ORIGINAL RESEARCH

Age, time living with diagnosed HIV infection, and self-rated health

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Objectives

An increasing proportion of people living with HIV are older adults, who may require specialized care. Adverse physical and psychological effects of HIV infection may be greatest among older people or those who have lived longer with HIV.

Methods

The ASTRA study is a cross-sectional questionnaire study of 3258 HIV-diagnosed adults (2248 men who have sex with men, 373 heterosexual men and 637 women) recruited from UK clinics in 2011–2012. Associations of age group with physical symptom distress (significant distress for at least one of 26 symptoms), depression and anxiety symptoms (scores $\geq$ 10 on PHQ-9 and GAD-7, respectively), and health-related functional problems (problems on at least one of three domains of the Euroqol 5D-3L)) were assessed, adjusting for time with diagnosed HIV infection, gender/sexual orientation and ethnicity.

Results

The age distribution of participants was: < 30 years, 5%; 30–39 years, 23%; 40–49 years, 43%; 50–59 years, 22%; and $\geq$ 60 years, 7%. Overall prevalences were: physical symptom distress, 56%; depression symptoms, 27%; anxiety symptoms, 22%; functional problems, 38%. No trend was found in the prevalence of physical symptom distress with age [adjusted odds ratio (OR) for trend across age groups, 0.96; 95% confidence interval (CI) 0.89, 1.04; $P = 0.36$]. The prevalence of depression and anxiety symptoms decreased with age [adjusted OR 0.86 (95% CI 0.79, 0.94; $P = 0.001$) and adjusted OR 0.85 (95% CI 0.77, 0.94; $P = 0.001$), respectively], while that of functional problems increased (adjusted OR 1.28; 95% CI 1.17, 1.39; $P < 0.001$). In contrast, a longer time with diagnosed HIV infection was strongly and independently associated with a higher prevalence of symptom distress, depression symptoms, anxiety symptoms, and functional problems ($P < 0.001$ for trends, adjusted analysis).

Conclusions

Among people living with HIV, although health-related functional problems were more common with older age, physical symptom distress was not, and mental health was more favourable. These results suggest that a longer time with diagnosed HIV infection, rather than age, is the dominating factor contributing to psychological morbidity and lower quality of life.

Keywords: ageing, anxiety, depression, HIV, symptoms, wellbeing.

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Introduction

As a consequence of advances in treatment, people diagnosed with HIV infection have greatly improved life expectancy [1]. In the UK, an estimated 27% of people living with diagnosed HIV infection were aged 50 years or over in 2013; this percentage has doubled in the past decade [2], with newly diagnosed infections among older people doubling in the same time period [2]. The Joint United Nations Programme on HIV/AIDS (UNAIDS) surmised that, world-wide by 2013, 10% of people diagnosed with HIV infection were over 50 years old and that in high-income countries this was nearer a third [3]. Research into this population's requirements and experiences is important [4–6]. However, few studies have examined the effect of older age on wellbeing in people living with HIV.

Symptom prevalence is high in people living with HIV even in the era of combination antiretroviral therapy (cART) [7,8]. It has been suggested that adverse physical and psychological effects of HIV infection may be greatest among older people [4]. Older people with HIV infection may have been living with the diagnosis for many years and may have ongoing health problems or disability related to HIV infection, in addition to the age-related morbidities common in the general population. HIV infection and/or treatment has been implicated in a number of chronic conditions generally prevalent among older people, including cardiovascular disease, dyslipidaemia and osteoporosis [9–11] and a high medication burden is common among older people living with HIV [12]. Immune activation and chronic inflammation are associated with HIV infection and may be more prevalent among older adults [13]. Later HIV diagnosis in older adults can result in a lower likelihood of achieving immune recovery with cART [6,14]. It is conceivable, therefore, that HIV infection and older age could have cumulative detrimental effects on health [15].

Depression is common among people living with HIV [16,17]. Although there is a perception that older people with HIV may be particularly vulnerable to depression as a consequence of issues such as stigma and lack of social support [4], the association between age and psychological symptoms among people with HIV is unclear [6,16,18,19]. Quality of life has been defined as 'multidimensional in construct including physical, emotional, mental, social, and behavioural components' [6] and has been found to be lower among older compared with younger people with HIV [17], but the role of psychological, physical and functional problems in this relationship is unclear.

As HIV infection is now a chronic condition, research into the impact of age on wellbeing is increasingly relevant to patient care. However, few studies have examined the association of both age and time since HIV diagnosis with self-rated health and symptoms. We examined these questions in the Antiretrovirals, Sexual Transmission Risk and Attitudes (ASTRA) study, a multicentre study of people living with HIV in the UK. We have previously reported that the health-related quality-of-life utility score was lower among people with diagnosed HIV compared with the UK general population, accounting for major demographic factors [17]. The aim of this present analysis was to assess, among people with diagnosed HIV, the association of age with: (a) the prevalence of physical symptoms causing distress, (b) the prevalence of depression and anxiety symptoms and (c) the prevalence of health-related functional problems, taking into account time since HIV diagnosis and other demographic factors.

Methods

The ASTRA study recruited 3258 individuals diagnosed with HIV infection from eight HIV out-patient clinics in the UK from February 2011 to December 2012 (64% response rate). Participants completed a self-administered questionnaire on a range of socio-demographic, health, HIV-related and lifestyle issues, and the clinic-recorded viral load and CD4 count were documented. Further details have been published [20].

In this analysis, information on physical symptoms, depression and anxiety symptoms, and health-related functional problems is reported in relation to age group, time with diagnosed HIV infection, gender/sexual orientation and ethnicity.

Symptom measures

Physical symptoms were quantified using a modified Memorial Symptom Assessment Scale-Short Form (MSAS-SF) scale [21], listing 26 common symptoms (Table 1). Participants were asked to report whether each symptom was present in the past 2 weeks, and, if so, to rank their distress on a four-point scale: 'did not bother me'; 'bothered/distressed a little bit'; 'bothered/distressed quite a bit'; 'bothered/distressed very much'. Symptoms were classified in two ways: 'present' (if the symptom was reported) and 'distressing' (if the symptom 'bothered/distressed quite a bit' or 'very much'). 'Physical symptom distress' was defined as reporting at least one of the 26 symptoms as distressing. Several symptom subgroups were considered (Table 1) where participants were classified as positive if they reported at least one of the symptoms in that category as distressing.

