PE3/18

Distinct groupings of people with HIV and pain associate differently with pain-related healthcare use and health-related quality-of-life (HRQoL): findings from the POPPY study

Caroline A Sabin[1,2], Richard Harding[3], Memory Sachikonye[4], Adam Geressu[1], Patrick Mallon[5], Frank Post[6], Marta Boffito[7], Jaime Vera[8], Ian Williams[1], Margaret Johnson[9], Jane Anderson[10], Margarita Durkina[11], Alan Winston[12], for the POPPY study group

[1]Institute for Global Health, UCL; [2]NIHR HPRU in Blood-Borne and Sexually Transmitted Infections at UCL; [3]Kings College London; [4]UK Community Advisory Board (UK-CAB); [5]University College Dublin; [6]Kings College Hospital, London; [7]Chelsea and Westminster Hospital, London; [8]Brighton and Sussex University Hospital, Brighton; [9]Royal Free Hospital, London; [10]Homerton University Hospital, London; [11]Imperial Clinical Trials Unit, London; [12]Imperial College London, London.

POPPY
Pharmacokinetic and clinical observations in people over 50

Background

- Whilst the widespread use of antiretroviral treatment (ART) means that people with HIV (PWH) now have a near-normal life expectancy, those living with HIV are now ageing and are increasingly experiencing age-associated comorbidities.
- In a previous analysis of the POPPY study, we reported substantially higher rates of widespread pain in PWH than in people without HIV [1].
- Despite being associated with depressive symptoms, HRQoL and functional impairment [1,2], little research has been undertaken on chronic pain in the modern ART era and little is known about the patterns of pain that may be present.

Aim: To investigate pain profiles and their associations with pain-related healthcare use and patient-reported outcomes among PWH participating in the POPPY Study.

Methods

- The POPPY study recruited 1,073 PWH from the UK and Ireland [3], collecting information on socio-demographic and clinical factors at each study visit; historic information on ART exposure, CD4 counts and HIV viral loads are obtained through linkage with the UK Collaborative HIV Cohort (UK CHIC) and UCD ID cohorts.
- Self-reported pain information was collected through a pain manikin identifying affected body sites (as in [4]); for the purposes of analysis, right and left sides were combined, resulting in 14 distinct sites (see Table 2).
- Spearman's correlation explored the association between the presence of pain at each pair of body sites, and latent class analysis was used to identify pain profiles
- Pain profiles were linked to demographics, pain assessments, pain-related healthcare use (analgesic use, GP or other healthcare attendance), depressive symptoms (CES-D, PHQ-9) and HRQoL (SF-36), using Chi-squared and Kruskal-Wallis tests

Table 1: Demographic and lifestyle characteristics of included participants, overall and stratified by pain class

		Total	Pain class 1	2	3	4	p-value
N		683	391	125	104	63	
Male, n (%)		593 (86.8)	339 (86.7)	111 (88.8)	86 (82.7)	57 (90.5)	0.44
MSM, n (%)		541 (79.2)	314 (80.3)	98 (78.4)	74 (71.2)	55 (87.3)	0.07
White ethnicity, n (%)		600 (87.9)	340 (87.0)	113 (90.4)	87 (83.7)	60 (95.2)	0.11
Age, years	Median (IQR)	53 (47-59)	52 (46-58)	54 (46-61)	55 (48-61)	53 (48-60)	0.03
Educational attainment*, n (%)	Low	182 (26.7)	85 (21.7)	32 (25.6)	41 (39.4)	24 (38.1)	
	Moderate	95 (13.9)	61 (15.6)	16 (12.8)	12 (11.5)	6 (9.5)	
	High	406 (59.4)	245 (62.7)	77 (61.6)	51 (49.0)	33 (52.4)	0.005
Employment status, n (%)	Employed	363 (53.2)	250 (63.9)	58 (46.4)	41 (39.4)	14 (22.2)	
	Student	7 (1.0)	3 (0.8)	2 (1.6)	1 (1.0)	1 (1.6)	
	Unemployed/off sick	161 (23.6)	53 (13.6)	38 (30.4)	40 (38.5)	30 (47.6)	
	Other/unknown	152 (22.3)	85 (21.7)	27 (21.6)	22 (21.2)	18 (28.6)	0.0001
Smoking status, n (%)	Current	166 (24.3)	89 (22.8)	35 (28.0)	25 (24.0)	17 (27.0)	
	Ex-smoker	239 (35.0)	133 (34.0)	40 (32.0)	37 (35.6)	29 (46.0)	
	Never smoker/unknown	278 (40.7)	169 (43.2)	50 (40.0)	42 (40.4)	17 (27.0)	0.28
BMI (kg/m^2)	Median (IQR)	25.4 (23.1-28.0)	25.4 (23.2-28.0)	25.0 (22.7-27.4)	25.7 (23.1-29.0)	26.0 (22.6-28.3)	0.48

