EPH126

Higher mortality for generalized pustular psoriasis compared with plaque psoriasis highlights the need for improved treatments: Insights from a meta-analysis

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Conclusions

- These meta-analyses demonstrated that GPP all-cause mortality risk was approximately 2–3-fold higher than that for plaque psoriasis and the general population
- This underscores the substantial unmet need for improved GPP treatment options and patient management to reduce flares and severe complications

Aim

- To understand how all-cause mortality risk in GPP compares to that of plaque psoriasis and the general population

Introduction

- GPP is a serious, chronic, systemic, neutrophilic inflammatory skin disease, with a heterogeneous and unpredictable clinical course[1-4]
- The mortality burden of GPP remains substantial due to life-threatening complications from GPP flares and chronic comorbidities, including sepsis, multiorgan failure, and cardiovascular disease[1-4]
- With the introduction of highly effective therapies for plaque psoriasis, which can coexist with GPP but is clinically and pathologically distinct, all-cause and cardiovascular-related mortality have improved[2–5]
- Despite the considerable burden that GPP places on patients, progress in its management has been much slower, with only one targeted treatment approved for GPP in Europe (spesolimab)[1,6-8]

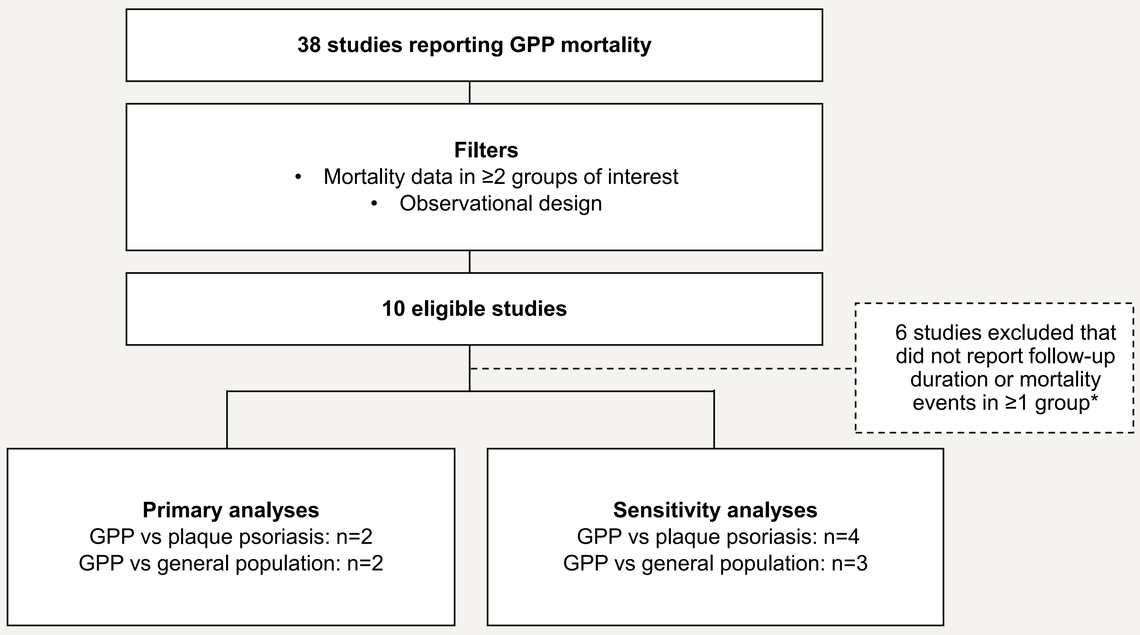
Methods

- A systematic literature review and review of unpublished data were conducted in July 2023 to identify studies reporting mortality data for GPP plus plaque psoriasis and/or the general population
- Two independent reviewers performed study screening and data extraction, and the quality of each study was assessed using the Newcastle–Ottawa Scale (NOS)
- Pooled HRs with 95% CIs were calculated for mortality risk for GPP vs plaque psoriasis and the general population using RE models. Sensitivity analyses evaluated the robustness of the primary results

Results

Study selection

- Following review of available evidence, the analysis was limited to observational studies due to their longer follow-up duration than interventional studies and to increase comparability between studies
- Studies were excluded if they did not report:
  - Mortality data for ≥1 comparator group
  - Follow-up duration*
  - Mortality events in one group of interest*
- **Of 38 studies reporting GPP mortality, four were included in the meta-analyses**



*HRs could not be calculated without these data.

