

# A Systematic Literature Review of the Prevalence, Risk Factors, and Short- and Long-term Impact on Health Care Resource Utilization of Delayed Graft Function in Patients Receiving Kidney Allografts

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## CONCLUSIONS

- The rate of delayed graft function after kidney transplant has increased in the past decade, partly driven by increased utilization of donor kidneys with higher kidney donor profile index and longer cold ischemia time following implementation of kidney allocation system and the 2021 revision to reduce organ travel time as a factor in kidney transplant recipient selection
- Delayed graft function significantly decreases graft and patient survival, and predisposes the kidney transplant recipient to comorbidities
- Delayed graft function is associated with significantly increased healthcare resource utilization, including length of stay and readmissions after kidney transplant, and higher overall medical costs. Further studies are warranted on the impact of delayed graft function duration and severity on graft and patient outcomes, rather than the effects of delayed graft function incidence alone
- Development of strategies and new therapies to reduce the incidence, duration, and severity of delayed graft function remain an unmet need in kidney transplant

## INTRODUCTION

- Kidney transplantation (KT) is the optimal form of renal replacement therapy (RRT) because it offers patients the best long-term outcomes at the lowest overall health care cost;<sup>1,2</sup> however, donor kidney demand is much higher than availability, with ~75% of patients on the KT waitlist not receiving a graft within any given year<sup>3</sup>
- In late 2014, a new kidney allocation system (KAS) was introduced to address inequity and improve donor-recipient biological compatibility,<sup>4</sup> and refined in 2021 to remove donor distance from the recipient as a factor in candidate selection<sup>5</sup>
- After KAS was implemented, the rate of early graft dysfunction (ie, delayed graft function [DGF]) rose during the ensuing decade in the United States in part, because use of grafts with high kidney donor profile indices (KDPI, range: 0% [best quality] to 100% [lowest quality]) and transport times increased<sup>2,6,7</sup>
- DGF, defined as the need for dialysis within 7 days after KT, reflects acute kidney injury (AKI) of the allograft, primarily through ischemia-reperfusion injury, and is associated with multiple donor, organ preservation, and recipient factors<sup>8,9</sup>
- Although DGF negatively impacts graft and patient survival,<sup>8,9</sup> there is a lack of approved therapies to prevent DGF or accelerate resolution of the injury<sup>10</sup>
- Reflecting this unmet need, the literature on DGF has grown substantially over the past decade and most full-text articles are published by US-based authors compared with other countries<sup>10</sup>

## OBJECTIVE

To conduct a systematic literature review (SLR) to describe DGF epidemiology, risk factors, impact on short- and long-term graft and patient outcomes, health care resource utilization (HCRU), and medical costs in the United States

