

Tufts Center for the Study of Drug Development

Briefing

Cost of Developing a New Drug

November 18, 2014

Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs

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R&D Cost Study Briefing
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Agenda

- “ **Main Finding**
- “ **Data and Methods**
- “ **Clinical approval rates, phase transition rates, and out-of-pocket costs per approved compound**
- “ **Development times, the discount rate, and capitalized costs per approved compound**
- “ **Post-approval cost estimates**
- “ **R&D cost growth rates**
- “ **Cost drivers**

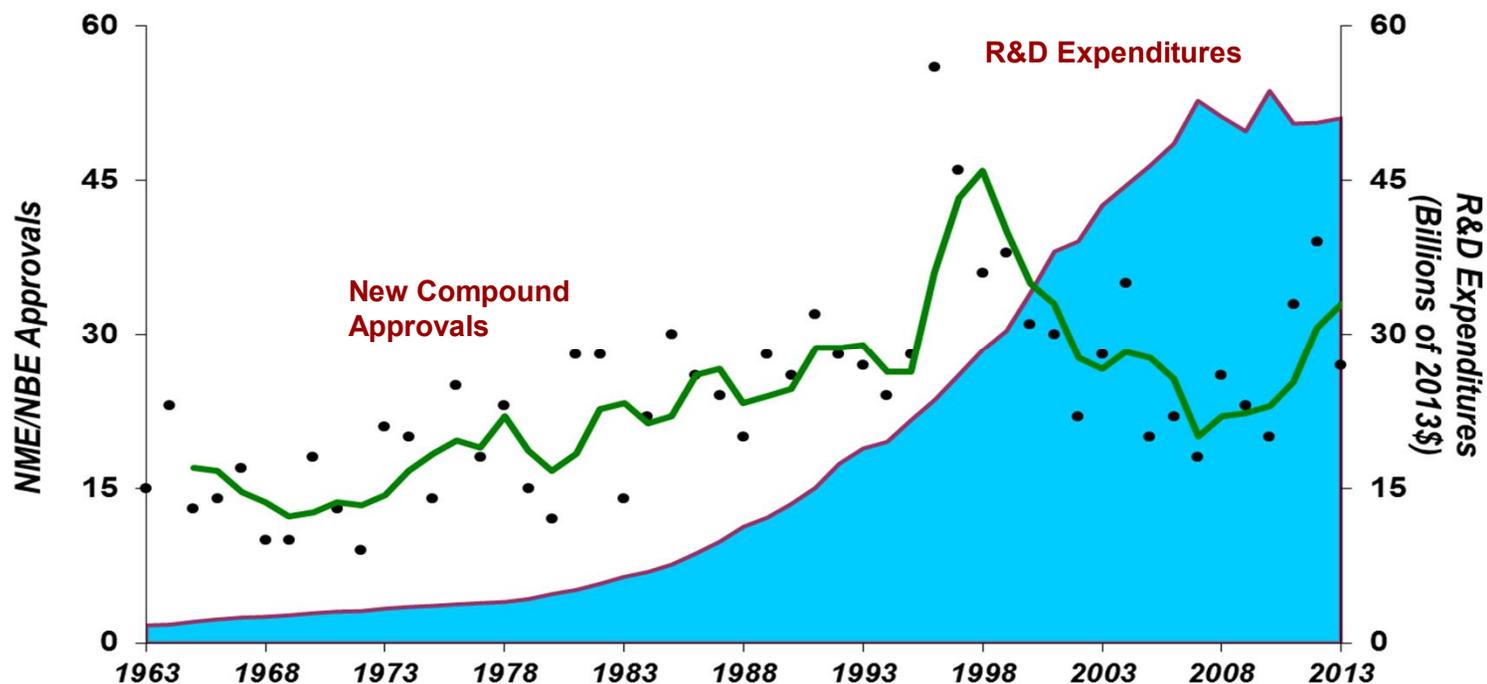
Main Finding:

The estimated average pre-tax industry cost per new prescription drug approval (inclusive of failures and capital costs) is:

\$2,558 million

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New Drug and Biologics Approvals and R&D Spending



R&D expenditures are adjusted for inflation; curve is a 3-year moving average for NME/NBEs
Sources: Tufts CSDD; PhRMA, 2014 Industry Profile

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Data and Methods

Outline of Study Cost Dataset

- “ 106 investigational new drugs and biologics from 10 firms first tested in humans anywhere in the world, 1995-2007
- “ Clinical period development cost data up to 2013
- “ Five compounds still active at the time of data collection.
- “ Compounds that lasted late in development oversampled to increase the amount of information for late development stages. Results then weighted to reflect the population distribution.
- “ Annual company biopharmaceutical R&D expenditures from 1990 to 2010 broken down in various ways (used to estimate pre-human R&D costs).

