

Appendix 1. Literature searching and PICO (population, intervention, comparator and outcome) questions

Search strategy

The Medline, Embase and Cochrane Library databases were searched in May 2019 using the following terms:

(HIV OR AIDS) AND ("pyrexia of unknown origin" or "pyrexia of unexplained origin" or "pyrexia of uncertain origin" or "fever of unknown origin" or "fever of unexplained origin" or "fever of uncertain origin" or "fever without source").

Abstracts from the following conferences using the same search terms were searched between January 2017 and June 2019: Conference on Retrovirus and Opportunistic Infections (CROI), International AIDS Society (IAS), International AIDS Conference, European AIDS Clinical Society (EACS), British HIV Association (BHIVA) and HIV Drug Therapy Glasgow.

PICO questions

The literature searches were based on the following PICO questions:

What is the prevalence/incidence of PUO in people (adults and adolescents) living with HIV in the ART era?

Which investigations for PUO in people (adults and adolescents) living with HIV have the greatest yield?

What is the spectrum of diagnoses made in PUO in people (adults and adolescents) living with HIV?

Appendix 2. Frequency of PUO in people living with HIV

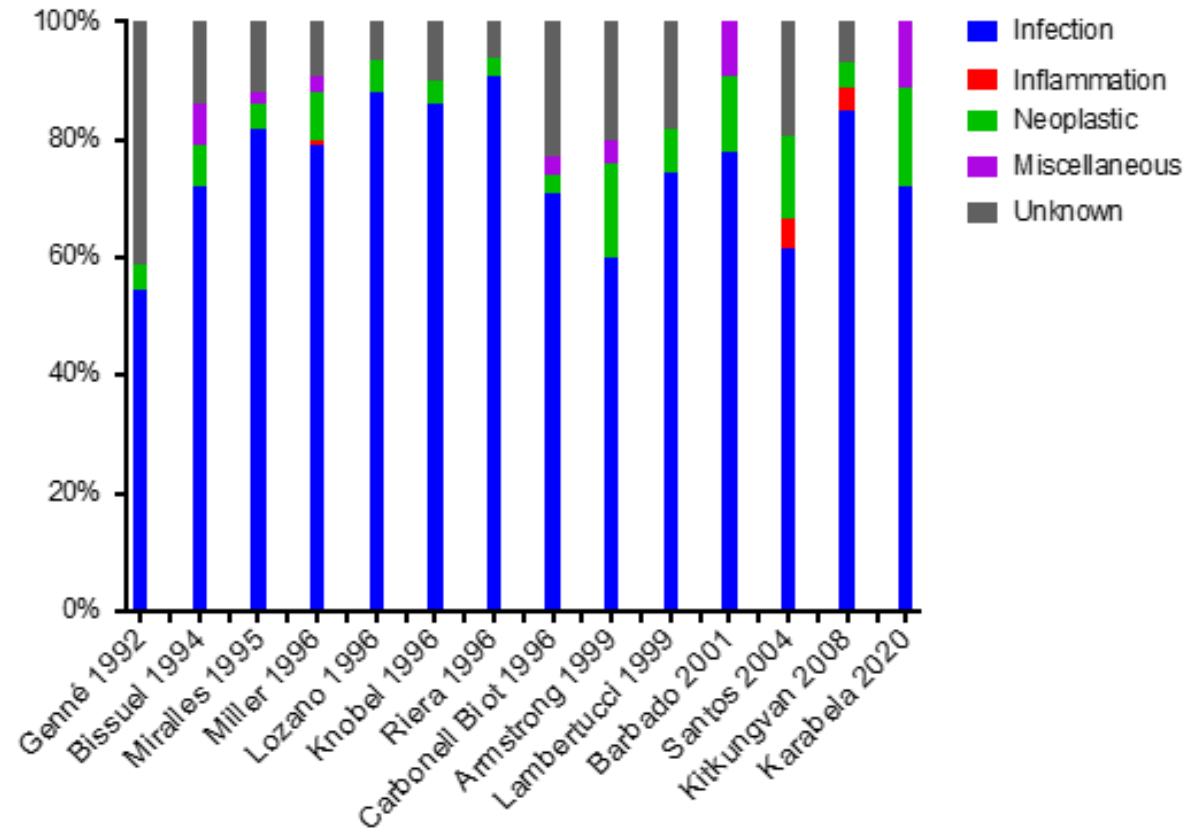
Reference	Study design	Population type	Country	Population size (n)	Main findings	Comments	Quality of evidence
Knobel <i>et al.</i> 1996 [1]	Prospective observational	Living with HIV hospitalised for any reason	Spain	100	8.3 cases:100 patients/year	Full text unavailable - sample mean CD4 count = 61 cells/mm ³ ; unable to determine proportion with CD4 count <200 cells/mm ³	Low
Lozano <i>et al.</i> 1996 [2]	Prospective observational	Living with HIV hospitalised for any reason	Spain	128	1.1 cases:100 patients/year	Median CD4 = 46 cells/mm ³ ; CD4 <100 cells/mm ³ in 73.4%	Low
Miller <i>et al.</i> 1996 [3]	Retrospective observational	Living with HIV hospitalised for any reason	UK	75	26.3 cases:100 patients/year	Median CD4 = 40 cells/mm ³	Very low
Lambertucci <i>et al.</i> 1999 [4]	Retrospective observational	Living with HIV hospitalised for any reason	Brazil	55	21.5 cases:100 patients/year	Mean CD4 = 98 cells/mm ³ ; CD4 <100 cells/mm ³ in 67.5%	Very low
Barbado <i>et al.</i> 2001 [5]	Prospective observational	Living with HIV hospitalised for any reason	Spain	48	7.8 cases:100 patients/year	Median CD4 = 113 cells/mm ³	Low
Abellán-Martínez <i>et al.</i> 2009 [6]	Retrospective observational	Living with HIV hospitalised for any reason	Spain	276	7.3 cases per 100 patients	Median CD4 = 28 cells/mm ³	Moderate