Depression symptoms and anxiety symptoms were measured using standard symptom inventories (the Patient Health Questionnaire, 9 item scale (PHQ-9) [22]

Table 1 Prevalence of 26 physical symptoms and physical symptom distress in the past 2 weeks in the study participants ($N = 3258$)

Symptom	Present n (%)	Distressing¶	
		n (%)	% of 'present'
Lack of energy	2116 (64.9)	844 (25.9)	39.9
Feeling drowsy/tired	2105 (64.6)	790 (24.2)	37.5
Difficulty sleeping	1890 (58.0)	796 (24.4)	42.1
Muscle aches or joint pains	1740 (53.4)	678 (20.8)	39.0
Trouble remembering things	1676 (51.4)	569 (17.5)	33.9
Problems with sexual interest/activity	1530 (47.0)	627 (19.2)	41.0
Difficulty concentrating	1514 (46.5)	462 (14.2)	30.5
Skin problems (e.g. rash, itching or dryness)	1375 (42.2)	430 (13.2)	31.3
Numbness, tingling or pain in hands or feet	1338 (41.1)	514 (15.8)	38.4
Headache	1294 (39.7)	343 (10.5)	26.5
Pain	1282 (39.3)	586 (18.0)	45.7
Feeling bloated	1253 (38.5)	366 (11.2)	29.2
Diarrhoea	1201 (36.9)	358 (11.0)	29.8
Sweats/fever	1192 (36.6)	412 (12.6)	34.6
Shortness of breath	1056 (32.4)	340 (10.4)	32.2
Cough	981 (30.1)	242 (7.4)	24.7
Dry mouth	970 (29.8)	226 (6.9)	23.3
Dizziness	961 (29.5)	293 (9.0)	30.5
Changes in fat in face or body	947 (29.1)	428 (13.1)	45.2
Nausea	811 (24.9)	221 (6.8)	27.3
Lack of appetite	754 (23.1)	204 (6.3)	27.1
Constipation	663 (20.3)	199 (6.1)	30.0
Changes in way food tastes	564 (17.3)	159 (4.9)	28.2
Weight loss	543 (16.7)	191 (5.9)	35.2
Mouth sores	531 (16.3)	155 (4.8)	29.2
Vomiting	392 (12.0)	125 (3.8)	31.9
Combined symptom categories			
Sleep/energy/tiredness problems*	2522 (77.4)	1140 (35.0)	45.2
Concentration/memory problems†	1927 (59.1)	736 (22.6)	38.2
Pain/headache‡	1746 (53.6)	688 (21.1)	39.4
Gastrointestinal symptoms§	1986 (61.0)	704 (21.6)	35.4

*Includes 'lack of energy', 'feeling drowsy/tired' and 'difficulty sleeping'.
†Includes 'trouble remembering things' and 'difficulty concentrating'.
‡Includes 'pain' and 'headache'.
§Includes 'feeling bloated', 'diarrhoea', 'nausea', 'constipation' and 'vomiting'.
¶Symptom causes 'quite a bit of' or 'very much' distress.

and Generalized Anxiety Disorder 7 item scale (GAD-7) [23]) that inquire about the frequency of occurrence of specific symptoms in the past 2 weeks: depression and anxiety were defined according to standard algorithms based on a total score of 10 or more in each case.

A 'health-related functional problem' was defined as reporting 'some' or 'severe' problems (rather than 'no problems') on one of three functional domains (mobility, self-care and daily activities) of a standard health-related quality of life (HrQoL) measure, the Euroqol 5D 3L (EQ-5D-3L) [24]. In addition, the three domains of the EQ-5D-3L were considered separately.

Missing values for individual questions on symptom/HrQoL questionnaires were counted as the absence of

symptoms. PHQ-9, GAD-7, modified MSAS-SF and the three domains of the EQ-5D-3L are shown in Appendix 2. Of note, both PHQ-9 and modified MSAS-SF incorporate questions on tiredness, sleep, appetite and concentration.

Statistical analysis

Age was grouped as follows: < 30, 30–39, 40–49, 50–59 and ≥ 60 years. Differences in participant characteristics by age group were assessed using χ^2 tests for trend.

Prevalences of physical symptom distress, depression, anxiety and health-related functional problems were calculated overall and by age group. Logistic regression was used to assess the association between age group and each of the health measures (dependent variables), adjusting for gender/sexual orientation [men who have sex with men (MSM), heterosexual men and women], ethnicity [white and nonwhite/missing] and years with diagnosed HIV infection [< 2, 2-<5, 5-<10, 10-<15, 15-<20 and ≥ 20 years]. Age was fitted as a categorical variable in the models. Tests for linear trend across categories were also performed for age and years with diagnosed HIV infection. Results are presented as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). Statistical significance was assessed using likelihood ratio tests. Sensitivity analyses: (i) treating age and years with diagnosed HIV infection as continuous rather than categorical variables (ii) additionally adjusting for university education and (iii) additionally adjusting for clinical centre yielded the same conclusions regarding trends (data not shown).

Results

Subject characteristics

Of the 3258 study participants, 2248 (69.0%) were MSM, 373 (11.4%) were heterosexual men and 637 (19.6%) were women. The mean age was 45 years [standard deviation (SD) 9.6 years; range 18–88 years). Of 3190 participants with age information, 172 (5.4%) were under 30 years old, 745 (23.4%) 30–39 years old, 1370 (42.9%) 40–49 years old, 689 (21.6%) 50–59 years old and 214 (6.7%) ≥ 60 years old. Time since diagnosis of HIV infection ($n = 3230$) was: 0–2 years for 373 patients (11.5%), 2–5 years for 498 (15.4%), 5–10 years for 893 (27.6%), 10–15 years for 647 (20.0%), 15–20 years for 488 (15.1%) and ≥ 20 years for 331 (10.2%). In terms of ethnic origin, 2220 (68.1%) participants were white, 614 (18.8%) were of black African ethnicity, 125 (3.8%) were of other black ethnicity and 299 (9.2%) were of other/missing ethnicity; 56.1% (1785 of 3183) of all partici-

pants were born in the UK. Over half of participants (1821 of 3174; 57.4%) were employed, 577 (18.2%) were unemployed, 420 (13.2%) were not working because of sickness/disability, 192 (6.0%) were retired, and 164 (5.2%) were students, took care of the home, or other. A high proportion of participants were university educated (1317; 40.4%). Overall, 86.5% (2771 of 3202) of participants were on ART, 76.2% (2466 of 3237) had viral load (VL) ≤ 50 HIV-1 RNA copies/mL and 18.5% (599 of 3235) had CD4 count < 350 cells/μL.

