Impact of FDA Expedited Review Programs on New Drug Approval Time

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Research Questions

01 How do the FDA's four expedited programs affect review time?

02 What factors are associated with receiving any expedited review designation?

Background

- The US FDA has four expedited programs to facilitate the development and regulatory review of new drugs.[1]
  - Of these, priority review is explicitly intended to reduce application review time from 10 to 6 months.
  - The other programs include features to help expedite the clinical development process, but do not directly affect review time.
  - A drug may qualify for one or more expedited programs.

	Accelerated Approval	Breakthrough Therapy	Fast-track	Priority Review
Qualifying criteria	▪ Serious condition ▪ Meaningful advantage over available therapies ▪ Demonstrates effect on surrogate endpoint or intermediate clinical endpoint that is likely to predict clinical benefit	▪ Serious condition ▪ Preliminary clinical evidence demonstrates substantial improvement on clinically significant endpoint over available therapies	▪ Serious condition ▪ Nonclinical or clinical data demonstrate the potential to address unmet medical need, or has been designated as a qualified infectious disease product	▪ Serious condition ▪ Would provide significant improvement in safety or effectiveness, or has been designated as a qualified infectious disease product, or has been submitted with a priority review voucher
When to submit request	During development to support the use of the planned endpoint as basis for approval	Before pre-BLA or pre-NDA meeting	Before pre-BLA or pre-NDA meeting	With BLA, NDA, or efficacy supplement
Features	Approval based on effect on a surrogate endpoint	▪ Guidance on efficient drug development ▪ Organizational commitment ▪ Rolling review	▪ Actions to expedite development and review ▪ Rolling review	Shorter time for review of marketing application

1. FDA. Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014. Available at https://www.fda.gov/media/86377/download. Accessed March 2024.
Abbreviations: BLA = biologics license application; NDA = new drug application