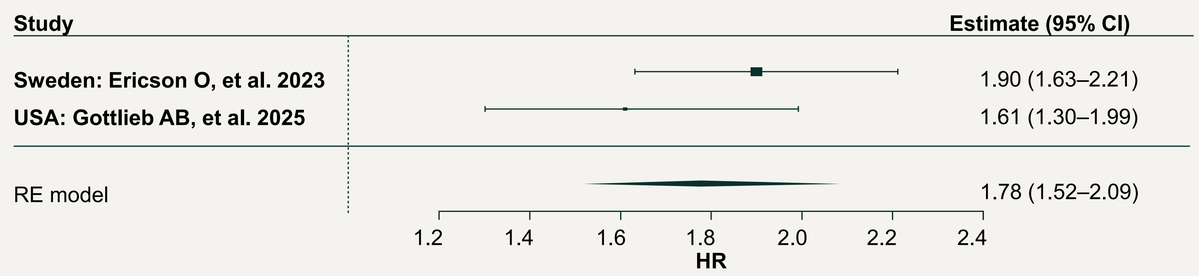
Study characteristics and quality

- Primary analyses included two comparable studies in Sweden and the USA[9,10]
- Sensitivity analyses included a study in France with a non-comparable psoriasis reference group (any type of severe psoriasis rather than plaque psoriasis) and a study in Germany with potential miscoding issues[11,12]
- All studies were conducted before the introduction of spesolimab in 2022[8] and the plaque psoriasis and general population cohorts were matched to GPP
- NOS quality assessments indicated high quality for the Swedish, USA, and French studies (7 or 8/9 stars), and lower quality for the German study (3/9 stars)

	Swedish population-based study	USA medical claims-based study	German medical claims-based study	French population-based study
Study period	2004–2020	2016–2020	2016–2020	2010–2018
Mortality events/total people, n				
GPP	315/1,022	150/2,630	13/976	515/1,842
Plaque psoriasis	679/3,048	190/5,260	14/1,952	159/1,842
General population	1,027/4,842	65/5,260	136/4,880	NR
Follow-up duration, mean (SD)				
GPP	9.3 (4.6)	4.4 (1.4)	1.0 (NR)	4.7 (1.4)
Plaque psoriasis	10.1 (4.1)	4.3 (1.4)	1.0 (NR)	5.2 (1.3)
General population	10 (4.3)	2.0 (1.2)	1.0 (NR)	NR
NOS, total stars (max 9)	8	8	3	7

Mortality for GPP vs plaque psoriasis

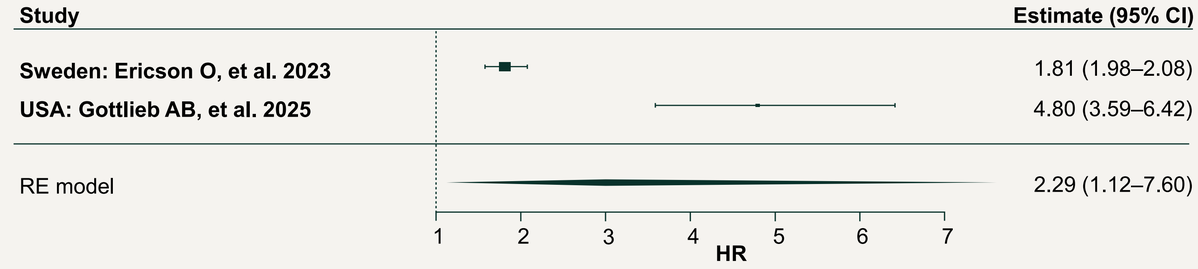
- The primary analysis indicated **all-cause mortality for GPP was 1.8x higher** (n=3,652) vs plaque psoriasis (n=8,308) (p<0.0001)



- A sensitivity analysis including all four studies (GPP, n=6,470; plaque psoriasis n=12,102) **supported the primary results**, with a pooled HR of 2.23 (95% CI: 1.43–3.49; p=0.0004)

Mortality for GPP vs general population

- The primary analysis indicated **all-cause mortality for GPP was 2.9x higher** (n=3,652) vs the general population (n=10,102) (p=0.03)



- The pooled HR reduced to 1.63 in a sensitivity analysis including the German study (GPP, n=4,628; general population, n=14,982; 95% CI: 0.45–5.97; p=0.46); however, the German study found GPP to be protective on mortality, with a HR of 0.47 (95% CI: 0.27–0.84) relative to the general population, potentially due to miscoding issues[12]

Abbreviations CI, confidence interval; GPP, generalized pustular psoriasis; HR, hazard ratio; NOS, Newcastle–Ottawa Scale; NR, not reported; RE, random effects; SD, standard deviation.

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