Older participants were more likely to be male (88.8% for age ≥ 60 years *vs.* 68.6% for age < 30 years; $P < 0.001$, χ^2 test for trend across all age groups), of white ethnicity (77.1% *vs.* 58.1%, respectively; $P < 0.001$), to have been born in the UK (70.0% *vs.* 51.5%, respectively; $P < 0.001$), to have been diagnosed with HIV infection for more than 10 years (63.0% *vs.* 5.3%, respectively; $P < 0.001$), to be on ART (93.8% *vs.* 60.9%, respectively; $P < 0.001$) and to have VL ≤ 50 copies/mL (88.7% *vs.* 48.8%, respectively; $P < 0.001$). Older people were less likely to be employed (19.7% *vs.* 60.9% for age ≥ 60 years *vs.* < 30 years, respectively; $P < 0.001$) No significant trend with age was found for university education (33.6% *vs.* 35.5%, respectively; $P = 0.11$) or CD4 count < 350 cells/μL (19.3% *vs.* 23.4%, respectively; $P = 0.69$).

Physical symptom distress

Table 1 reports the prevalence of each symptom according to whether it was (i) present and (ii) distressing. At least one symptom was reported as 'distressing' by 55.6% of participants (1811 of 3258), while 11.0% reported ten or more distressing symptoms. The five most prevalent distressing symptoms were 'lack of energy' (25.9%), 'difficulty sleeping' (24.4%), 'feeling drowsy/tired' (24.2%), 'muscle aches or joint pains' (20.8%) and 'problems with sexual interest/activity' (19.2%). Although lower in prevalence, 'pain' and 'changes in fat' were more likely to cause distress when present than other symptoms.

The three most prevalent distressing symptoms within age groups were the same for each of the four age groups under 60 years: 'lack of energy' (22.1–30.9%), followed by 'feeling drowsy/tired' (20.0–28.4%) and 'difficulty sleeping' (21.7–26.7%), and the proportion who reported no distressing symptoms ranged from 38.8% to 48.6%. Among participants aged ≥ 60 years the pattern was different: 'muscle ache/joint pains' was the most prevalent distressing symptom (23.8%), followed by 'pain' (18.2%) and 'lack of energy' (18.2%), but 47.7% of participants reported no distressing symptoms.

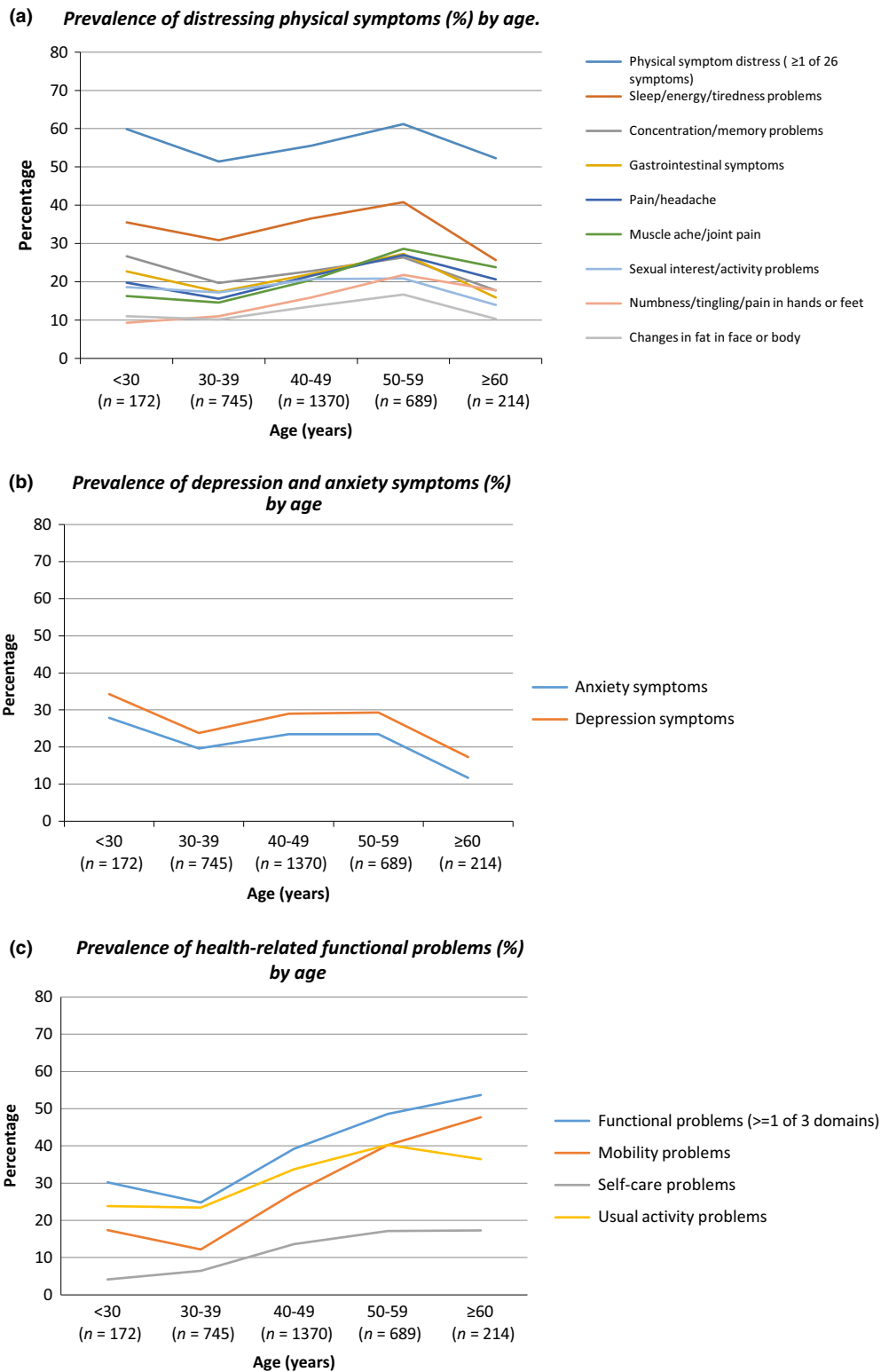Figure 1a shows the prevalence of physical symptom distress overall and for selected common symptoms and symptom subgroups by age group. The prevalence of overall symptom distress tended to increase slightly with age over the 30–59-year age range, but was lower in the ≥ 60-year age group. Interestingly, participants aged < 30 years tended to have a higher prevalence of distressing symptoms compared with those aged 30–40 years, and compared with the ≥ 60-year age group. Most of the symptom groups followed this pattern, with 'muscle-ache/joint pain', 'numbness/tingling/pain in the hands/feet' and 'pain' having the strongest increases with age.