* Low: O-levels or lower; Moderate: A-levels; High: Higher than A-levels/unknown

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POPPY Management Team: Marta Boffito, Paddy Mallon, Frank Post, Caroline Sabin, Memory Sachikonye, Alan Winston, Amalia Ndoutoumou, Daphne Babalis. **POPPY Scientific Steering Committee:** Jane Anderson, David Asboe, Marta Boffito, Lucy Garvey, Paddy Mallon, Frank Post, Anton Pozniak, Caroline Sabin, Memory Sachikonye, Jaime Vera, Ian Williams, Alan Winston **POPPY Sites and Trials Unit:** Caldecot Centre, King's College Hospital (Frank Post, Lucy Campbell, Selin Yurdakul, Sara Okumu, Louise Pollard, Beatriz Santana Suárez) Department of Infection and Population Health, UCL (Ian Williams, Damilola Otiko, Laura Phillips, Rosanna Laverick, Michelle Beynon, Anna-Lena Salz, Abigail Severn) Elton John Centre, Brighton and Sussex University Hospital (Martin Fisher, Amanda Clarke, Jaime Vera, Andrew Bexley, Celia Richardson, Sarah Kirk, Rebecca Gleig) HIV Molecular Research Group, School of Medicine, UCD (Paddy Mallon, Alan Macken, Bijan Ghavani-Kia, Joanne Maher, Maria Byrne, Ailbhe Flaherty, Aoife McDermott) Homerton Sexual Health Services, Homerton University Hospital (Jane Anderson, Sifiso Mguni, Rebecca Clark, Rhiannon Nevin-Dolan, Sambasivarao Peiluri) Ian Charleson Day Centre, Royal Free Hospital (Margaret Johnson, Nnenna Ngwu, Nargis Hemat, Anne Carroll, Sabine Kinloch, Mike Youle and Sara Madge) Imperial Clinical Trials Unit, Imperial College London (Amalia Ndoutoumou, Daphne Babalis) St. Mary's Hospital London, Imperial College Healthcare NHS Trust (Alan Winston, Lucy Garvey, Jonathan Underwood, Lavender Tembo, Matthew Stott, Linda McDonald, Felix Dransfield) St Stephen's Centre, Chelsea and Westminster Hospital (Marta Boffito, David Asboe, Anton Pozniak, Margherita Bracchi, Nicole Pagani, Maddalena Cerrone, Daniel Bradshaw, Francesca Ferretti, Chris Higgs, Elisha Seah, Stephen Fletcher, Michelle Anthonipillai, Ashley Moyes, Katie Deats, Irtiza Syed, Clive Matthews, Peter Fernando) **POPPY methodology/statistics:** Caroline Sabin, Nicholas Bakewell, Hajra Okhai, Luxsena Sukumaran **Funders:** The POPPY study is funded from investigator initiated grants from BMS, Gilead Sciences, Janssen, MSD and ViiV Healthcare

