to the physicians, the variables were SJC (OR = 0.43 [0.32–0.59]), TJC (OR = 0.53 [0.37–0.75]) and the patient's VAS disease activity (OR = 0.46 [0.34–0.62]), but not the ESR, CRP or joint pain VAS. The patients in remission according to the DAS28-ESR and ACR/EULAR criteria, compared to patients not in remission, were younger, were treated less with corticosteroids and more with anti-TNF therapy but the difference was not significant regarding biologics generally.

Finally, the management of RA by rheumatologists in routine practice complied with the guidelines, since almost all of the RA patients were receiving a DMARD, some 80% had at least achieved low disease activity, and around a half (between 30 and 60%, depending on the criteria) were in remission.

## Authors contribution

Drs. Dominique Meyer, Denis Verriere, Sylvie Melac Ducamp, Baptiste Glace, Florence Demarquilly, Milly Gendey, Bernard Maillet, Karim Zbadi, Christine Voquer, Jean Paul Monghal, Abdelkarim Kabchou, Julie Ledoux Eberst, Stella Cechetti, Jean Meloux, Marielle Vayssade are investigators in the study and are co-authors of this article.

## Disclosure of interest

The authors declare that they have no competing interest.

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## Uptrend in mortality from systemic connective tissue diseases: A joinpoint regression analysis among the general population of Brazil, 1996–2016

Previous population-based studies of mortality trends related to connective tissue diseases (CTDs) have focussed their analyses on a single systemic disorder [1–3]; hence, they failed to capture the dynamics of mortality in the general population from the large spectrum of systemic CTDs. Therefore, we performed a nationwide population-based study to primarily assess the temporal trend of mortality with CTDs overall as underlying cause in Brazil from 1996 to 2016 [the earliest and latest years to date with national-level mortality data available according to the International Classification of Diseases, 10th revision (ICD-10)] [4].

For this study, population and death counts (corresponding ICD-10 codes for systemic CTDs: M30-M36) across age groups were both obtained from the Ministry of Health at www.datasus.saude.gov.br. Annual age-standardised mortality rates (ASMRs, per 100,000 population) for all CTDs, the major disease categories, and all other ICD-10 causes (i.e., non-CTD causes) were calculated via the direct method using the 2000 US general population as standard [Appendix A, Document S1; see the supplementary material associated with this article online]. Then, a joinpoint regression analysis (program version 4.6.0.0) was conducted to examine temporal trends in ASMRs [5]. Briefly, the joinpoint model:

- identifies the time points (calendar years) at which the change in the slope of the ASMR is statistically significant, i.e., the joinpoints;
- estimates the regression function with joinpoints previously identified, i.e., determines the magnitude of the change by estimating the average annual percent change (APC) in mortality rate [6].

Over the study period, deaths related to systemic CTDs ($n = 27{,}305$; 79% women and 61% at age 20–59 years) accounted for 0.12% of fatalities ($n = 22{,}366{,}860$) in the Brazilian general population. When comparing years 1996 and 2016, significant increases were found in the proportion of deaths from systemic CTDs among men (16% [$n = 131/810$] to 22% [$n = 383/1764$]; $P = 0.001$, $Chi^2$) and the elderly ($\geq 60$ years old) (20% [$n = 164/807$] to 33% [$n = 587/1764$]; $P < 0.0001$, $Chi^2$). The ASMR (standard error) for all CTDs increased from 0.67 (0.03) in 1996 to 0.98 (0.02) in 2016 (46% cumulative increase). In contrast, the ASMR for non-CTD causes declined by 17% over the same time (1087.89 [1.29] to 906.43 [0.83]).

Results of the joinpoint trend analysis (Table 1 and Fig. 1) showed that although the ASMR for non-CTD causes continuously decreased from 1996 to 2016 at an APC of −1.1% (95% CI: −1.4% to −0.8%), the ASMR for all CTDs increased, on average, at an APC of 2.0% (95% CI: 0.9% to 3%) (APC, 95% CI of 4.2% [2.8% to 5.7%], 1996–2008 and −1.3% [−3.2% to 0.6%],

**Table 1**
Characteristics of deaths from systemic connective tissue diseases as underlying cause among the general population of Brazil, 1996–2016.