The adjusted association of age with physical symptom distress is presented in Table 2. After adjustment for gender/sexual orientation, time with diagnosed HIV infection and ethnicity, there was no trend with age group in the prevalence of overall physical symptom distress. For 'numbness/tingling/pain in the hands or feet' and 'muscle ache/joint pain', however, there was a significant increase in prevalence with age, while for 'problems with sexual interest/activity' there was a significant decrease with age. However, for all symptom subgroups, the prevalence of distressing symptoms was lower among those aged ≥ 60 years than those aged 50–60 years. In fact, for many symptom groups, participants aged ≥ 60 years had the lowest prevalence of distressing symptoms overall.

Time with diagnosed HIV infection was strongly related to the prevalence of overall physical symptom distress and each symptom subgroup: those diagnosed for longer were more likely to report distressing symptoms (test for trend across categories $P < 0.001$ for overall symptom distress and all symptom measures in adjusted models, Table 2). There were also differences by gender/sexual orientation. For many symptom subgroups, the pattern was similar: compared with MSM, the prevalence of distressing symptoms tended to be somewhat lower among heterosexual men, and somewhat higher among women. There were few significant differences according to ethnicity.

Psychological symptoms

Depression (assessed using PHQ-9) was apparent in 27.1% (884 of 3258) of participants and anxiety (assessed using GAD-7) in 21.9% (715 of 3258). Figure 1b shows the associations with age. The prevalence of symptoms of depression tended to decrease with age, being highest in the < 30-year age group, similar across the three age groups from 30 to 59 years, and lowest in those aged ≥ 60 years. The prevalence of anxiety also tended to decrease with age, following a similar pattern and being lowest among the ≥ 60-year age group. These patterns of decreasing prevalence with age were stronger in the adjusted analysis (Table 3). However, in contrast to older age, longer time

(a)   *Prevalence of distressing physical symptoms (%) by age.*

Legend:
- Physical symptom distress (≥1 of 26 symptoms)
- Sleep/energy/tiredness problems
- Concentration/memory problems
- Gastrointestinal symptoms
- Pain/headache
- Muscle ache/joint pain
- Sexual interest/activity problems
- Numbness/tingling/pain in hands or feet
- Changes in fat in face or body

x-axis: Age (years): <30 (n = 172), 30-39 (n = 745), 40-49 (n = 1370), 50-59 (n = 689), ≥60 (n = 214)

(b)   *Prevalence of depression and anxiety symptoms (%) by age*

Legend:
- Anxiety symptoms
- Depression symptoms

(c)   *Prevalence of health-related functional problems (%) by age*

Legend:
- Functional problems (>=1 of 3 domains)
- Mobility problems
- Self-care problems
- Usual activity problems

Fig. 1 Prevalences (%) of (a) distressing physical symptoms, (b) depression and anxiety symptoms, and (c) health-related functional problems by age group. Physical symptom distress was defined using modified MSAS-SF (see Table 1); depression symptoms were defined as a PHQ-9 score ≥ 10; anxiety symptoms were defined as a GAD-7 score ≥ 10; health-related functional problems were defined using the three domains of Euro-qol 5D 3. N = 3190 participants with information on age..

Table 2 Adjusted association of age, time with diagnosed HIV infection, gender/sexual orientation and ethnicity with physical symptom distress (N = 3167)

Independent variable	Physical symptom distress*			Sleep/energy/tiredness problems			Concentration/memory problems			Gastrointestinal symptoms			Pain/headache		
	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjustd odds ratio[+]	95% CI
Age[+]	0.022			< 0.001			0.022			0.002			0.008		
< 30 years		1.84	(1.20, 2.82)		2.36	(1.49, 3.76)		2.04	(1.22, 3.41)		2.15	(1.25, 3.68)		1.22	(0.71, 2.07)
30–39 years		1.23	(0.89, 1.69)		1.74	(1.21, 2.51)		1.33	(0.88, 2.01)		1.40	(0.91, 2.14)		0.87	(0.58, 1.31)
40–49 years		1.25	(0.93, 1.68)		1.91	(1.36, 2.67)		1.42	(0.97, 2.08)		1.60	(1.08, 2.37)		1.13	(0.78, 1.62)
50–59 years		1.46	(1.06, 2.01)		2.08	(1.46, 2.95)		1.67	(1.12, 2.47)		1.98	(1.31, 2.97)		1.44	(0.99, 2.11)
≥ 60 years¶		1			1			1			1			1	
Test for trend‡	0.36	0.96	(0.89, 1.04)	0.080	0.93	(0.85, 1.01)	0.42	0.96	(0.87, 1.06)	0.77	0.99	(0.89, 1.09)	0.070	1.10	(0.99, 1.21)
Years with diagnosed HIV infection	< 0.001			< 0.001			< 0.001			< 0.001			< 0.001		
0–2 years¶		1			1			1			1			1	
2–5 years		1.08	(0.82, 1.41)		1.12	(0.82, 1.51)		1.14	(0.80, 1.64)		1.05	(0.72, 1.53)		1.35	(0.91, 2.01)
5–10 years		1.13	(0.89, 1.45)		1.33	(1.01, 1.75)		1.48	(1.07, 2.03)		1.49	(1.07, 2.09)		1.67	(1.17, 2.39)
10–15 years		1.35	(1.04, 1.76)		1.59	(1.19, 2.12)		1.40	(0.99, 1.96)		1.72	(1.21, 2.44)		1.82	(1.25, 2.64)
15–20 years		1.86	(1.39, 2.47)		1.97	(1.45, 2.68)		1.91	(1.34, 2.71)		2.05	(1.43, 2.95)		2.47	(1.69, 3.62)
≥ 20 years		2.73	(1.96, 3.79)		2.72	(1.95, 3.80)		2.52	(1.73, 3.66)		2.41	(1.64, 3.55)		3.58	(2.40, 5.35)
Test for trend‡	< 0.001	1.21	(1.14, 1.27)	< 0.001	1.22	(1.15, 1.29)	< 0.001	1.19	(1.11, 1.26)	< 0.001	1.21	(1.13, 1.28)	< 0.001	1.26	(1.18, 1.35)
Gender/sexual orientation	0.047			0.11			0.012			0.002			0.002		
MSM¶		1			1			1			1			1	
Heterosexual men		0.75	(0.58, 0.97)		0.75	(0.57, 0.99)		0.89	(0.65, 1.22)		0.63	(0.44, 0.89)		0.72	(0.51, 1.00)
Women		1.02	(0.81, 1.28)		0.97	(0.76, 1.23)		1.37	(1.06, 1.78)		1.17	(0.89, 1.54)		1.28	(0.98, 1.67)
Ethnicity	0.77			0.19			0.22			0.096			0.005		
White¶		1			1			1			1			1	
Other ethnicity		1.03	(0.84, 1.26)		0.87	(0.70, 1.07)		1.16	(0.92, 1.47)		0.81	(0.63, 1.04)		1.41	(1.11, 1.80)