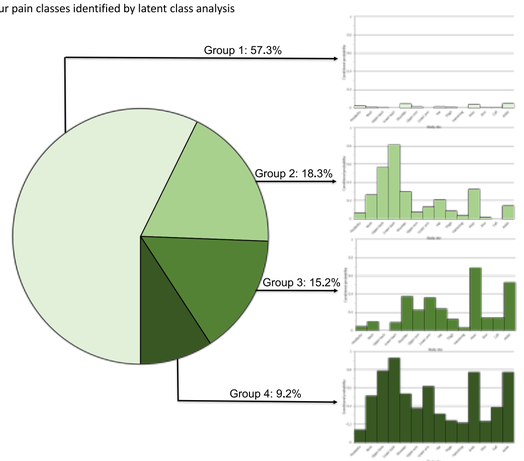
Results

- 683 PWH with complete pain manikin data were included in analyses (**Table 1**)
- Pain was most commonly reported at the knees (26.8%), lower back (25.6%), ankles (21.5%), shoulders (19.2%) and upper back (18.5%) (**Table 2**)
- Exploratory analyses suggested that pain often co-occurred in the upper (neck, upper/lower back, shoulder, upper/lower arm) or lower (hamstring, knee, calf, ankle) body.

Table 2: Reported pain sites and pairwise (Spearman) correlations

Site of pain	N (%)	Headache	Neck	U. back	L. back	Shoulder	U. arm	L. arm	Hip	Thigh	Hamstring	Knee	Shin	Calf	Ankle
Headache	31 (4.5)	1	0.14	0.11	0.13	0.09	0.07	0.07	0.01	-0.03	0.04	0.04	0.11	0.15	0.07
Neck	82 (12.0)	-	1	0.47	0.36	0.37	0.24	0.27	0.14	0.09	0.11	0.24	0.06	0.16	0.21
U. back	126 (18.5)	-	-	1	0.67	0.31	0.22	0.24	0.20	0.15	0.18	0.26	0.12	0.19	0.26
L. back	175 (25.6)	-	-	-	1	0.27	0.18	0.31	0.27	0.23	0.26	0.33	0.14	0.19	0.28
Shoulder	131 (19.2)	-	-	-	-	1	0.38	0.35	0.12	0.11	0.14	0.28	0.08	0.15	0.22
U. arm	64 (9.4)	-	-	-	-	-	1	0.37	0.12	0.08	0.11	0.24	0.04	0.16	0.26
L. arm	99 (14.5)	-	-	-	-	-	-	1	0.21	0.11	0.11	0.33	0.17	0.15	0.35
Hip	78 (11.4)	-	-	-	-	-	-	-	1	0.26	0.14	0.21	0.09	0.15	0.19
Thigh	44 (6.4)	-	-	-	-	-	-	-	-	1	0.35	0.26	0.27	0.25	0.12
Hamstring	23 (3.4)	-	-	-	-	-	-	-	-	-	1	0.22	0.18	0.35	0.12
Knee	183 (26.8)	-	-	-	-	-	-	-	-	-	-	1	0.26	0.35	0.12
Shin	34 (5.0)	-	-	-	-	-	-	-	-	-	-	-	1	0.41	0.26
Calf	43 (6.3)	-	-	-	-	-	-	-	-	-	-	-	-	1	0.27
Ankle	147 (21.5)	-	-	-	-	-	-	-	-	-	-	-	-	-	1

Figure 1: Four pain classes identified by latent class analysis



- Latent class analyses revealed four pain classes (**Figure 1**)
  - ❖ Group 1: Low rates of pain at all body sites – 57.3% of cohort
  - ❖ Group 2: Predominantly back pain – 18.3% of cohort
  - ❖ Group 3: Joint (non-back) pain – 15.2% of cohort
  - ❖ Group 4: High rates of pain at all sites - 9.2% of cohort
- Other measures of pain increased progressively as the pain class increased. In particular, 88.9% of those in Group 4 also met the 2019 American College of Rheumatology fibromyalgia criteria [5] for widespread pain; this criteria was only met by 10.4% and 21.2% of those in Groups 2 and 3, respectively, and none of those in Group 1 (p=0.0001) (**Table 3**).
- Use of pain-related healthcare use also increased progressively through pain classes 1 to 4 (**Table 3**).