Elements Used to Determine Fully Allocated New Compound R&D Costs

- “ **Out-of-pocket clinical costs (all indications, long-term animal testing, overhead, CMC during clinical testing and prior to first approval)**
- “ **Out-of-pocket discovery research and preclinical development costs**
- “ **Clinical approval success and phase attrition rates**
- “ **Development times**
- “ **Cost of capital**

Out-of-Pocket Clinical Costs

- “ Survey data on costs by phase and year for a sample of investigational compounds.
- “ Oversampled compounds that proceeded to late-stage testing: stratified random sample.
- “ Weight survey response to reflect actual population distribution for strata.
- “ Calculate weighted average phase costs.

Out-of-Pocket Discovery and Preclinical Development Costs

- “ Cannot attribute all pre-human R&D costs to specific compounds.
- “ Use time series data on company annual aggregate spending on pre-human and clinical R&D.
- “ Apply lag structure on data based on gap between pre-human and clinical expenditures (difference in median phase times).
- “ Determine ratio of pre-human to clinical expenditures from lagged data.
- “ Apply ratio to clinical phase cost estimate to obtain a pre-human cost estimate.

Clinical Approval Success Rates

- “ Since many compounds fail in testing, phase costs must be weighted by the probability of entering the phase (expected costs) to obtain costs per investigational compound.
- “ Overall clinical approval success rates used to translate cost per investigational compound to cost per approved compound.
- “ Tufts CSDD database of investigational compounds used to estimate these probabilities (subset relevant to cost study sample period).
- “ Other interesting results obtained: attrition rates and distribution of failures by phase.

Phase Development Times

- “ Use survey data to find average time in phase (across indications).
- “ Use survey data to find average time between start of one phase and beginning of the next phase.
- “ Average phase-to-phase times used to establish a representative development time profile from synthesis to approval.
- “ Representative time profile, along with average phase lengths, used to determine how expenditures are distributed over time.

Cost of Capital and Capitalization

- “ **Cost of capital is the expected return required by investors to get them to invest in drug development.**
- “ **Capital Asset Pricing Model (CAPM) applied to data on biopharmaceutical firms over relevant period to determine an industry cost of capital.**
- “ **Estimate is based on data on stock market returns and debt-equity ratios for a sample of biopharmaceutical firms.**
- “ **Used as the discount (interest) rate to capitalize R&D expenditures to marketing approval according to the estimated development timeline.**