Independent variable	Sexual interest/activity problems			Muscle ache/joint pain			Changes in fat in face or body			Numbness/tingling/pain in hands or feet		
	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI	P-value	Adjusted odds ratio[+]	95% CI
Age	0.041			0.001			0.15			0.001		
< 30 years		2.18	(1.23, 3.85)		0.85	(0.50, 1.48)		1.56	(0.79, 3.08)		0.65	(0.34, 1.24)
30–39 years		1.70	(1.09, 2.66)		0.70	(0.47, 1.04)		1.26	(0.75, 2.12)		0.68	(0.44, 1.06)
40–49 years		1.81	(1.19, 2.74)		0.87	(0.61, 1.24)		1.40	(0.87, 2.25)		0.90	(0.61, 1.33)
50–59 years		1.66	(1.07, 2.55)		1.27	(0.88, 1.82)		1.71	(1.05, 2.79)		1.30	(0.87, 1.93)
≥ 60 years¶		1			1			1			1	
Test for trend‡	0.032	0.89	(0.81, 0.99)	0.001	1.18	(1.07, 1.31)	0.80	1.02	(0.90, 1.15)	< 0.001	1.22	(1.09, 1.36)
Years with diagnosed HIV infection	< 0.001			< 0.001			< 0.001			< 0.001		
0–2 years¶		1			1			1			1	
2–5 years		1.34	(0.91, 1.97)		1.45	(0.95, 2.20)		0.79	(0.48, 1.30)		1.37	(0.84, 2.21)
5–10 years		1.43	(1.00, 2.04)		1.84	(1.26, 2.69)		1.31	(0.86, 1.98)		1.81	(1.18, 2.78)
10–15 years		1.85	(1.28, 2.67)		2.20	(1.50, 3.25)		1.58	(1.02, 2.44)		2.46	(1.59, 3.81)
15–20 years		1.97	(1.34, 2.90)		3.09	(2.07, 4.60)		2.58	(1.66, 4.00)		2.62	(1.67, 4.11)

Table 2 (Continued)

Independent variable	Sexual interest/activity problems			Muscle ache/joint pain			Changes in fat in face or body			Numbness/tingling/pain in hands or feet		
	P-value	Adjusted odds ratio†	95% CI	P-value	Adjusted odds ratio†	95% CI	P-value	Adjusted odds ratio†	95% CI	P-value	Adjusted odds ratio†	95% CI
≥ 20 years	< 0.001	2.88	(1.92, 4.32)	< 0.001	4.07	(2.68, 6.18)	0.001	2.45	(1.53, 3.94)	< 0.001	3.38	(2.12, 5.41)
Test for trend‡		1.21	(1.13, 1.29)	< 0.001	1.31	(1.22, 1.40)	0.001	1.28	(1.18, 1.38)	0.002	1.26	(1.17, 1.35)
Gender/sexual orientation	0.15			0.29			0.54			0.070		
MSM¶		1			1			1			1	
Heterosexual men		0.92	(0.67, 1.28)		0.75	(0.54, 1.06)		0.93	(0.63, 1.39)		0.70	(0.48, 1.02)
Women		0.75	(0.56, 1.01)		1.48	(1.13, 1.94)		1.71	(1.25, 2.34)		1.36	(1.01, 1.84)
Ethnicity	0.69											
White¶		1			1			1			1	
Other ethnicity		0.95	(0.74, 1.23)		1.14	(0.89, 1.46)		1.10	(0.82, 1.47)		1.29	(0.98, 1.69)

For symptom subgroup definitions, see Table 1.
*Reports one or more distressing symptoms out of 26.
†Multivariable logistic regression model including all factors in table. P-values obtained using likelihood ratio tests.
‡Linear trend across groups.
¶Reference group.
CI, confidence interval; MSM, men who have sex with men.
'other ethnicity' includes missing values.

with diagnosed HIV infection was strongly associated with a higher prevalence of both depression and anxiety ($P < 0.001$, for trend across categories for each in adjusted models). There were no significant differences according to gender/sexual orientation or ethnicity.

Health-related functional problems

The prevalence of health-related functional problems was 38.1% (1240 of 3258) overall and the prevalence of individual domains was: mobility problems, 27.1%; self-care problems, 12.3%; and problems performing usual activity, 32.1%. Few participants (< 3%) reported 'extreme' problems with mobility, self-care or usual activities. Figure 1c shows that the prevalence of health-related functional problems tended to increase with age for the overall measure and all three domains.

Table 4 shows that patterns were similar in adjusted analysis. The prevalence of functional problems significantly increased with age. As was the case for the physical and psychological symptom measures, longer time since HIV diagnosis was strongly associated with a greater prevalence of functional problems, both overall and for each domain ($P < 0.001$ for trend across categories in adjusted models). In addition, mobility problems tended to be more common among women compared with MSM. There were no significant differences by ethnicity.

Discussion

In this large multicentre cross-sectional UK study, with older age, people living with HIV reported a higher prevalence of health-related functional problems, but a lower prevalence of depression and anxiety symptoms. There was no trend with age in the prevalence of overall physical symptom distress, but the pattern varied according to the specific symptom. Longer time with diagnosed HIV infection, however, was related to a higher prevalence of all self-rated health problems: symptom distress, depression, anxiety and each domain of functional problems, independently of age.