| Diseases | ICD-10 code | Death count[a] | | | | | | | Overall ASMR (95% CI) per $10^5$ population[b] | AAPC (95% CI)[c] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | < 1 y | 1–19 y | 20–59 y | ≥ 60 y | All ages | Female | Male | | |
| Systemic connective tissue disorders | M30-M36 | 28 | 2378 | 16646 | 8241 | 27305 | 21547 | 5749 | 0.90 (0.83 to 0.97) | 2.0 (0.9 to 3.0)d |
| Necrotising vasculopathies | M30-M31 | 14 | 252 | 2034 | 3759 | 6063 | 3308 | 2752 | 0.26 (0.22 to 0.29) | 3.3 (0.9 to 5.7)[d] |
| Systemic lupus erythematosus | M32 | 7 | 1860 | 11209 | 1876 | 14959 | 13481 | 1475 | 0.42 (0.39 to 0.44) | 2.0 (1.1 to 2.9)[d] |
| Dermatopolymyositis | M33 | 0 | 95 | 690 | 466 | 1 251 | 838 | 413 | 0.04 (0.041 to 0.046) | 0.5 (−0.3 to 1.3) |
| Systemic sclerosis | M34 | 3 | 38 | 1677 | 1526 | 3244 | 2564 | 679 | 0.12 (0.11 to 0.13) | 1.8 (0.9 to 2.7)[d] |
| Other systemic involvement of connective tissue | M35 | 4 | 133 | 1036 | 614 | 1788 | 1356 | 430 | – | – |

No underlying cause of death was assigned to ICD-10 code M36 ("Systemic disorders of connective tissue in diseases classified elsewhere") over the study period. We merged the ICD-10 categories M30 ("Polyarteritis nodosa and related conditions") and M31 ("Other necrotising vasculopathies") into one category "Necrotising vasculopathies" (M30-M31).
AAPC: average annual percent change; ASMR: age-standardised mortality rate; ICD-10: International Classification of Diseases, 10th revision; 95% CI: 95% confidence interval.
[a] Data for age and sex at death were missing for 12 and 9 persons, respectively.
[b] Two-step calculation. We first computed the age-specific crude mortality rate among the population of interest by dividing the number of deaths by the respective population in each age group. Then, we multiplied each age-specific crude rate by the proportion of the 2000 US general population (standard) belonging to that particular age group. The overall age-standardised mortality rate was finally obtained by adding the resulting numbers.
[c] Summary measure of the trend over a pre-specified fixed interval. It is computed as a weighted average of the annual percent changes from the joinpoint model, with the weights equal to the length of the annual percent change interval.
[d] AAPC is significantly different from zero at the alpha = 0.05 level.