## METHODS

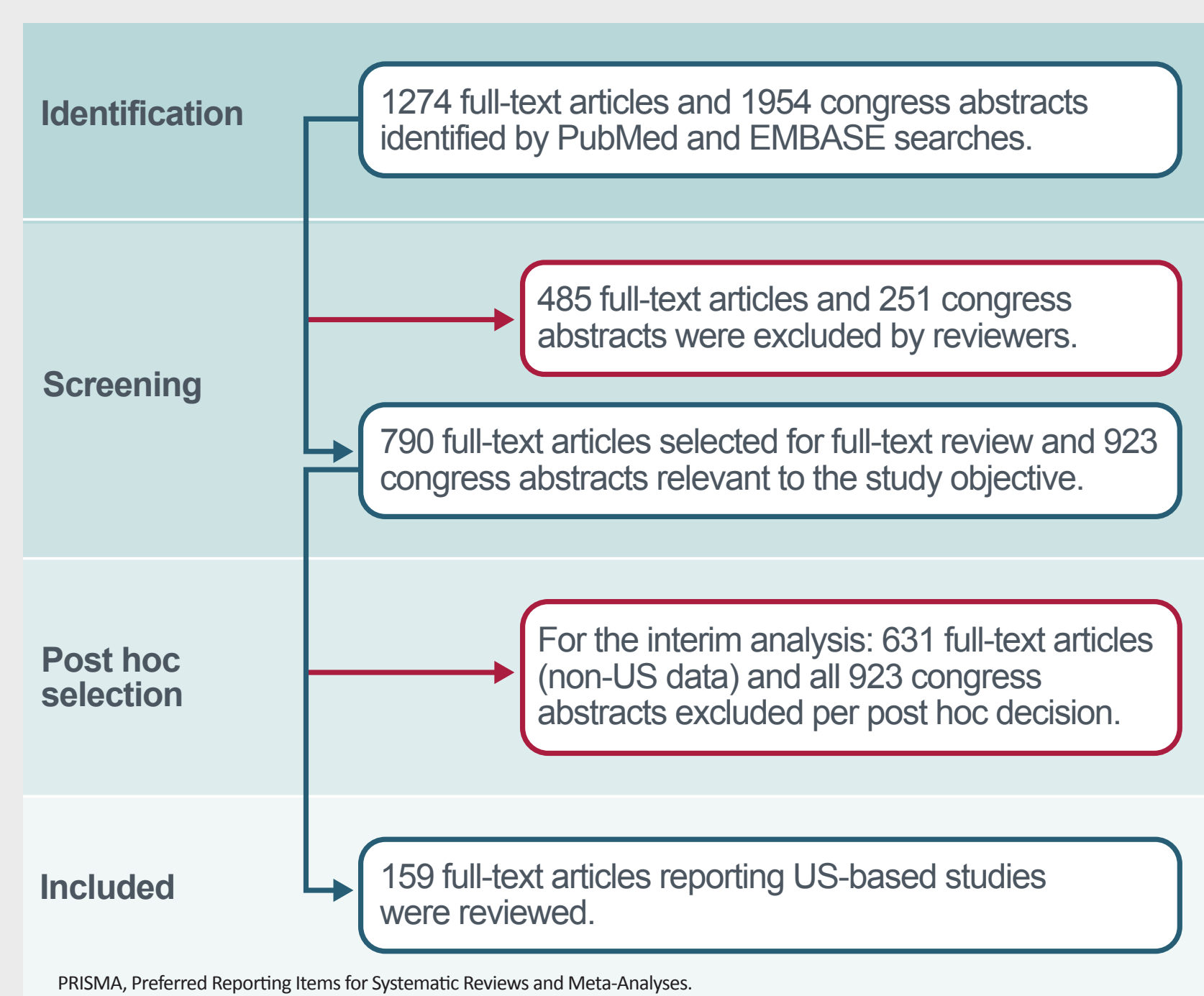
- An SLR was conducted per PRISMA guidelines<sup>11</sup> based on literature searches using the PubMed and EMBASE databases over a 10-year look-back period from October 1, 2015 to September 30, 2025
- Search terms to find articles and congress abstracts were selected to meet the objective of the SLR
- Two independent reviewers reviewed abstracts for relevance to the study objective, and a third reviewer adjudicated any discrepancies between the initial choice of abstracts to include; full-text articles of the selected abstracts were obtained and reviewed in their entirety
- For this interim SLR analysis, a post hoc decision was made to include only full-text articles and omit congress abstracts, in part, to assess the full methods and robustness of statistical testing (ie, univariate versus multivariate), and report only data from US-based transplantation centers, US national databases, and US registries
- Percentages may not total 100% due to rounding to the nearest whole number

## RESULTS

### Search results

- Database searches yielded 1274 original full-text articles and 1954 congress abstracts (Figure 1); 790 full-text articles and 923 congress abstracts remained after review
  - Focusing on US-based studies, 159 full-text articles were reviewed (the list of articles is available via QR code)

