.0±0.1
Lack of exercise	29.9	32.6	27.6	21.5	19.9	24.9
Suffering from stress	50.2	61.1	59.2	48.6	23.6	16.7
Household income, €						
<1500	31.5	19.6	14.4	24.8	32.0	32.3
1500–3200	57.6	53.3	52.2	53.3	59.1	60.2
>3200	10.9	27.0	33.3	21.9	9.0	7.6

Values are presented as mean±SE of the mean for continuous variables and as percentages otherwise.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index.

Table 2 Comorbidities according to the claims data in patients with axial spondyloarthritis in different age groups

	Age (years)					
	18–29, n=80	30–39, n=207	40–49, n=361	50–59, n=376	60–69, n=372	70–79, n=340
Cardiovascular diseases (%)						
Hypertensive diseases (I10–I15)	2.1	13.6	31.7	48.9	65.4	84.7
Ischaemic heart diseases (I20–I25)	–	–	1.6	6.4	16.5	33.7
Diseases of arteries (I70–I79)	1.4	1.4	3.6	4.8	15.6	19.7
Diseases of veins (I80–I89)	4.2	7.5	14.4	17.5	22.2	27.2
Mental disorders (%)						
Depressive disorders (F32, F33)	13.9	17.6	21.6	27.9	20.9	20.5
Anxiety disorders (F40, F41)	6.4	9.0	8.1	12.5	8.9	8.1
Reaction to severe stress and adjustment disorders (F43)	6.0	10.6	11.2	13.5	9.1	4.9
Somatoform disorders (F45)	13.1	16.3	23.3	25.2	17.7	21.8
Neurological disorders (%)						
Nerve, nerve root and plexus disorders (G50–G59)	3.5	5.7	9.6	14.0	13.2	13.4
Polyneuropathies (G60–G64)	–	2.0	3.6	6.4	10.5	17.4
Sleep disorders (G47)	–	4.9	6.9	9.6	11.3	15.8
Obstructive sleep apnoea (G47.31)	–	–	1.4	2.4	4.6	5.0
Musculoskeletal disorders (other than axSpA) (%)						
Osteoarthritis (M15–M19)	3.9	11.6	19.4	34.8	47.0	57.6
Spondylosis (M47)	17.7	16.4	20.4	24.4	25.8	30.4
Other soft tissue disorders, not elsewhere classified (M79)	20.9	29.5	27.8	28.4	25.7	22.8
Fibromyalgia (M79.7)	2.1	2.5	4.0	5.8	4.8	4.3
Disorders of bone density (M80–M85)	2.1	4.2	5.5	13.6	19.6	18.6
Metabolic and endocrine disorders (%)						
Disorders of thyroid gland (E00–E07)	9.2	14.9	26.4	29.6	36.4	29.5
Diabetes mellitus (E10–E14)	–	4.8	9.0	13.1	21.3	30.6
Type 2 diabetes mellitus (E11)	–	1.8	7.7	11.3	18.6	28.0
Overweight (E65–E68)	5.7	10.8	13.0	14.6	15.6	19.2
Respiratory tract diseases (%)						
Chronic obstructive pulmonary disease (J44)	–	1.0	5.2	7.4	13.2	14.2
Asthma bronchiale (J45)	8.1	10.7	11.7	9.8	10.7	7.7
Gastrointestinal diseases (%)						
Diseases of oesophagus, stomach and duodenum (K20–K31)	19.2	13.7	19.7	25.3	25.8	32.6

disorders according to the claims data, in middle-aged persons (40–59 years of age) with axSpA. These persons reported the highest prevalences of stress and lack of exercise which is likely related to factors such as career-oriented and family demands. The mentioned factors together with the impact of the disease—that was very similar across the age groups—are likely to be responsible to the higher level of depressive symptoms in the mid-aged population. Therefore, according to our data, a careful evaluation of depressive symptoms can be recommended in particular in individuals with axSpA aged between 40 and 59. In this age group, disease specific, socioeconomic and lifestyle factors were associated with the highest risk of a depressive disorder.

Table 3 Factors associated with the presence of symptoms suggestive of depression (WHO-5 score of ≤28) in the multivariable regression analysis in different age groups

	Reference	All patients*, n=1736, OR (95% CI)	Age 18–39, n=287,OR (95% CI)	Age 40–49, n=361, OR (95% CI)	Age 50–59, n=376, OR (95% CI)	Age 60–69, n=372, OR (95% CI)	Age 70–79, n=340, OR (95% CI)
Age	Per 10 years	**0.98 (0.97 to 0.99)**	–	–	–	–	–
Sex, female	Male	1.00 (0.77 to 1.29)	1.29 (0.68 to 2.43)	0.70 (0.42 to 1.18)	1.01 (0.59 to 1.72)	0.86 (0.48 to 1.56)	1.57 (0.85 to 2.91)
BASDAI	Per unit	**1.37 (1.27 to 1.49)**	1.11 (0.91 to 1.35)	**1.40 (1.21 to 1.63)**	**1.28 (1.06 to 1.54)**	**1.74 (1.40 to 2.16)**	**1.38 (1.13 to 1.67)**
BASFI	Per unit	**1.25 (1.17 to 1.33)**	**1.37 (1.13 to 1.66)**	**1.17 (1.02 to 1.34)**	**1.35 (1.18 to 1.56)**	1.15 (0.99 to 1.34)	**1.23 (1.06 to 1.42)**
Lack of exercise	No	**1.50 (1.14 to 1.98)**	**1.91 (1.02 to 3.55)**	1.26 (0.73 to 2.15)	1.23 (0.66 to 2.32)	1.84 (0.93 to 3.64)	1.77 (0.90 to 3.49)
Suffering from stress	No	**2.03 (1.55 to 2.64)**	**3.39 (1.66 to 6.94)**	**2.01 (1.19 to 3.37)**	**2.04 (1.19 to 3.50)**	1.20 (0.62 to 2.33)	1.87 (0.87 to 4.01)
Household income, < € 1500	> € 3200	**1.88 (1.27 to 2.78)**	2.42 (0.95 to 6.20)	1.25 (0.55 to 2.81)	**2.52 (1.13 to 5.61)**	1.65 (0.50 to 5.39)	2.06 (0.45 to 9.4)
Household income, € 1500–3200	> € 3200	**1.54 (1.08 to 2.19)**	**3.12 (1.42 to 6.85)**	1.37 (0.78 to 2.42)	1.83 (0.88 to 3.82)	0.76 (0.24 to 2.41)	2.20 (0.49 to 9.92)

*The original model including age as a continuous covariate is shown for a reference purpose.
Odds ratios of variables associated with a WHO-5 score of ≤ 28 are shown in bold.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; WHO-5, five-item WHO Well-Being Index.

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