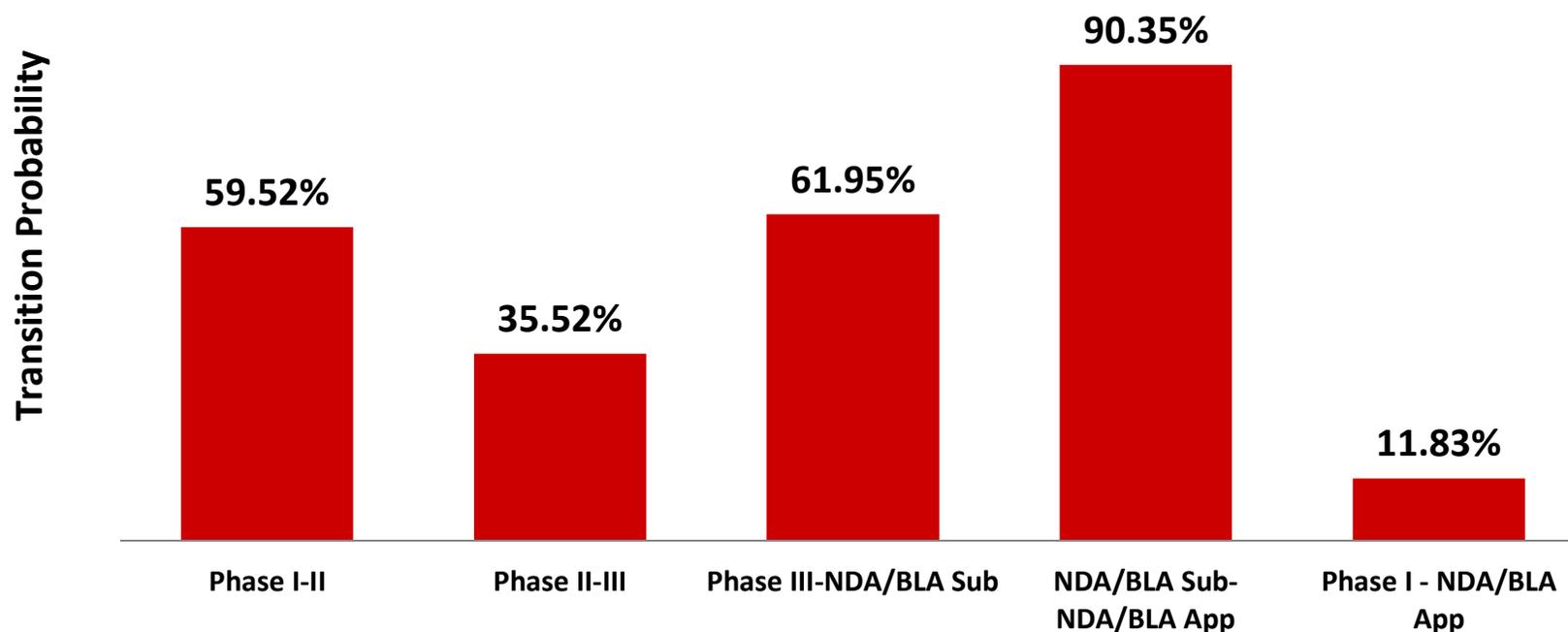
Results

Data for Phase Transition and Approval Success Rate Estimates

- “ Dataset of investigational compounds in the portfolios of top 50 firms (several commercial pipeline databases, published company pipelines, clinicaltrials.gov, web searches).
- “ Subset of self-originated compounds first tested in humans anywhere in the world from 1995 to 2007.
- “ 1,442 compounds met study inclusion criteria.
- “ Development status checked through end of 2013.
- “ For this set of compounds, 7.1% were approved, 80.3% had been discontinued in some phase, and 12.6% were still active in some phase.

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Clinical Phase Transition Probabilities and Overall Clinical Approval Success Rate*



*Therapeutic new molecular entities and new therapeutically significant biologic entities first tested in humans, 1995-2007

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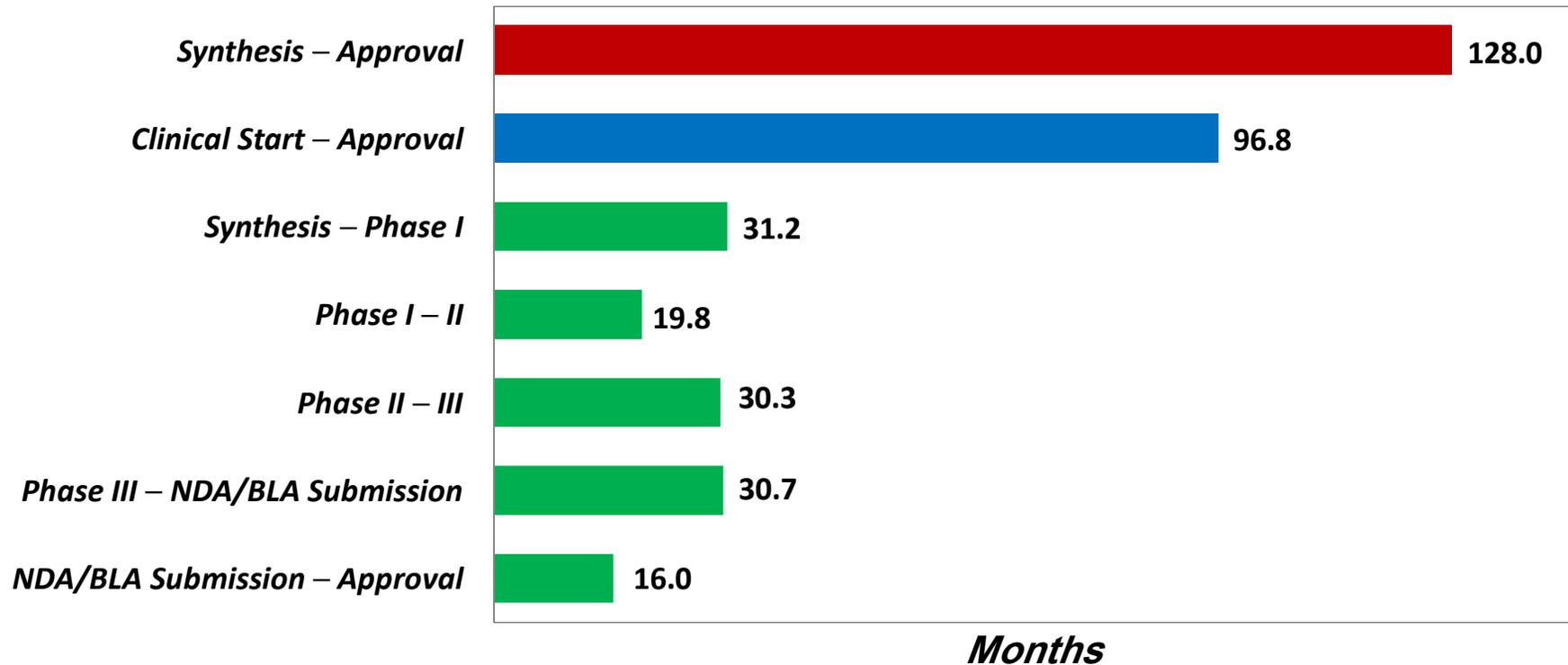