Figure 1. PRISMA flow diagram of search results

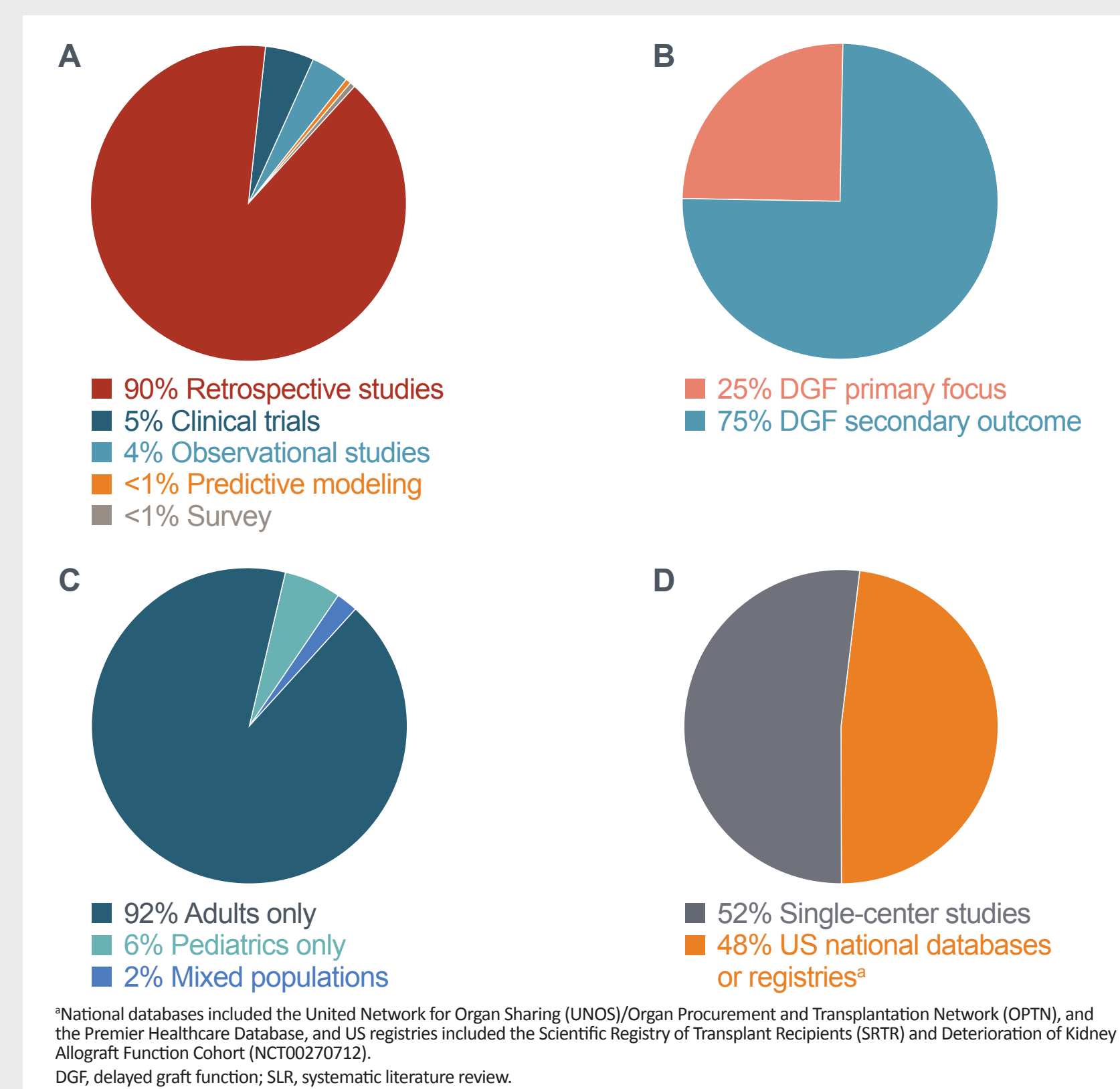


### Types of US-based studies and populations

- Of the 159 articles, the majority (90%) reported retrospective studies (Figure 2A)
- Data spanning KAS implementation (2014) were reported by 55% of articles; the remaining only reported data pre-KAS (30%) or after KAS (26%)
- DGF was the focus (primary outcome or key dependent variable) of only 25% of articles (Figure 2B)
- Only adults were evaluated by 92% of studies (Figure 2C); 52% reporting single-center studies, and 48% reported multicenter data from US national databases or registries (Figure 2D)