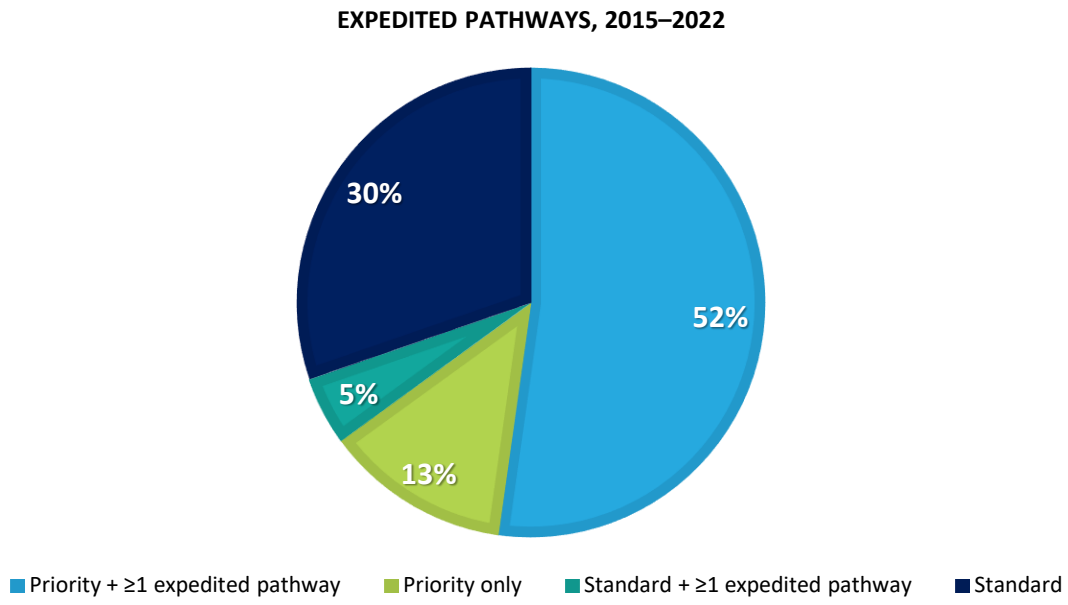
Methods

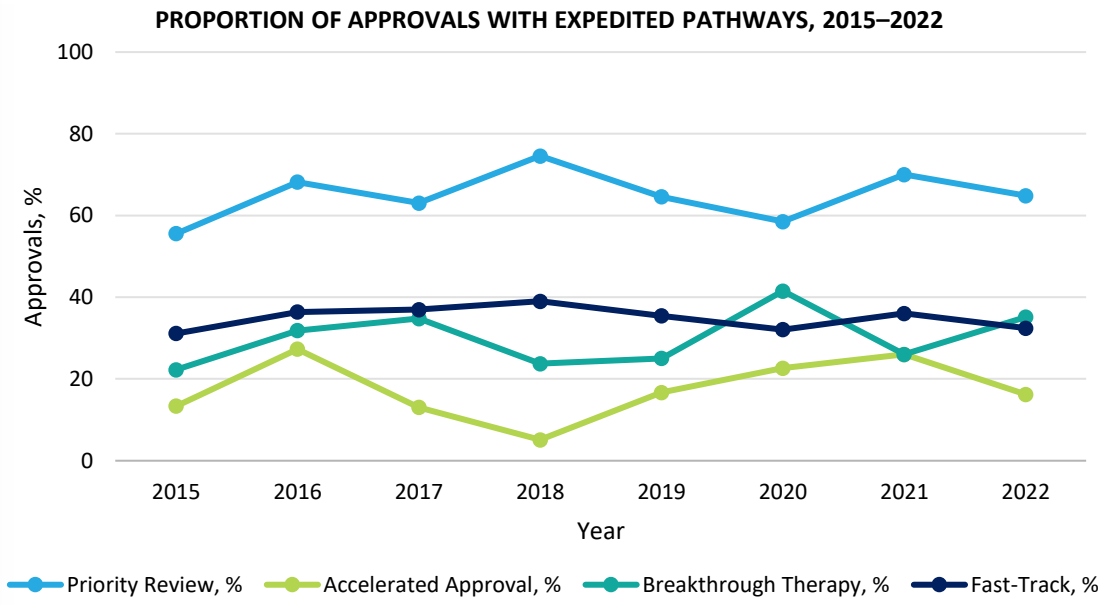
- All New Drug Applications (NDA) and Biologic License Applications (BLAs) approved from January 2015 to December 2022 were obtained from the FDA website.[1]
- The total review time for each drug was calculated based on the difference between the FDA approval and application receipt dates.
- Each approval's indication was categorized by therapy area based on International Classification of Diseases, 10th Revision (ICD-10) codes.
- Review times associated with priority review and other expedited programs were compared with standard review with no expedited programs. The likelihood of receiving any expedited program based on first-in-class status, orphan drug status, and therapy area was also compared. Relative risks (RRs) and 95% CIs were calculated for comparisons of interest.

1. FDA. Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals. March 2023. Available at https://www.fda.gov/drugs/drug-approvals-and-databases/compilation-cder-new-molecular-entity-nme-drug-and-new-biologic-approvals. Accessed October 2023.

Expedited Pathway Designation Trends

- Of 360 approvals, priority review was applied to 65% of applications.
- Fifty-seven percent of applications had accelerated, breakthrough, and/or fast-track designation.
- Proportions of approvals with various expedited pathways were generally constant over time.