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Representative Development and Regulatory Review Time Profile (synthesis to approval)



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Pre-human Cost Estimates

- “ Annual data on pre-human and clinical period company R&D expenditures on self-originated investigational compounds aggregated across companies.
- “ Need to impose a lag structure between pre-human and clinical expenditures.
- “ Based on development time data, we used a 5-year lag between median pre-human and median clinical expenditures .
- “ Implies that pre-human expenditures are 30.8% of costs per approved compound.
- “ Results are not very sensitive to assumed lag within reason (4 and 6-year lags applied in sensitivity analysis)

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**Nominal and Real Cost of Capital (COC) for the
Biopharmaceutical Industry, 1994-2010**

	1994	2000	2005	2010
Nominal COC	14.2%	14.9%	13.3%	11.4%
Inflation Rate	3.1%	3.1%	2.5%	2.0%
Real COC	11.1%	11.8%	10.8%	9.4%

Implication: R&D costs were capitalized at a 10.5% real COC

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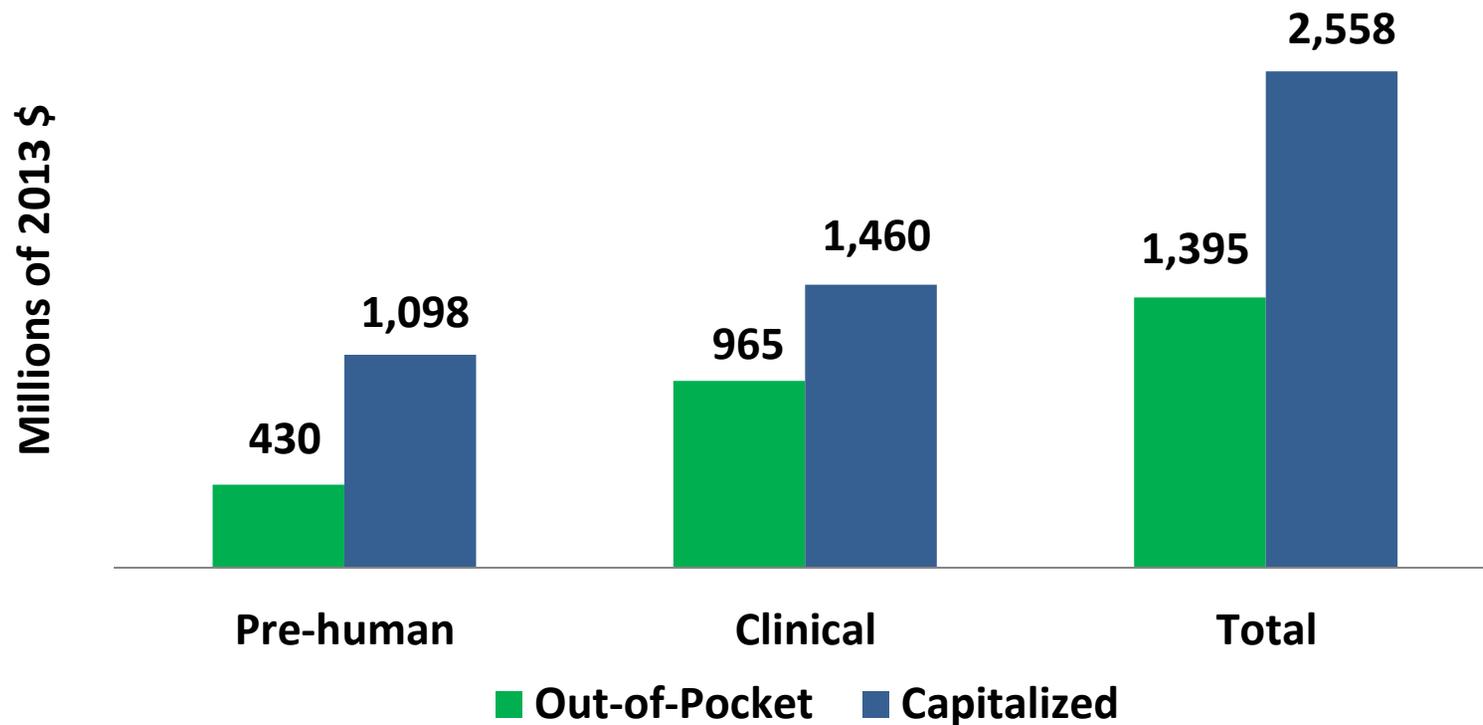