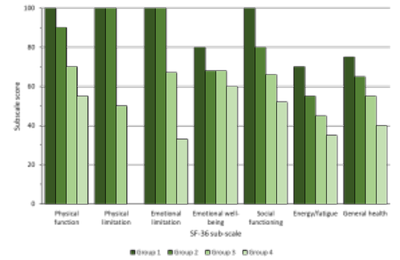
Table 3: Other measures of pain and pain-related healthcare use, overall and stratified by pain class

		Total	Pain class 1	2	3	4	p-value
N		683	391	125	104	63	
Widespread pain (fibromyalgia), n (%)	None	330 (48.3)	329 (84.1)	0 (-)	1 (1.0)	0 (-)	
	Regional	262 (38.4)	62 (15.9)	112 (89.6)	81 (77.9)	7 (11.1)	
	Widespread	91 (13.3)	0 (-)	13 (10.4)	22 (21.2)	56 (88.9)	0.0001
Aches and pains, n (%)		359 (52.6)	68 (17.4)	125 (100.0)	103 (99.0)	63 (100.0)	0.0001
Bodily pain in past month, n (%)		449 (66.3)	177 (45.6)	117 (93.6)	93 (92.1)	62 (98.4)	0.0001
Current pain, n (%)		245 (35.9)	37 (9.5)	88 (70.4)	72 (69.2)	48 (76.2)	0.0001
Moderate/severe pain, n (%)		175 (25.9)	34 (8.8)	46 (36.8)	49 (48.5)	46 (73.0)	0.0001
Moderate/severe interference of pain, n (%)		173 (38.5)	36 (20.3)	45 (38.5)	50 (53.8)	42 (67.7)	0.0001
Any joint problem, n (%)		306 (44.8)	120 (30.7)	72 (57.6)	62 (59.6)	52 (82.5)	0.0001
Use of analgesics, n (%)		100 (14.6)	40 (10.2)	19 (15.2)	24 (23.1)	17 (27.0)	0.0002
Any pain-related GP visit, n (%)		113 (16.5)	44 (11.3)	32 (25.6)	24 (23.1)	13 (20.6)	0.0002
Any pain-related healthcare resource use*, n (%)		182 (26.7)	75 (19.2)	42 (33.6)	40 (38.5)	25 (39.7)	0.0001
Any falls, n (%)		90 (13.2)	29 (7.4)	17 (13.6)	26 (25.0)	18 (28.6)	0.0001

* Any use of analgesics, pain-related GP visit or specialist pain visit

- CESD scores increased progressively as pain class increased with median (inter-quartile range) scores of 6 (3-14), 12 (6-20), 13 (7-26) and 25 (13-33) for those in classes 1, 2, 3 and 4 respectively (p=0.0001). PHQ-9 scores increased similarly: 2 (0-6), 5 (2-10), 7 (2-11) and 10 (5-16), respectively (p=0.0001).
- Measures of HRQoL from the SF-36 tool decreased progressively as pain class increased (p=0.0001 for each sub-scale) (**Figure 2**)

Figure 2: Median scores on each of the SF-36 sub-scales stratified by pain class



Conclusion

We have identified four distinct pain profiles among PWH with different associations with healthcare resource use; whilst there is agreement between these pain classes and existing pain classification scales (e.g. [5]), our four classes demonstrate a stronger correlation with patient-reported outcomes, including depressive symptoms and HRQoL. These findings emphasise the need for targeted approaches to assess and manage pain in PWH, and call for greater research to understand the underlying pathology of pain among PWH.

We note that there may be inconsistencies in the way that participants indicated the site of their pain on the manikin, which may induce correlations between sites.

References: [1]Sabin CA, *et al. AIDS* 2020;34:2071-9; [2]Sabin CA, *et al. AIDS* 2018;32:2697-706; [3]Bagkeris E, *et al. Int J Epidemiol* 2018;47:1391-1392e; [4]Lawson E, *et al. Clin J Pain* 2015;31:813-9; [5]Wolfe F, *et al. Scand J Pain* 2019; doi.org/10.1515/sjpain-2019-0054.

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