References

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2. Lozano F, Torre-Cisneros J, Bascuñana A *et al.*; the Grupo Anduluz para el Estudio de las Enfermedades Infecciosas. Prospective evaluation of fever of unknown origin in patients infected with the human immunodeficiency virus. *Eur J Clin Microbiol Infect Dis* 1996; **15**: 705–711.
3. Miller RF, Hingorani AD, Foley NM. Pyrexia of undetermined origin in patients with human immunodeficiency virus infection and AIDS. *Int J STD AIDS* 1996; **7**: 170–173.
4. Lambertucci JR, Rayes AA, Nunes F *et al.* Fever of undetermined origin in patients with the acquired immunodeficiency syndrome in Brazil: report on 55 cases. *Rev Inst Med Trop Sao Paulo* 1999; **41**: 27–32.
5. Barbado FJ, Gómez-Cerezo J, Peña JM *et al.* Fever of unknown origin: classic and associated with human immunodeficiency virus infection. A comparative study. *J Med* 2001; **32**: 152–162.
6. Abellán-Martínez J, Guerra-Vales J-M, Fernández-Cotarelo M-J, González-Alegre M-T. Evolution of the incidence and aetiology of fever of unknown origin (FUO), and survival in HIV-infected patients after HAART (highly active antiretroviral therapy). *Eur J Intern Med* 2009; **20**: 474–477.

Appendix 3. Cause of PUO in people living with HIV in 14 studies from 1992 to 2020



Reference	Study period	Country	Individuals (n)	Cause of PUO				
				Infection (%)	Inflammation (%)	Neoplastic (%)	Miscellaneous (%)	Unknown (%)
Genné 1992 [1]	1987–1990	Switzerland	22	55	0	5	0	41
Bissuel 1994 [2]	1989–1991	France	57	72	0	7	7	14
Miralles 1995 [3]	1991–1992	Spain	35	82	9	4	2	12
Miller 1996 [4]	1989–1993	UK	75	79	1	8	3	9
Lozano 1996 [5]	1992–1993	Spain	128	88	0	6	0	6
Knobel 1996 [6]	1993–1995	Spain	95	86	0	4	0	10
Riera 1996 [7]	Not reported	Spain	35	91	0	3	0	9
Carbonell Biot 1996 [8]	1989–1994	Spain	27	71	0	3	3	23
Armstrong 1999 [9]	1992–1997	USA	72	64	0	11	4	20
Lambertucci 1999 [10]	1989–1997	Brazil	55	75	0	8	0	18
Barbado 2001 [11]	1991–1996	Spain	46	78	0	13	9	0
Santos 2004 [12]	1996–1999	USA	72	64	5	10	19	0
Kitkungvan 2008 [13]	2003–2004	Thailand	72	85	4	4	0	7
Karabela 2020 [14]	2006–2016	Turkey	18	72	0	17	11	0

References

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