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Out-of-Pocket and Capitalized Cost per Approved New Compound



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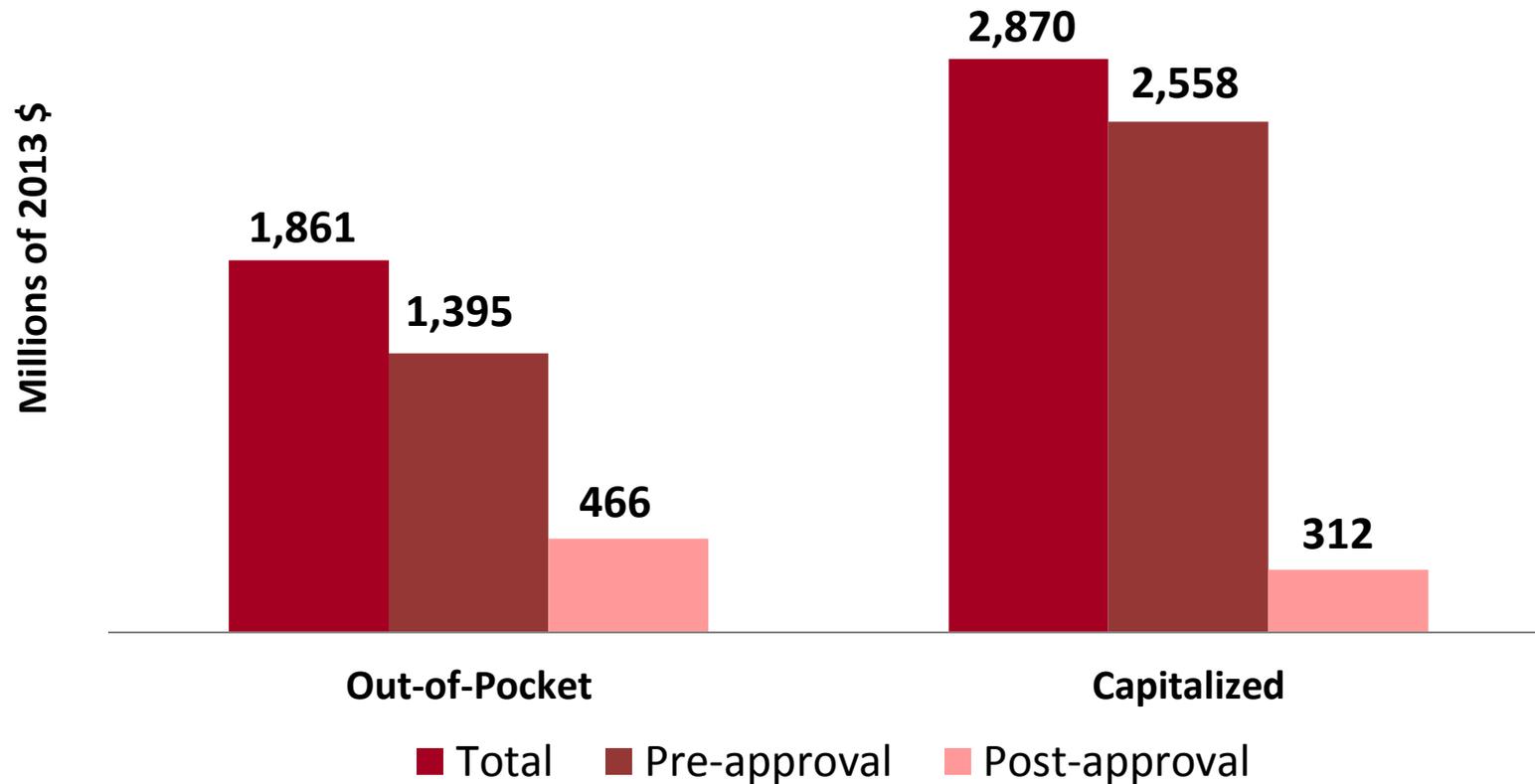