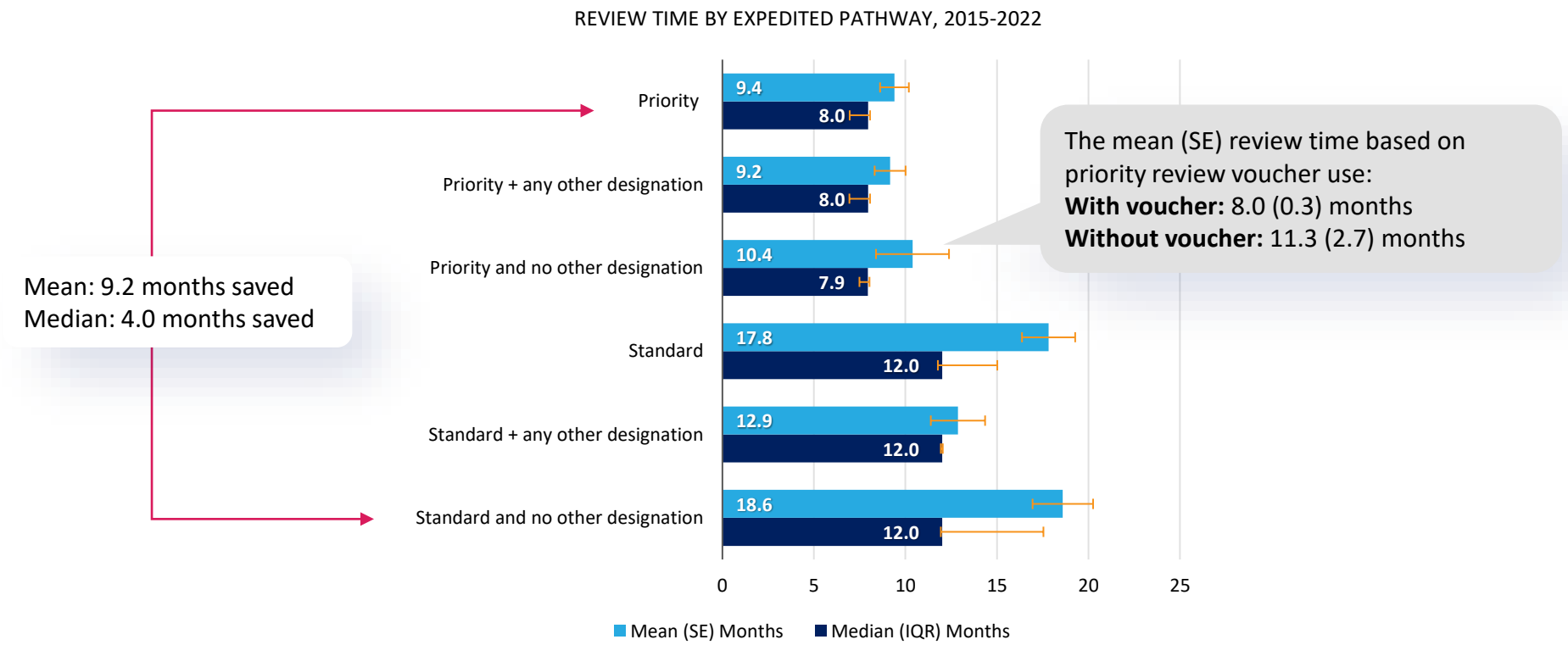




Note: 28% of drugs with priority only designation used a priority review voucher. No drugs using priority review vouchers had other expedited pathway designations.