## RESULTS (cont.)

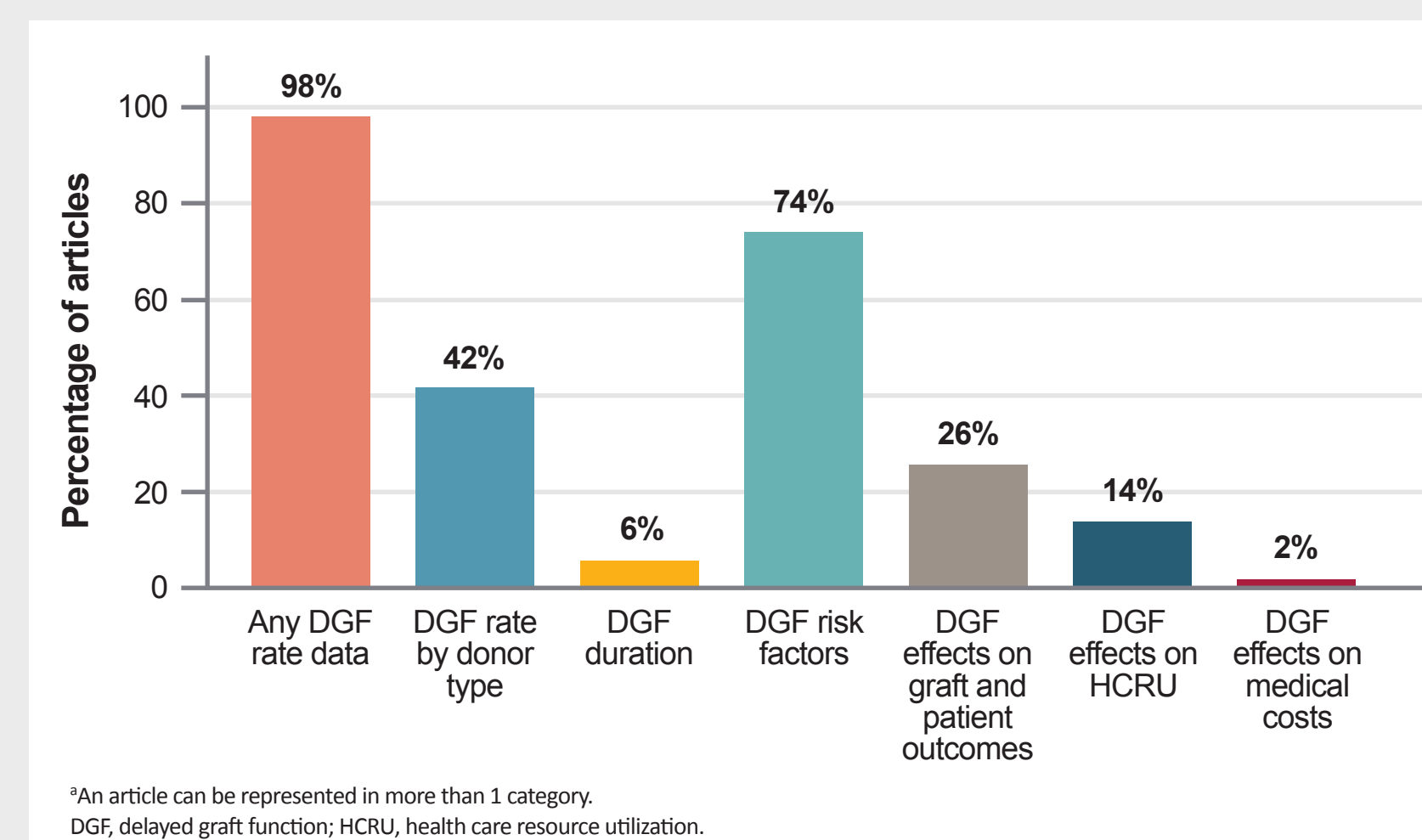
Figure 2. Types of US-based studies (A), outcome measures (B), populations (C), and data sources (D) in articles in the SLR