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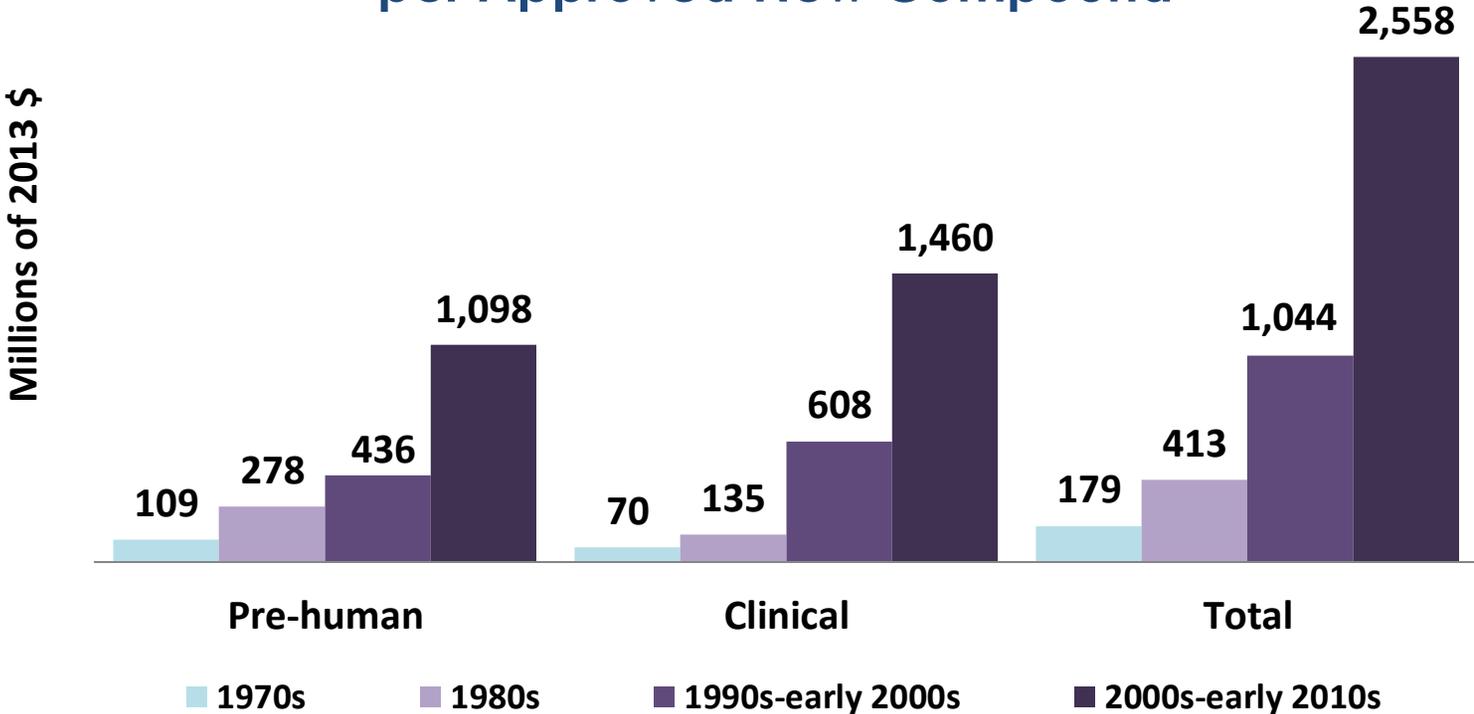
**Pre-approval, Post-approval and Total Lifecycle Cost
per Approved New Compound**