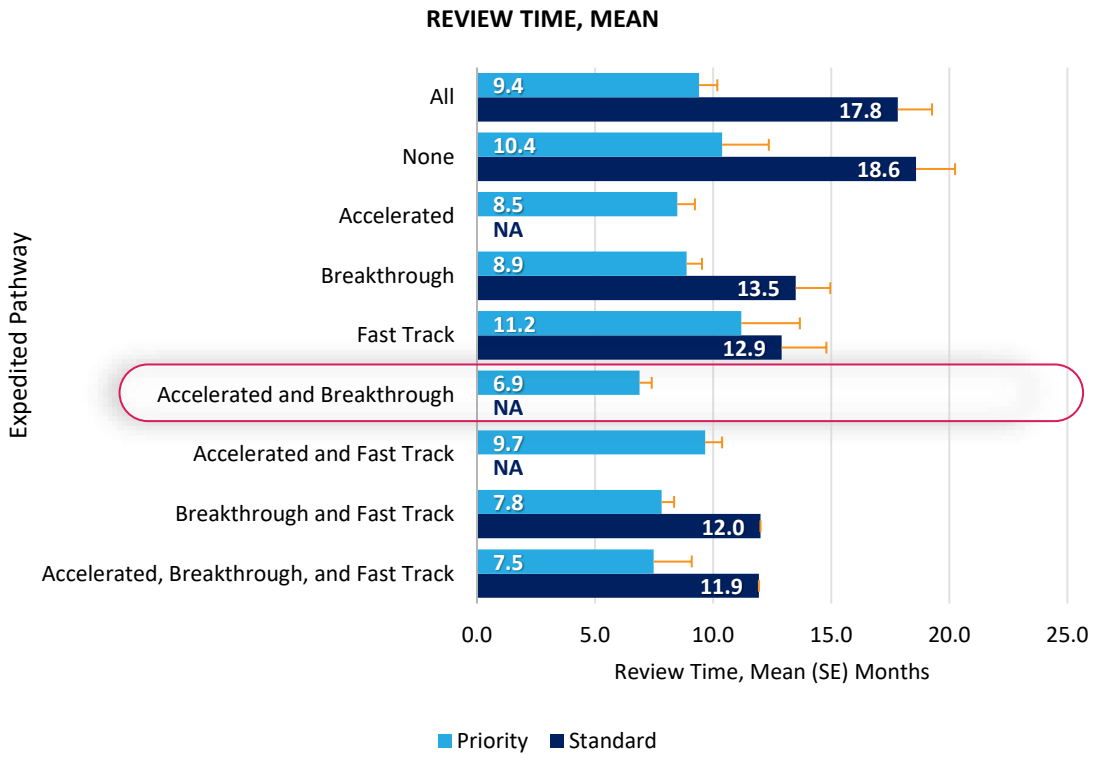
Approval Time

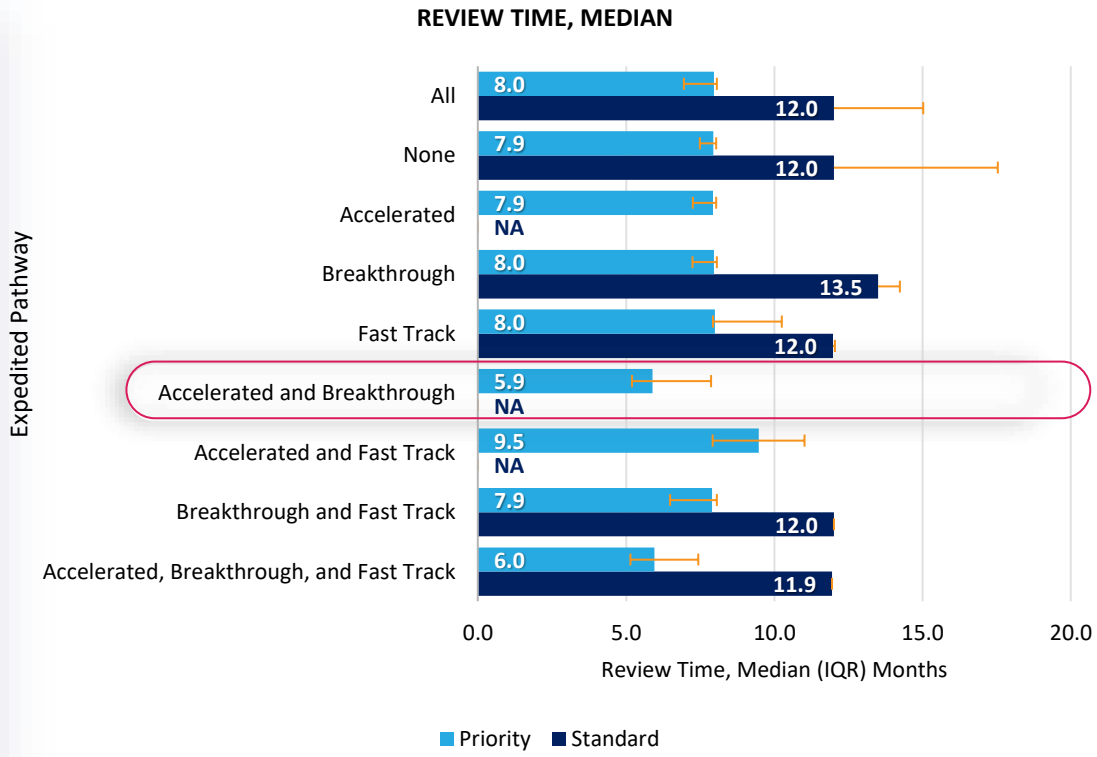
- Therapies with priority review had a shorter mean (median) review time of 9.4 (8.0) months compared with 18.6 (12.0) months for therapies under standard review only, equating to 9.2 (4.0) months saved.



Approval Time (cont.)

- Individually, fast-track, breakthrough, and accelerated approval designations had little impact on review time for therapies under priority review, but the combination of priority review, accelerated approval, and breakthrough therapy designations provided the shortest overall mean (median) time to approval: 6.9 (5.9) months.