In our study, as found in the international START (Strategic Timing of AntiRetroviral Treatment) trial population at baseline, [25], the prevalence of problems with physical mobility and daily function (assessed using the EQ-5D-3L) increased with age, probably as a result primarily of an increasing prevalence of chronic illness and disability. Age was not significantly associatied with overall physical symptom distress, but prevalence did increase with age for specific symptom groups (muscle ache/joint pain, and numbness/tingling/pain in hands or

Table 3 Adjusted association of age, time with diagnosed HIV infection, gender/sexual orientation and ethnicity with psychological symptoms
(*N* = 3167)

Independent variable	Depression (score ≥ 10 on PHQ-9)			Anxiety (score ≥ 10 on GAD-7)		
	P-value	Adjusted odds ratio*	95% CI	*P*-value	Adjusted odds ratio*	95% CI
Age	< 0.001			< 0.001		
< 30 years		3.52	(2.13, 5.81)		4.13	(2.35, 7.26)
30–39 years		1.93	(1.28, 2.91)		2.35	(1.46, 3.79)
40–49 years		2.17	(1.48, 3.19)		2.59	(1.65, 4.06)
50–59 years		2.06	(1.38, 3.07)		2.48	(1.56, 3.94)
≥ 60 years‡		1			1	
Test for trend†	0.001	0.86	(0.79, 0.94)	0.001	0.85	(0.77, 0.94)
Years with diagnosed HIV infection	< 0.001			< 0.001		
0–2 years‡		1			1	
2–5 years		0.93	(0.67, 1.30)		1.20	(0.83, 1.73)
5–10 years		1.36	(1.01, 1.82)		1.75	(1.26, 2.44)
10–15 years		1.41	(1.03, 1.93)		1.48	(1.04, 2.11)
15–20 years		1.85	(1.33, 2.55)		2.23	(1.55, 3.20)
≥ 20 years		2.31	(1.63, 3.28)		2.85	(1.93, 4.20)
Test for trend†	< 0.001	1.20	(1.13, 1.27)	< 0.001	1.21	(1.13, 1.29)
Gender/sexual orientation	0.63			0.22		
MSM‡		1			1	
Heterosexual men		0.95	(0.71, 1.27)		1.02	(0.74, 1.39)
Women		1.10	(0.85, 1.41)		1.25	(0.96, 1.62)
Ethnicity	0.56			0.16		
White‡		1			1	
Other ethnicity		1.07	(0.86, 1.33)		1.19	(0.94, 1.50)

*Multivariable logistic regression model including all factors in table. *P*-values obtained using likelihood ratio test.
†Linear trend across groups.
‡Reference group.
CI, confidence interval; MSM, men who have sex with men.
'other ethnicity' includes missing values.

feet). However, we found a lower prevalence of distressing symptoms in the over-60s group compared with younger age groups, both overall and for many symptom subgroups. This could, in part, be attributable to older adults attributing health changes to natural ageing and therefore not rating them as distressing [26,27]. Previous research also posits that older adults may face fewer high-demand situations as a consequence of retirement, leaving increased time and mental reserves for coping with physical distress [28]. It could also reflect 'resilience' in older HIV-diagnosed people, lower expectations of good health, or greater tolerance of poor health function [29].

In terms of mental health, the prevalence of depression and anxiety, assessed using standardized symptom questionnaires, tended to decrease with age, a trend that became more marked after adjustment for time with diagnosed HIV infection. In particular, the prevalences of depression and anxiety were lower in the over-60s compared with all other age groups. Interestingly, when analysed by individual questions, the decreasing prevalence with age was more apparent for 'psychological' symptoms of depression such as 'feeling down' or 'thoughts you would be better off dead', than for 'physical' symptoms of depression, such as 'feeling tired' or 'appetite problems' (data on request). It is possible that deteriorating physical

health in older age, or ageing with HIV infection, in addition to depression contributes to these 'physical' symptoms [30], or that in older adults depression is defined more often by somatic, rather than psychological, symptoms [31]. It has been suggested that the burden of psychological symptoms is high among older people living with HIV [6,32,33], although few studies have assessed the association between age and anxiety. Our results showed a lower prevalence of psychological symptoms among older people living with HIV, which could be mediated by improved social, behavioural or economic circumstances in the older population (such as reduced recreational drug use). It is possible that the lower prevalences of anxiety and depression among older compared with younger people living with HIV reflect better adaptation to hardship in older adults, developed through their lifespan [34,35], or 'resilience' [36], which has been found to be high in older HIV-diagnosed people [28,37]. Alternatively, this could be an example of 'successful ageing' in HIV-diagnosed people; the ability to maintain mental health despite age-related health losses [37]. However, it could also reflect a 'survivor' selection effect towards psychological wellbeing.

The overall prevalence of health-related functional problems, as assessed by three domains of the EQ-5D-3L,

Table 4 Adjusted association of age, time with diagnosed HIV infection, gender/sexual orientation and ethnicity with health-related function problems (N = 3167)