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Growth in Capitalized R&D Costs per Approved New Compound

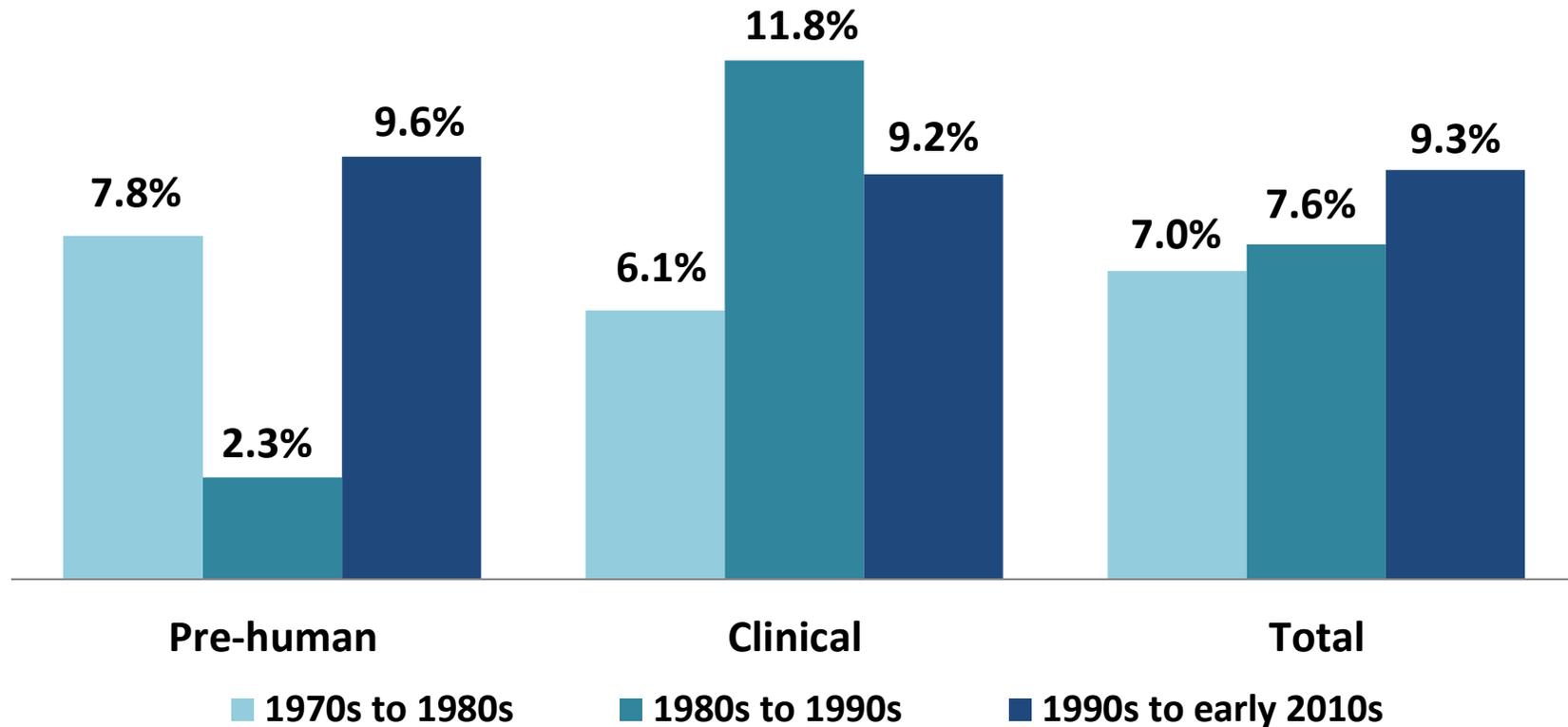


Sources: 1970s, Hansen (1979); 1980s, DiMasi et al. (1991); 1990s-early 2000s, DiMasi et al. (2003); 2000s-early 2010s, Current Study

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Compound Annual Inflation-Adjusted Growth Rates for Out-of-Pocket R&D Costs