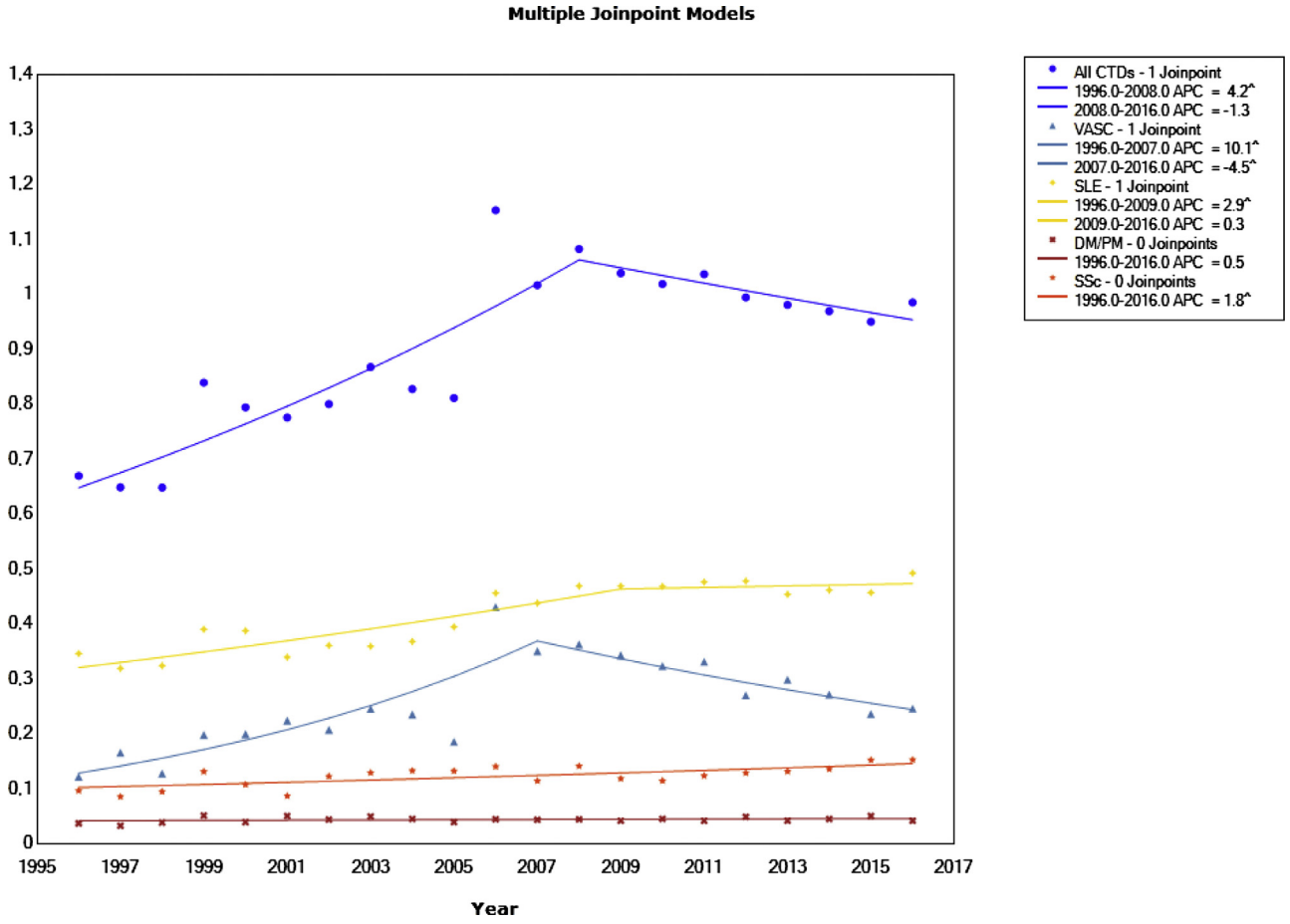


**Fig. 1.** ASMR per 100,000 population for systemic CTDs overall and the major ICD-10 disease categories (VASC, SLE, DM/PM, and SSc). Data are shown per calendar year of death, with lines fitted on the basis of joinpoint analysis. APC: annual percent change; ASMR: age-standardised mortality rate; CTDs: systemic connective tissue diseases; DM/PM: dermatopolymyositis; ICD-10: International Classification of Diseases, 10th revision; SLE: systemic lupus erythematosus; SSc: systemic sclerosis; VASC: necrotising vasculopathies; ^indicates that the APC is significantly different from zero at the alpha = 0.05 level.

2008–2016). Distinct patterns in mortality trends were seen across systemic lupus erythematosus, necrotising vasculopathies, systemic sclerosis, and dermatopolymyositis. However, the average APC in the mortality rate from each of these disorders either increased or remained stable between 1996 and 2016 (Table 1 and Fig. 1).

In conclusion, this population-based study is the first to report on the mortality trends of the whole spectrum of systemic CTDs. Based on our results, future researches are warranted to investigate the reasons for the disconnect in mortality trends between systemic CTDs and non-CTD causes.

## Authors' contributions

RR conceived and designed the study. All authors analysed the data, wrote the manuscript and approved the final version.

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## Patient consent for publication

Not applicable.

## Ethics approval

Not required.

## Data sharing statement

No additional data available.

## Disclosure of interest

The authors declare that they have no competing interest.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at https://doi.org/10.1016/j.jbspin.2019.03.010.

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# There is no season for infectious spondylodiscitis

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The belief that osteoarticular infections are more common in summer is widely-held among rheumatologists. Studies have demonstrated that *Staphylococcus aureus* infections, especially manifesting as skin infections or bursitis, are apparently more common in summer [1,2]. For prosthesis infections and postoperative spinal infections, however, studies have produced conflicting results regarding seasonality [3–8]. One study involving 159 cases of septic arthritis in native joints reported no seasonal influence at all [9], yet there have been no studies so far of primary spondylodiscitis.

With this study, we sought to evaluate any potential seasonal distribution of primary infectious spondylodiscitis. To this end, we reviewed the records of patients admitted to our rheumatology department between 2000 and 2015 for spondylodiscitis. Cases of tuberculosis infection and iatrogenic inoculation were excluded from analysis. For each case, the month of admission was recorded, with the trimester linked to a season. The cohort included 100 men and 45 women of a mean age of 66.2 ± 14.8 years. Spondylodiscitis presented in the forms of cervical ($n = 15$), dorsal ($n = 41$), and lumbar ($n = 94$) involvement. The causative bacteria were identified by blood cultures or disco-vertebral biopsy in 113/145 cases (78%). The main bacteria were: *Staphylococcus* (57, including 29 *S. aureus*), *Streptococcus* (25), and Gram-negative bacilli (23). The number of spondylodiscitis cases varied from 8 to 18 depending on the month of admission, with a non-significant ($P = 0.45$) difference in distribution. Seasonal distribution as evaluated by trimester was: 37 in winter (25.5%), 30 in spring (20.7%), 42 in summer (29%), and 36 in autumn (24.8%) (Fig. 1). There was no significant difference ($P = 0.44$) nor did the distribution of documented bacterial or *Staphylococcus* infections reveal any seasonal trend.