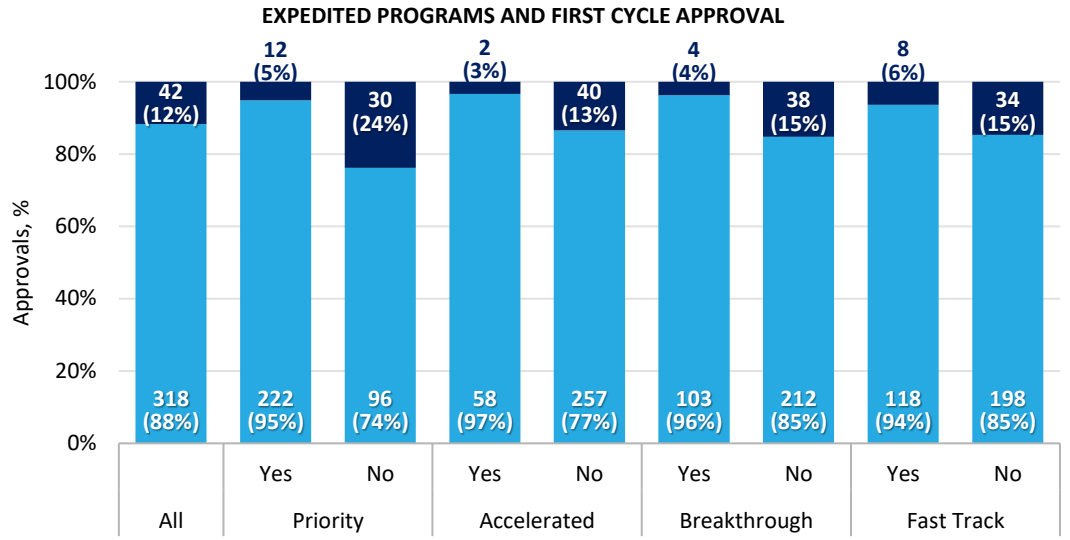


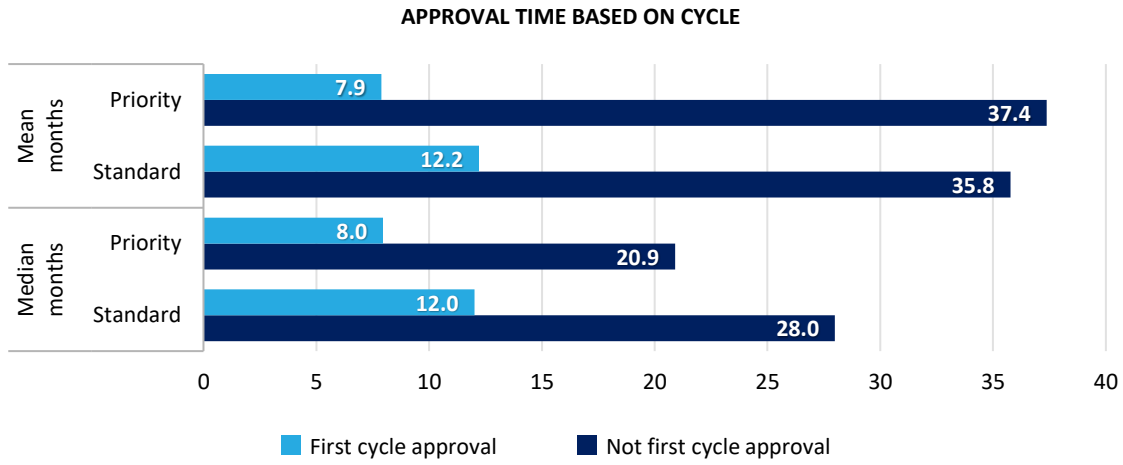
Abbreviation: NA = not applicable

Expedited Program Impact on Review Round

- Twelve percent of all approved drugs were not approved in the first round.
  - Among applications not approved in the first round, 71% were under standard review.
- Therapies were significantly more likely to be approved during the first review cycle if they underwent priority review, breakthrough therapy designation, or fast-track designation compared with therapies without the respective designation.
- The mean (median) approval time for drugs not approved in the first cycle was 36.2 (25.1) months vs. 9.2 (8.0) for drugs approved in the first cycle

	RR (95% CI)
Priority	**2.44 (1.51–3.96)**
Accelerated	3.87 (0.98–15.25)
Breakthrough	**3.43 (1.33–8.84)**
Fast-track	**1.96 (1.03–3.72)**

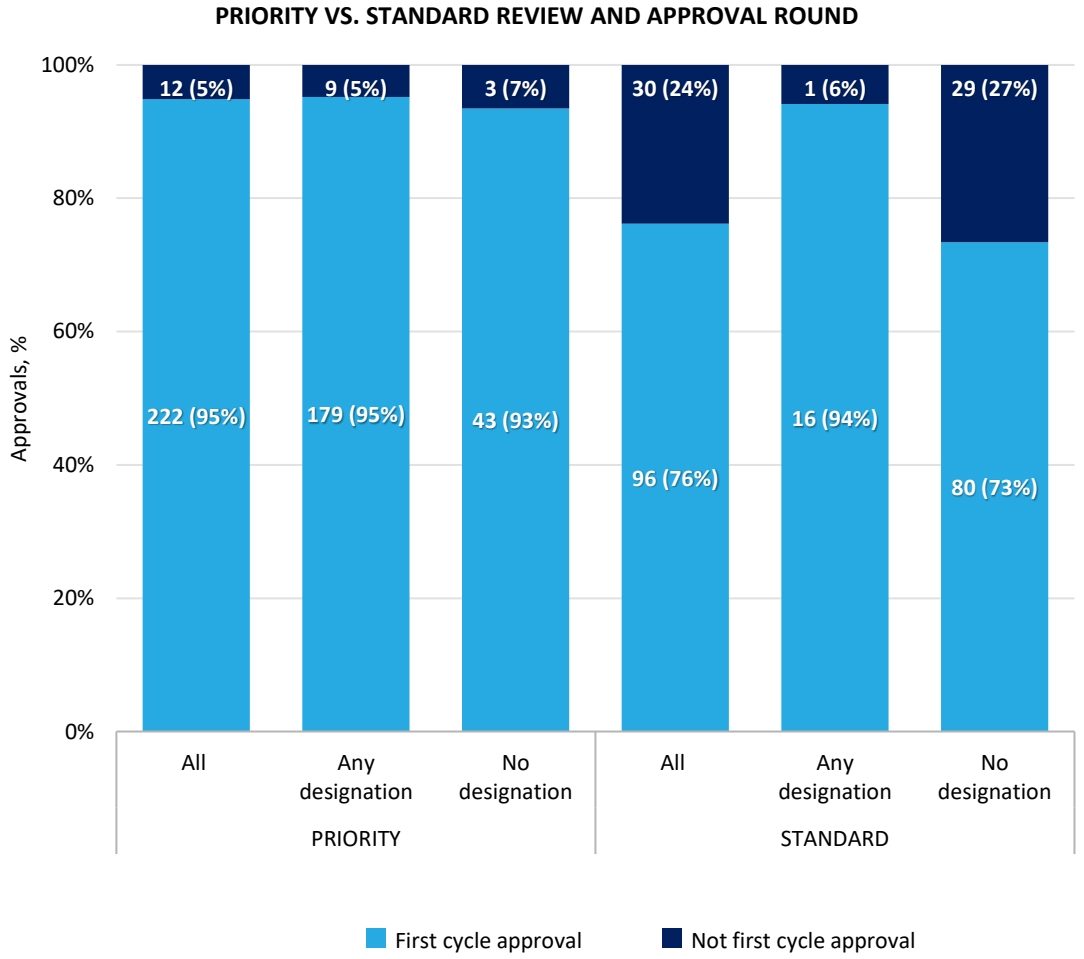




Abbreviation: RR = relative risk

Expedited Program Impact on Review Round (cont.)

