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Drought-associated woody-plant mortality has been increasing in most regions with multi-decadal records and is projected to increase in the future, impacting terrestrial climate forcing, biodiversity and resource availability. The mechanisms underlying such mortality, however, are debated, owing to complex interactions between the drivers and the processes. In this Review, we synthesize knowledge of drought-related tree mortality under a warming and drying atmosphere with rising atmospheric CO<sub>2</sub>. Drought-associated mortality results from water and carbon depletion and declines in their fluxes relative to demand by living tissues. These pools and fluxes are interdependent and underlay plant defences against biotic agents. Death via failure to maintain a positive water balance is particularly dependent on soil-to-root conductance, capacitance, vulnerability to hydraulic failure, cuticular water losses and dehydration tolerance, all of which could be exacerbated by reduced carbon supply rates to support cellular survival or the carbon starvation process. The depletion of plant water and carbon pools is accelerated under rising vapour pressure deficit, but increasing CO<sub>2</sub> can mitigate these impacts. Advancing knowledge and reducing predictive uncertainties requires the integration of carbon, water and defensive processes, and the use of a range of experimental and modelling approaches.

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