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LETTER TO THE EDITOR

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The impact of fibrotic diseases on global mortality from 1990 to 2019

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To the Editor,

Fibrosis, characterized by the excessive production and accumulation of extracellular matrix (ECM) proteins, is an integral part of numerous chronic diseases affecting vital organs such as the lungs, liver, heart, and kidneys [1]. Despite the diversity in their etiological underpinnings and clinical presentations, these disorders all lead to a common process of tissue remodeling and scarring. This results in the deterioration of organ structure, functional impairment, and ultimately organ failure, often requiring transplantation. While there has been a long-standing notion that fibrotic diseases might account for up to 45% of worldwide deaths, this estimate has lacked solid epidemiological backing. To address this knowledge gap, we turned to the 2019 Global Burden of Disease (GBD) study (https://www.healthdata.org) [2], aiming to uncover the actual impact of fibrotic diseases on global mortality.

From the myriad causes of death documented in the GBD, we specifically focused on conditions connected to ECM remodeling (Fig. 1A). Based on these data, a conservative estimate posits that fibrotic diseases contributed to 16.5% of all global deaths in 1990, and this percentage steadily increased over time to 17.8% in 2019 (Fig. 1A). However, emerging insights indicate that the majority of neoplasms should also be categorized as fibrotic disorders, as fibrosis plays a key role in tumor growth and metastasis [3–5]. When accounting for neoplasms, excluding acute lymphoid leukemia and acute myeloid leukemia, the overall impact of fibrotic diseases on global deaths in 1990 was 28.7%, which subsequently rose to 35.4% in 2019 (Fig. 1A, B). Among all fibrotic disorders, neoplasms and chronic obstructive pulmonary disease consistently ranked as the primary contributors to global mortality during this period (Fig. 1A). In contrast, the impact of various infectious diseases declined over time. For instance, tuberculosis, a significant contributor in 1990, saw its contribution nearly halved by 2019 (Fig. 1A, B), reflecting changing patterns in the global disease landscape over the years.

While the impact of fibrotic disorders on global mortality might be smaller than previously estimated, and we recognize that certain deaths involve factors beyond ECM remodeling and fibrosis, it remains evident that fibrotic diseases still contribute significantly to global mortality. This underscores the necessity for sustained research efforts aimed at developing effective antifibrotic treatments, as this critical need remains largely unaddressed.

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A

Rank 1990	Disease	% of all deaths
1	Neoplasms	12.15
2	Chronic obstructive pulmonary disease	5.40
3	Tuberculosis	3.81
4	Cirrhosis and other chronic liver diseases	2.17
5	Hypertensive heart disease	1.40
6	Chronic kidney disease	1.29
7	Rheumatic heart disease	0.78
8	Cardiomyopathy and myocarditis	0.51
9	HIV/AIDS - Drug-susceptible Tuberculosis	0.25
10	Gallbladder and biliary diseases	0.18
11	Interstitial lung disease and pulmonary sarcoidosis	0.14
12	Leishmaniasis	0.13
13	Non-rheumatic calcific aortic valve disease	0.11
14	Peripheral artery disease	0.06
15	Inflammatory bowel disease	0.05
16	Pneumoconiosis	0.05
17	Rheumatoid arthritis	0.05
18	Schistosomiasis	0.04
19	Multiple sclerosis	0.03
20	Decubitus ulcer	0.03
21	Chagas disease	0.02
22	Uterine fibroids	0.01
23	Cystic echinococcosis	0.01
24	Cysticercosis	2.82E-03
25	HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance	1.43E-03
26	Endometriosis	3.33E-04
27	HIV/AIDS - Extensively drug-resistant Tuberculosis	0.00
	Total	28.67
	Total (without neoplasms)	16.52

Rank 2019	Disease	% of all deaths
1	Neoplasms	17.58
2	Chronic obstructive pulmonary disease	5.80
3	Cirrhosis and other chronic liver diseases	2.60
4	Chronic kidney disease	2.53
5	Tuberculosis	2.09
6	Hypertensive heart disease	2.05
7	Cardiomyopathy and myocarditis	0.60
8	Rheumatic heart disease	0.54
9	HIV/AIDS - Drug-susceptible Tuberculosis	0.35
10	Interstitial lung disease and pulmonary sarcoidosis	0.30
11	Non-rheumatic calcific aortic valve disease	0.22
12	Gallbladder and biliary diseases	0.22
13	Peripheral artery disease	0.13
14	Rheumatoid arthritis	0.08
15	Inflammatory bowel disease	0.07
16	Decubitus ulcer	0.04
17	Pneumoconiosis	0.04
18	Multiple sclerosis	0.04
19	HIV/AIDS - Multidrug-resistant Tuberculosis without extensive drug resistance	0.03
20	Schistosomiasis	0.02
21	Chagas disease	0.02
22	Leishmaniasis	0.01
23	Uterine fibroids	0.01
24	Cystic echinococcosis	2.39E-03
25	Cysticercosis	1.85E-03
26	HIV/AIDS - Extensively drug-resistant Tuberculosis	1.43E-03
27	Endometriosis	1.59E-04
	Total	35.39
	Total (without neoplasms)	17.81

B

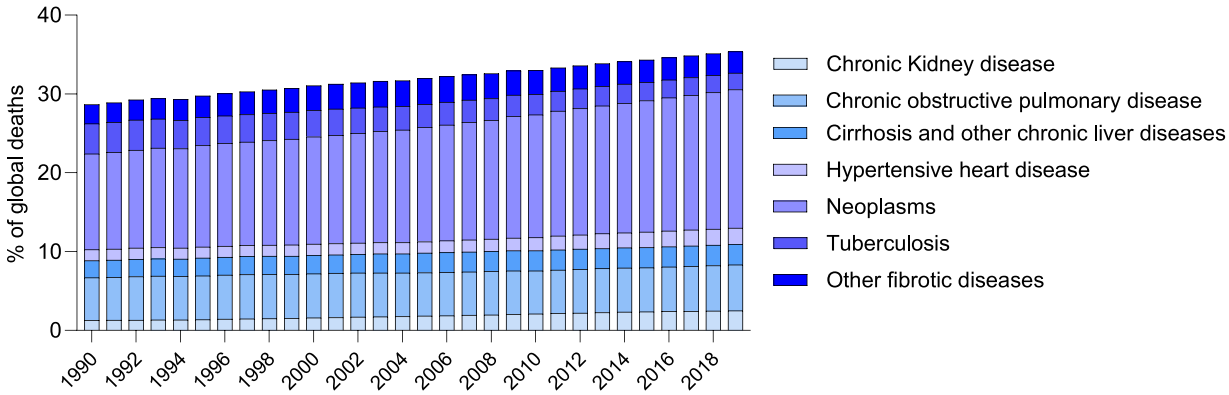

Fig. 1 Impact of Fibrotic Diseases on Global Mortality from 1990 to 2019. **A** Selected causes of death and their ranking in 1990 and 2019, based on their percentage contribution to global deaths. **B** Trend of percentage of global deaths attributable to fibrotic diseases from 1990 to 2019

Abbreviations

ECM Extracellular matrix
GBD Global Burden of Disease

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Declarations

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Not applicable.

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Competing interests
The authors declare that they have no competing interests.

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