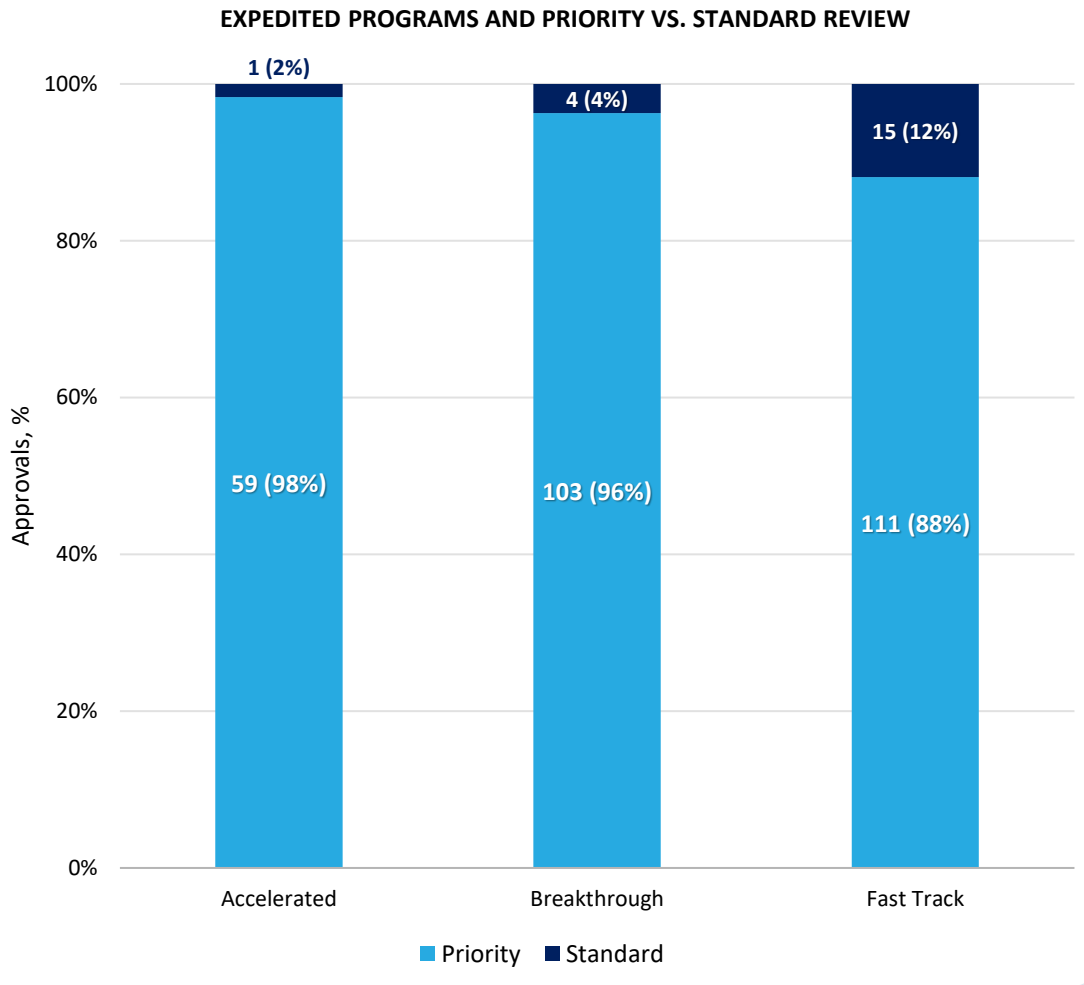
- The proportion of drugs approved in the first cycle is similar if accelerated, breakthrough, or fast-track designation have been applied, irrespective of priority or standard review (RR [95% CI] = 1.01 [0.89–1.14]).
- For drugs without accelerated, breakthrough, or fast-track designation, drugs with priority review are significantly more likely to be approved in the first round than drugs with standard review (RR [95% CI] = 1.27 [1.11–1.46]).



Expedited Designation Effect on Priority Review

- The likelihood of priority review increased for therapies with any expedited designation, with accelerated approval producing the largest impact and fast-track designation the smallest.
- Priority review was applied to:
  - **98%** of applications with accelerated designation.
  - **96%** of applications with breakthrough designation.
  - **88%** of applications with fast-track designation.