### Number of full-text articles reporting US-based DGF-related data

- The percentage of articles reporting outcomes of interest is presented in Figure 3

Figure 3. Percentage of articles reporting US-based DGF-related data<sup>a</sup>



### DGF rates reported in US-based studies

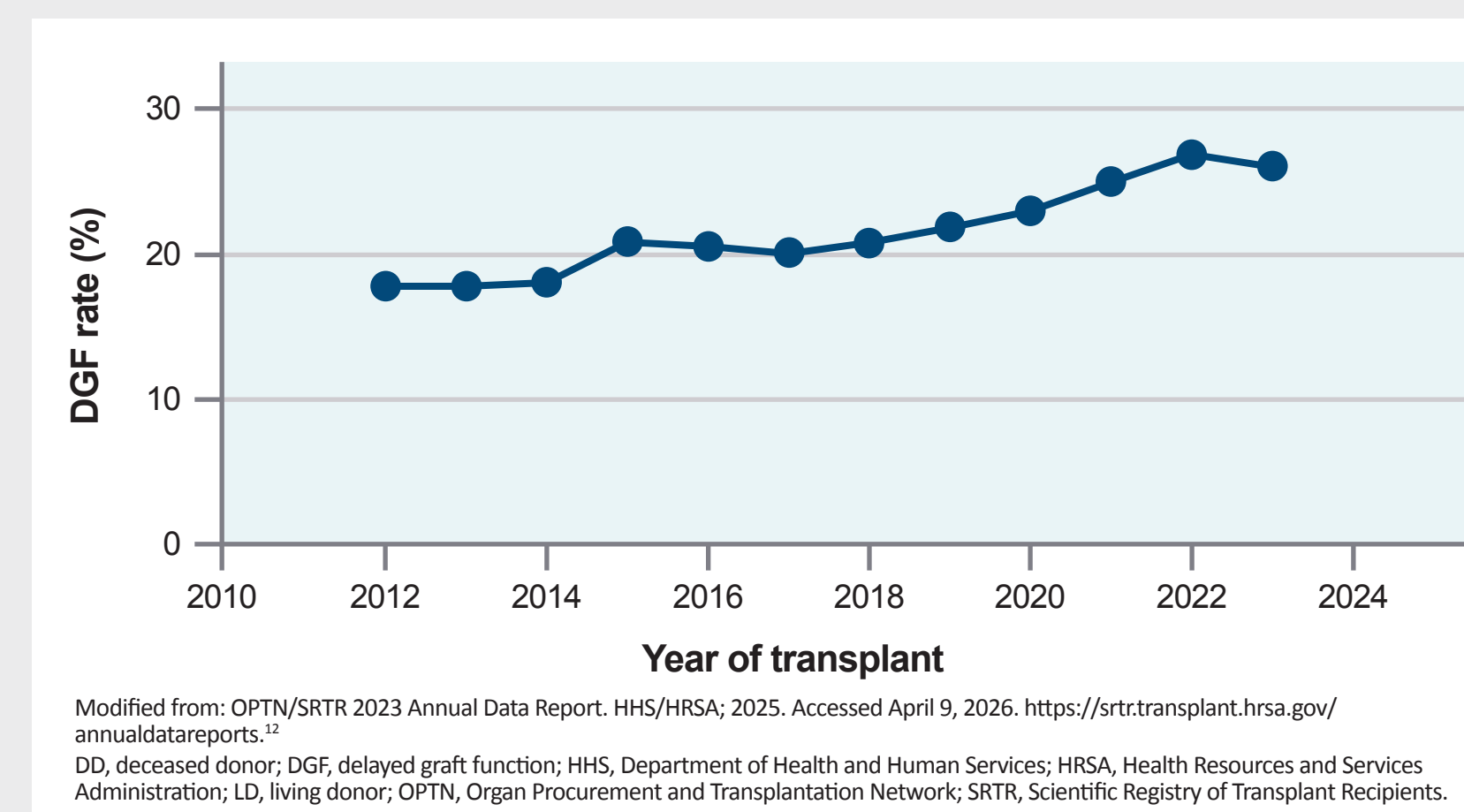
- Almost all articles (98%) reported DGF rates for an overall population or a subgroup of interest
- Of these, 66 (42%) articles reported DGF rates by donor type; 60 for DDs, of which 17 included rates from donation after circulatory (DCD), and 9 (15%) from donation after brain death (DBD)
  - The average (range) DGF rate after DD KT before subgroup stratification was 34% (7%–69%; n = 33 articles); corresponding values after DCD and DBD were 43% (20%–69%; n = 16 articles) and 20% (7%–32%; n = 8 articles)
- The average (range) DGF rate after living donor donation was 3.2% (0%–5.5%; n = 10 articles)