Independent variable	Functional problems (≥1 of 3 domains)*			Mobility problems			Self-care problems			Usual activities problems		
	P-value	Adjusted odds ratio[†]	95% CI	P-value	Adjusted odds ratio[†]	95% CI	P-value	Adjusted odds ratio[†]	95% CI	P-value	Adjusted odds ratio[†]	95% CI
Age	< 0.001			< 0.001			0.003			0.016		
<30 years		0.60	(0.38, 0.94)		0.39	(0.24, 0.65)		0.37	(0.15, 0.92)		0.88	(0.55, 1.41)
30–39 years		0.41	(0.29, 0.57)		0.22	(0.15, 0.32)		0.53	(0.33, 0.86)		0.78	(0.55, 1.10)
40–49 years		0.62	(0.46, 0.84)		0.45	(0.33, 0.61)		0.87	(0.59, 1.30)		1.02	(0.74, 1.39)
50–59 years		0.81	(0.59, 1.11)		0.73	(0.53, 1.00)		1.00	(0.66, 1.51)		1.19	(0.86, 1.66)
≥ 60 years§		1			1			1			1	
Test for trend‡	< 0.001	1.28	(1.17, 1.39)	< 0.001	1.54	(1.40, 1.70)	0.001	1.24	(1.10, 1.41)	0.011	1.12	(1.03, 1.22)
Years with diagnosed HIV infection	< 0.001			< 0.001			< 0.001			< 0.001		
0–2 years§		1			1			1			1	
2–5 years		1.29	(0.95, 1.77)		1.23	(0.83, 1.84)		1.29	(0.65, 2.55)		1.29	(0.93, 1.79)
5–10 years		1.43	(1.08, 1.90)		1.81	(1.28, 2.57)		2.92	(1.64, 5.21)		1.38	(1.02, 1.85)
10–15 years		1.94	(1.44, 2.60)		2.45	(1.7, 3.50)		3.14	(1.74, 5.65)		1.73	(1.27, 2.36)
15–20 years		3.14	(2.30, 4.28)		4.04	(2.80, 5.82)		4.99	(2.77, 9.00)		2.87	(2.08, 3.96)
≥ 20 years		4.55	(3.24, 6.41)		5.05	(3.42, 7.44)		6.88	(3.77, 12.56)		4.24	(3.00, 6.01)
Test for trend‡	< 0.001	1.36	(1.29, 1.44)	< 0.001	1.42	(1.33, 1.51)	< 0.001	1.44	(1.33, 1.56)	< 0.001	1.34	(1.26, 1.42)
Gender/sexual orientation	0.41			0.13			0.70			0.68		
MSM§		1			1			1			1	
Heterosexual men		1.03	(0.79, 1.35)		1.09	(0.81, 1.50)		1.18	(0.80, 1.74)		0.93	(0.70, 1.23)
Women		1.17	(0.92, 1.49)		1.31	(1.01, 1.71)		1.10	(0.77, 1.57)		1.06	(0.83, 1.36)
Ethnicity	0.80			0.43			0.34			0.64		
White§		1			1			1			1	
Other ethnicity		1.03	(0.83, 1.27)		1.10	(0.87, 1.39)		0.86	(0.63, 1.18)		0.95	(0.76, 1.18)

*Reports at least some difficulties with at least one of the three domains.
[†]Multivariable logistic regression model including all factors in table. P-values obtained using likelihood ratio test.
‡Linear trend across groups.
§Reference group.
CI, confidence interval; MSM, men who have sex with men.
'other ethnicity' includes missing values

increased with age. Similar patterns of results were found in other cross-sectional studies. A study using the WHO-QOL-HIV [38] across eight (mainly low-income) countries found physical symptoms tended to be more common for older HIV-diagnosed people but mental health aspects were more favourable. Similarly, in the international START trial population, overall quality of life and the physical health component decreased with age, but the mental health component improved [25]. A multicentre US study found few differences by age in health-related quality of life among HIV-diagnosed people [18] using the HAT-Quality of Life scale, but in this scale daily function has a smaller role and psychosocial measures take precedence [39]. These results highlight the sensitivity of quality of life analyses to the specific instrument used, and weighting of domains within that instrument, and emphasize the importance of understanding contrasting trends across different health domains.

In contrast to older age, longer time with diagnosed HIV infection was strongly and independently related to poorer physical and psychological health across all measures studied, suggesting it may be a more important factor than chronological age in determining wellbeing among people living with HIV. The association between longer time with diagnosed HIV infection and poorer health is likely to be related to earlier calendar time of diagnosis: having been diagnosed at a time when HIV prognosis was poor, treatments were less effective or more complex, HIV-related stigma was greater, and companions and supportive networks may have been lost. However, it may also be related to increased time living with a chronic disease and its health and social implications, younger age at HIV diagnosis, the effects of prolonged HIV treatment, or the effect of longer time with untreated HIV infection specifically. The fact that, for most of the health measures, an association with time with diagnosed HIV infection was apparent even within the group diagnosed in the last ten years (from 2001/2002 to 2011/2012; a time of good prognosis) may give some support to the latter explanations as contributing factors. Future studies are needed to explore whether the strong effect of time with diagnosed HIV on health measures is related to ageing with HIV infection, or whether it primarily represents a historical effect of diagnosis in the pre-cART or early cART eras. Research assessing the effects on health of cumulative time with detectable vs undetectable viral load may also be valuable.

Studies assessing self-reported symptoms among people living with HIV are an important addition to those based on clinic data, as they provide information on health from the participant's perspective. ASTRA is the largest questionnaire study of HIV-diagnosed individuals in the UK to date, and one of the few to examine associations of age with symptoms, having accounted for time with diagnosed HIV infection. However, our study has several limitations. We have previously compared health-related quality of life utility score (using EQ-5D-3L) between the ASTRA participants and a large UK general population sample [17], but unfortunately there is no corresponding contemporary information on the prevalence of symptoms assessed using PHQ-9/GAD-7/MSAS-SF from UK general population studies to compare with results for the ASTRA sample. The study response rate was 64% overall, but there may have been differential nonresponse according to age which could cause bias in the assessment of age trends. Very few of the participants had severe mobility problems, which may be correlated to the ability to attend the clinic, and so may exclude a group with very poor health. Grouping all adults over 60 years old together prevents us from identifying age differences within this subgroup.

We aimed to assess the association of age with self-reported health measures with adjustment for key demographic factors for which the causal direction of association would be uncontroversial. Socio-economic [40–42], HIV- and treatment-related [43,44], and lifestyle factors are worthy of future study as potential confounders or mediators of age effects.

Implications

This paper presents findings of age-related differences in wellbeing among people living with HIV and the independent effect of time with diagnosed HIV infection. Older people living with HIV are increasing in number globally [3] and health care systems will need to adapt to meet the needs of this ageing population. Quality of life, autonomy and self-rated health are essential components of successful ageing [34,45]; our findings should inform the development of appropriate services for older HIV-positive people. These data do not support the hypothesis that older compared with younger people living with HIV have a disproportionate burden of symptoms. As psychological health appeared to be better among older participants, further exploration of 'successful ageing' among people with HIV and the positive effects of age on coping would be of value.

However, the strong and consistent associations between longer time with diagnosed HIV infection and poorer self-reported health, even after accounting for age, suggest the need for supportive strategies for people who have lived with HIV for a long period of time (including those diagnosed in the pre-cART period, or as younger adults), and emphasize the importance of regular care,

and ongoing evaluation of psychological health, even for individuals who are virologically stable on ART. Independent associations of both older age and longer time since HIV diagnosis with physical health problems emphasize the importance of screening and assessment for age-related conditions among people under care for HIV infection, and prompt referral to suitable services.

For many symptom measures, we did not find continuous trends with age. Grouping older people together in an over-50s age group may miss important differences, such as possible improvements in symptom burden with older age. As the HIV-positive population ages, it will be important for future research to examine older age groups separately, as well as account for time since HIV diagnosis.