	RR (95% CI) for Priority Review
Accelerated	**37.62 (5.27–268.43)**
Breakthrough	**16.42 (6.19–43.57)**
Fast-track	**4.70 (2.86–7.71)**



Abbreviation: RR = relative risk

First-in-Class and Orphan Drugs

- First-in-class therapies were significantly more likely than non-first-in-class therapies to receive a priority review, breakthrough therapy designation, or fast-track designation.
- Orphan drugs were significantly more likely than non-orphan drugs to receive a priority review, accelerated approval, breakthrough therapy designation, or fast-track designation.

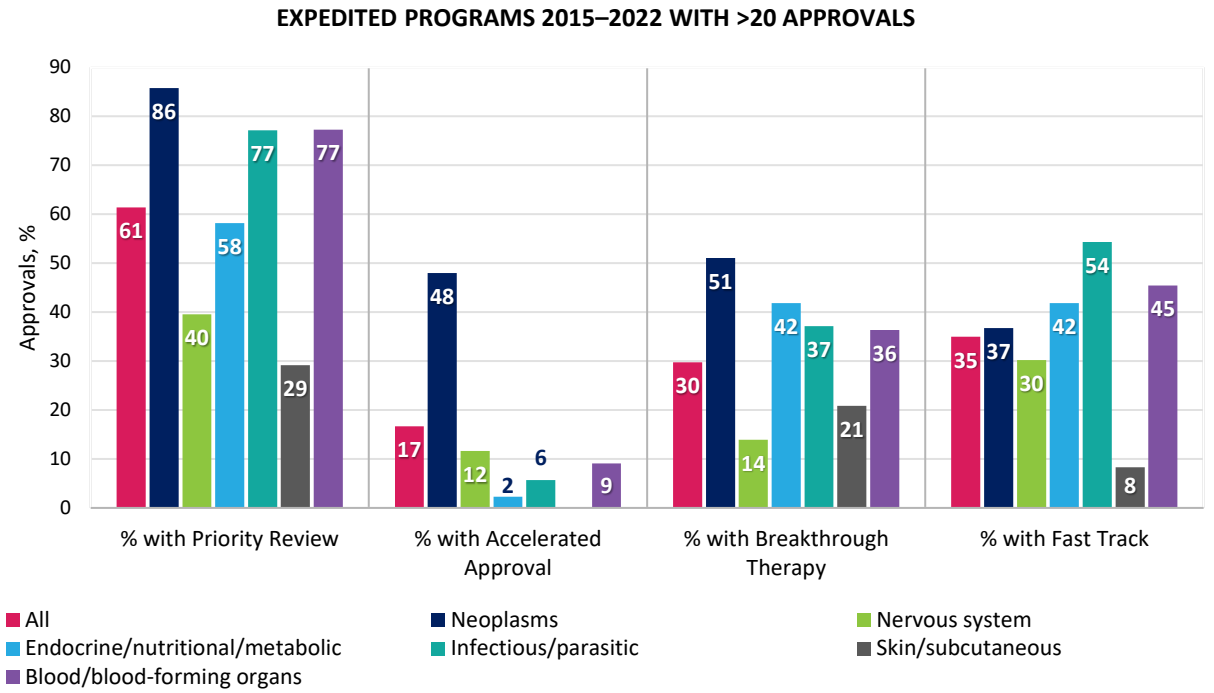
	RR (95% CI) for First-in-Class Therapies
Priority	**1.51 (1.28–1.77)**
Accelerated	1.11 (0.69–1.76)
Breakthrough	**2.01 (1.46–2.78)**
Fast-track	**1.34 (1.01–1.76)**

	RR (95% CI) for Orphan Conditions
Priority	**2.05 (1.70–2.48)**
Accelerated	**4.58 (2.46–8.52)**
Breakthrough	**2.90 (1.99–4.23)**
Fast-track	**1.84 (1.36–2.48)**

Abbreviation: RR = relative risk

Expedited Programs by Therapy Area

- Among therapy areas with >20 approvals:
  - Neoplasms and infectious and parasitic diseases were more likely to receive at least one expedited program designation
  - Nervous system diseases, skin and subcutaneous tissue diseases, and endocrine, nutritional, and metabolic diseases were less likely to receive at least one expedited program designation