## RESULTS (cont.)

### DGF rates reported in US-based studies (cont.)

- Six articles reported the effect of KAS implementation after KAS began in late 2014: DGF rates increased 3% to 20% above pre-KAS rates
- DGF rates over the past decade have increased<sup>12</sup> (Figure 4)

Figure 4. The rate of DGF in all adult recipients of kidneys (includes DD and LD transplantations)



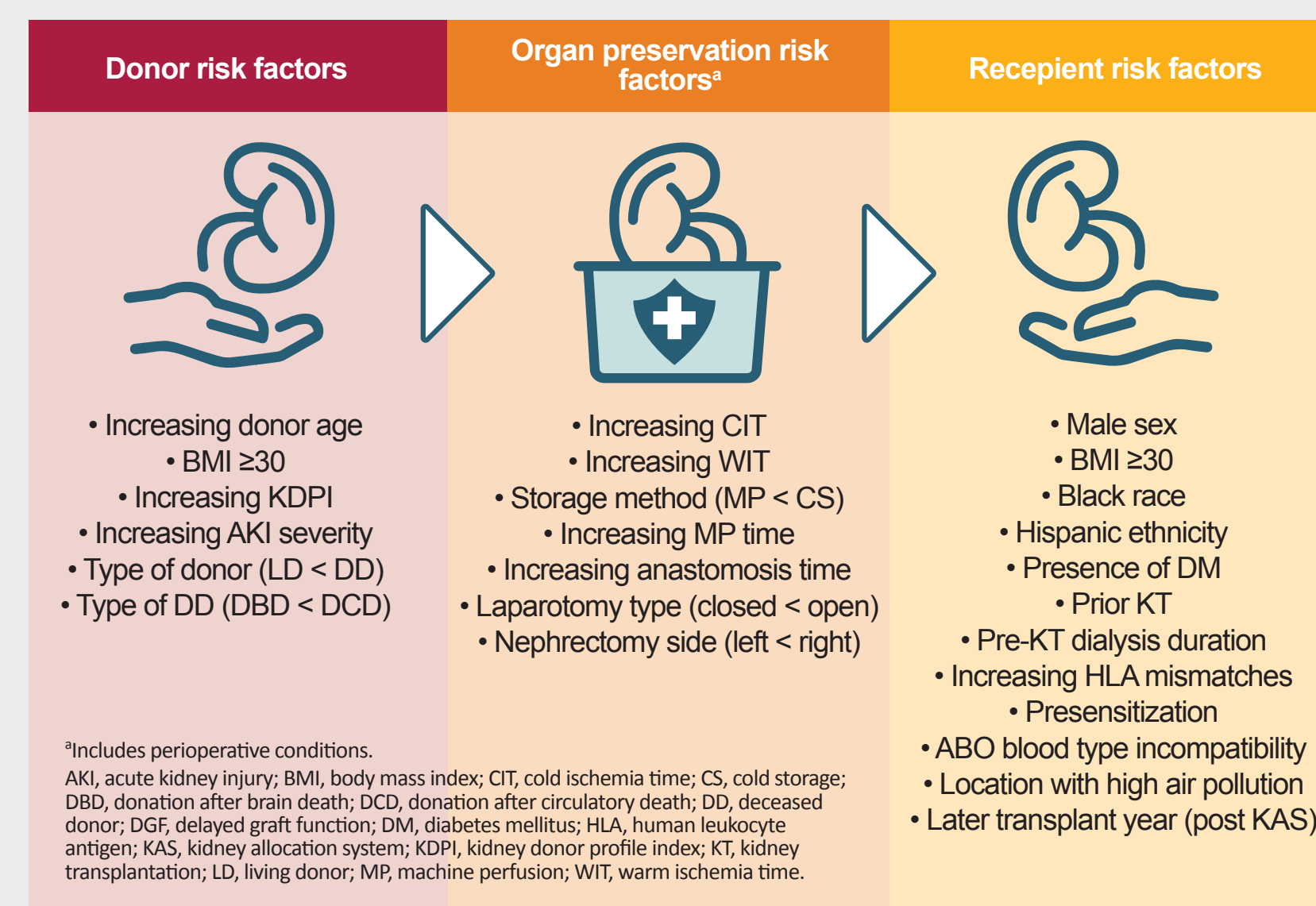
### DGF duration in US-based studies

- Ten (6%) articles described DGF duration, time to DGF resolution, or number of dialysis events required to resolve DGF
  - Median (interquartile range) duration was 10 (6–15) days (n = 1011 DGF events)<sup>13</sup> and 9 (5–19) days (n = 108 DGF events)<sup>14</sup>
  - In 1 multicenter study (n = 12,097 KT; 56 hospitals),<sup>15</sup> 52% of patients required ≥2 dialysis events, and a single-center study showed that 27% (269/1011) of patients continued dialysis 14 days after transplant<sup>13</sup>

### DGF risk factors

- Of 118 (74%) articles describing DGF risk factors, 29% used multivariate analyses, 18% were single-center or multicenter studies with >1000 KT recipients, and 11% were multicenter studies with ≥10,000 KT recipients
  - Significant predictors of DGF based on multivariate analyses of >1000 KT recipients (n = 22 articles) are depicted in Figure 5

Figure 5. Statistically significant predictors of DGF based on multivariate analyses in studies with >1000 KT recipients



## RESULTS (cont.)

### Impact of DGF on graft and patient outcomes in the United States

- DGF effects on graft and patient outcomes were reported by 42 (26%) studies; of these, 27, 13, and 14 assessed graft survival, patient survival, and other outcomes, respectively