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Appendix 1: The ASTRA Study Group and Advisory Board

ASTRA clinic teams

Royal Free Hospital: Alison Rodger, Margaret Johnson, Jeff McDonnell and Adebiyi Aderonke. Mortimer Market Centre: Richard Gilson, Simon Edwards, Lewis Haddow, Simon Gilson, Christina Broussard, Robert Pralat and Sonali Wayal. Brighton and Sussex University Hospital: Martin Fisher, Nicky Perry, Alex Pollard, Serge Fedele, Louise Kerr, Lisa Heald, Wendy Hadley, Kerry Hobbs, Julia Williams, Elaney Youssef, Celia Richardson and Sean Groth. North Manchester General Hospital: Ed Wilkins, Yvonne Clowes, Jennifer Cullie, Cynthia Murphy, Christina Martin, Valerie George and Andrew Thompson. Homerton University Hospital: Jane Anderson, Sifiso Mguni, Damilola Awosika and Rosalind Scourse. East Sussex Sexual Health Clinic: Kazeem Aderogba, Caron Osborne, Sue Cross, Jacqueline Whinney and Martin Jones. Newham University Hospital: Rebecca O'Connell and Cheryl Tawana. Whipps Cross University Hospital: Monica Lascar, Zandile Maseko, Gemma Townsend, Vera Theodore and Jas Sagoo.

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Fiona Lampe, Alison Rodger, Andrew Speakman and Andrew Phillips.

ASTRA data management

Andrew Speakman, Marina Daskalopoulou and Fiona Lampe.

ASTRA advisory group

Lorraine Sherr, Simon Collins, Jonathan Elford, Alec Miners, Anne Johnson, Graham Hart, Anna-Maria Geretti and Bill Burman.

CAPRA grant advisory board

Nick Partridge, Kay Orton, Anthony Nardone and Ann Sullivan.

Appendix 2: Symptom questionnaires

Modified MSAS–SF

Below is a list of symptoms. Did you have any of these symptoms during the PAST 2 WEEKS? Please tick one box in each row to tell us whether you have had the symptom and, if so, how much it DISTRESSED or BOTHERED you.

Did you have any of these symptoms during the PAST 2 WEEKS?	No did not have the symptom	Yes, had symptom but it DID NOT BOTHER ME	Yes, had symptom and was bothered/ distressed A LITTLE BIT	Yes, had symptom and was bothered/ distressed QUITE A BIT	Yes, had symptom and was bothered/ distressed VERY MUCH
1. Difficulty concentrating	☐	☐	☐	☐	☐
2. Difficulty sleeping	☐	☐	☐	☐	☐
3. Lack of energy	☐	☐	☐	☐	☐
4. Feeling drowsy/tired	☐	☐	☐	☐	☐
5. Trouble remembering things	☐	☐	☐	☐	☐
6. Pain	☐	☐	☐	☐	☐
7. Headache	☐	☐	☐	☐	☐
8. Numbness, tingling or pain in hands or feet	☐	☐	☐	☐	☐
9. Muscle aches or joint pains	☐	☐	☐	☐	☐
10. Nausea	☐	☐	☐	☐	☐
11. Vomiting	☐	☐	☐	☐	☐
12. Diarrhoea	☐	☐	☐	☐	☐
13. Constipation	☐	☐	☐	☐	☐
14. Feeling bloated	☐	☐	☐	☐	☐
15. Dizziness	☐	☐	☐	☐	☐
16. Sweats/fever	☐	☐	☐	☐	☐
17. Cough	☐	☐	☐	☐	☐
18. Shortness of breath	☐	☐	☐	☐	☐
19. Problems with sexual interest/activity	☐	☐	☐	☐	☐
20. Skin problems (e.g. rash, itching, dryness)	☐	☐	☐	☐	☐
21. Dry mouth	☐	☐	☐	☐	☐
22. Mouth sores	☐	☐	☐	☐	☐
23. Lack of appetite	☐	☐	☐	☐	☐
24. Changes in way food tastes	☐	☐	☐	☐	☐
25. Weight loss	☐	☐	☐	☐	☐
26. Changes in fat in face or body	☐	☐	☐	☐	☐

PHQ–9 and GAD–7

Over the PAST 2 WEEKS, how often have you been bothered by any of the following problems?
Please tick one box in each row.

	Not at all	Several days	More than half the days	Nearly every day
PHQ-9				
(1) Little interest or pleasure in doing things	☐	☐	☐	☐
(2) Feeling down, depressed, or hopeless	☐	☐	☐	☐
(3) Trouble falling or staying asleep, or sleeping too much	☐	☐	☐	☐
(4) Feeling tired or having little energy	☐	☐	☐	☐
(5) Poor appetite or overeating	☐	☐	☐	☐
(6) Feeling bad about yourself—or that you are a failure or have let yourself or your family down	☐	☐	☐	☐

Appendix 2: Continued

	Not at all	Several days	More than half the days	Nearly every day
(7) Trouble concentrating on things, such as reading the newspaper or watching television	☐	☐	☐	☐
(8) Moving or speaking so slowly that other people could have noticed. Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	☐	☐	☐	☐
(9) Thoughts that you would be better off dead, or of hurting yourself in some way	☐	☐	☐	☐

GAD–7

Over the PAST 2 WEEKS, how often have you been bothered by any of the following problems?
Please tick one box in each row.

	Not at all	Several days	More than half the days	Nearly every day
(1) Feeling nervous, anxious or on edge	☐	☐	☐	☐
(2) Not being able to stop or control worrying	☐	☐	☐	☐
(3) Worrying too much about different things	☐	☐	☐	☐
(4) Trouble relaxing	☐	☐	☐	☐
(5) Being so restless that it is hard to sit still	☐	☐	☐	☐
(6) Becoming easily annoyed or irritable	☐	☐	☐	☐
(7) Feeling afraid as if something awful might happen	☐	☐	☐	☐

EUROQOL 5D 3L – first three domains

Please indicate which statements best describes your own state of health TODAY.
Please tick one box in each section

(a) Mobility	☐ I have no problems in walking about
	☐ I have some problems in walking about
	☐ I am confined to bed
(b) Self-care	☐ I have no problems with self-care
	☐ I have some problems washing or dressing myself
	☐ I am unable to wash or dress myself
(c) Usual activities (e.g. work, study, housework, family or leisure activities)	☐ I have no problems with performing my usual activities
	☐ I have some problems with performing my usual activities
	☐ I am unable to perform my usual activities

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