	Neoplasms	Nervous System	Endocrine/Nutritional/ Metabolic	Infectious/Parasitic	Skin/Subcutaneous	Blood/Blood-forming Organs
Priority	**1.50 (1.31–1.71)**	**0.58 (0.40–0.84)**	0.88 (0.68–1.15)	1.21 (0.99–1.48)	**0.43 (0.23–0.81)**	1.20 (0.95–1.53)
Accelerated	**9.97 (5.65–17.59)**	**0.66 (0.28–1.57)**	**0.12 (0.02–0.87)**	0.32 (0.08–1.24)	0 (NE)	0.53 (0.14–2.01)
Breakthrough	**2.42 (1.79–3.26)**	**0.43 (0.20–0.93)**	1.48 (1.00–2.19)	1.27 (0.80–2.02)	0.68 (0.31–1.51)	1.23 (0.69–2.19)
Fast-track	1.08 (0.79-1.47)	0.87 (0.54-1.39)	1.22 (0.83–1.79)	**1.64 (1.16–2.31)**	**0.22 (0.06–0.85)**	1.32 (0.81–2.13)

Abbreviations: NE = not evaluable

Value of Expedited Review

Effect of Expedited Pathways on Development Time

- The median development time for drugs with accelerated, breakthrough, and/or fast-track designation was 6.0 years vs. 7.2 years for applications without these expedited designations.[1]

Effect of Expedited Pathways on FDA Review Time

- These expedited programs also increase the likelihood of priority review designation, first cycle approval, and overall shorter times from application submission to approval.

Monetary Value of Priority Review

- The value of priority review designation has been demonstrated through the subsequent sales of vouchers that were originally awarded for drugs to treat rare pediatric conditions, tropical diseases, and material threat medical countermeasures.
  - In a 2020 Government Accountability Office report, 17 of 31 priority review vouchers were sold for between $67–$350 million each.[2]

1. Wong AK, et al. *JAMA Network Open*. 2023 Aug 1;6(8):e2331753-.
2. United States Government Accountability Office. January 2020.

Conclusions

References and Acknowledgments

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- FDA. Expedited Programs for Serious Conditions – Drugs and Biologics. May 2014. Available at https://www.fda.gov/media/86377/download. Accessed March 2024.
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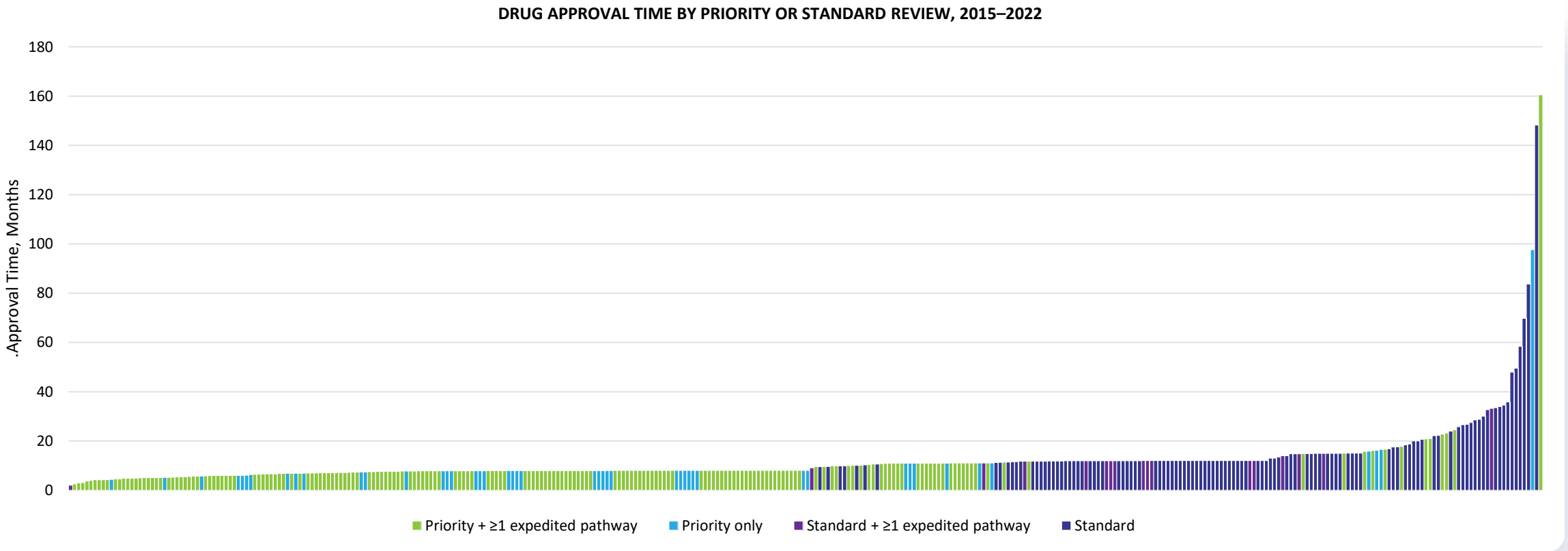
Approval Time

- Drugs with priority review generally have shorter review times than those with standard review.
- Approval times varied dramatically, mainly in drugs with standard review.



Approval Time

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- **71%** of submissions not approved in the first round were under standard review.