  - Collectively, DGF significantly decreased graft survival, significantly increased AKI risk, predicted renal insufficiency at 1 year after KT, and risk of pyelonephritis
  - DGF also significantly decreased 1- to 10-year patient survival and was a significant risk factor for developing anemia, inadequate blood pressure control, cytomegalovirus viremia, and thrombocytopenia

### Impact of DGF on HCRU

- Twenty-three (14%) articles reported HCRU data; DGF significantly increased the mean or median length of stay (LOS) by +1 to +13 days and DGF rate and duration were risk factors for readmission rates<sup>16,17</sup>
- In a survey of 70 US and 3 Canadian transplant centers,<sup>18</sup> 57% of respondents reported a LOS of 3–5 days for patients without DGF
  - DGF was most often managed as outpatient visits (with DGF: 2–3 outpatient visits/week; without DGF: 1–2 visits/week)—only 2% of respondents reported that patients remained hospitalized until DGF was resolved

### Impact of DGF on medical costs

- Only 2 articles reported the direct effect of DGF on medical costs
  - A multicenter study of the Premier Healthcare Database analyzed 12,907 KT from 56 unique US hospitals and found that DGF significantly increased the initial mean cost of KT by \$12,239 and the Annual cost plus any 90-day readmissions by \$17,894<sup>14</sup>
  - A single-center study that assessed the impact of the 2021 KAS revision<sup>19</sup> reported that the associated increase in DGF prevalence increased the estimated cost of hemodialysis after KT by more than \$100,000 for their program, reflecting a more than 2-fold higher number of dialysis sessions required within 30 days post KT

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