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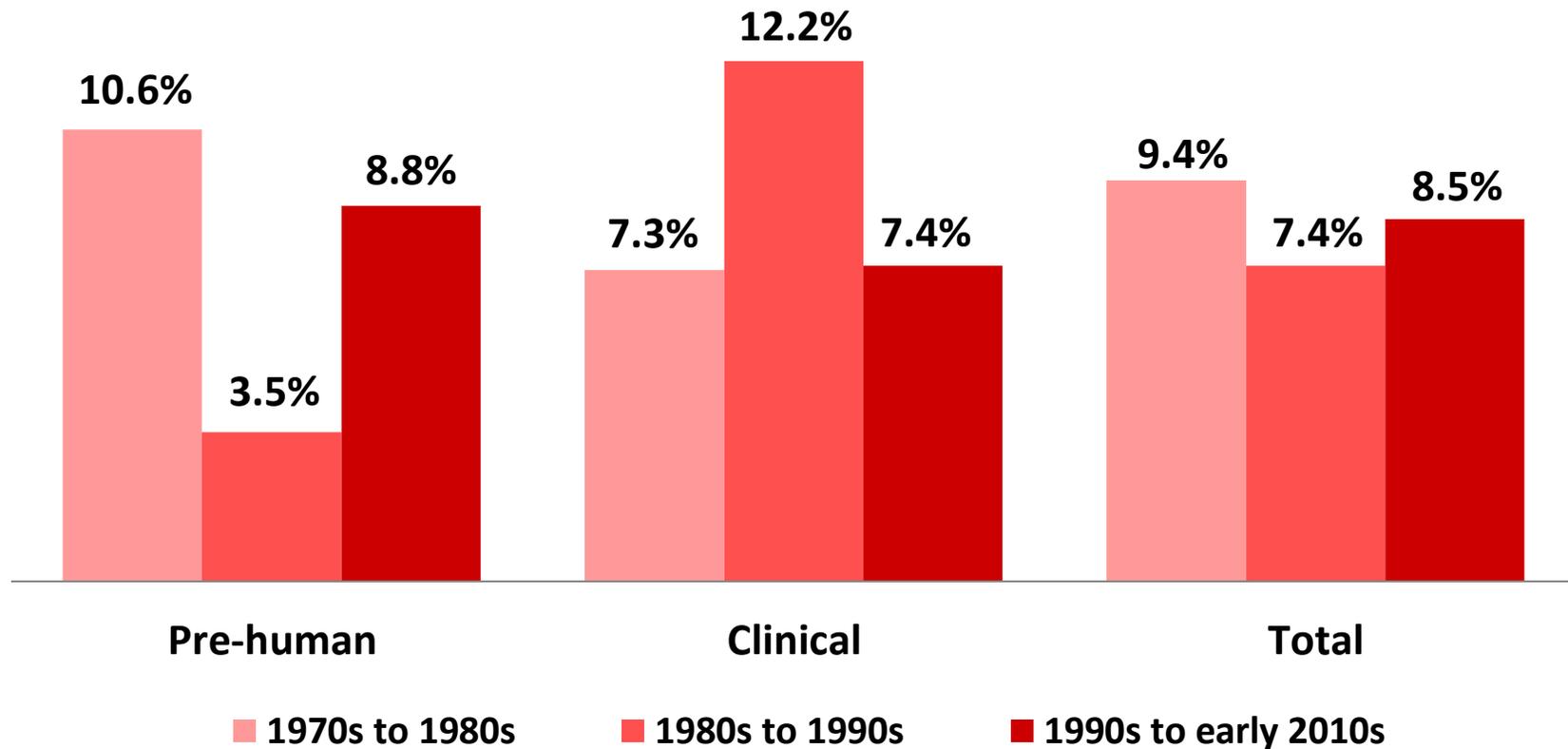


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Compound Annual Inflation-Adjusted Growth Rates for Capitalized R&D Costs



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Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (direct cash outlays)*

Factor Category	Factor	Percentage Change in Cost
<i>Cash Outlays</i>	Out-of-Pocket Clinical Phase Costs	82.5%
	Pre-human/Clinical Cost Ratio	1.6%
	Overall Out-of-Pocket Costs	85.5%

* Factor impact on current study cost relative to prior study cost (\$1,044 million in 2013 dollars)

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Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (development risk)*

Factor Category	Factor	Percentage Change in Cost
<i>Risk</i>	Clinical Approval Success Rate with Prior Study Distribution of Failures	57.3%
	Distribution of Failures with Prior Study Clinical Approval Success Rate	-6.0%
	Overall Risk Profile: Clinical Approval Success Rate plus Distribution of Failures	47.3%

* Factor impact on current study cost relative to prior study cost (\$1,044 million in 2013 dollars)

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Cost Drivers: Change in Capitalized Cost per Approved Compound by Factor (time and cost of capital)*

Factor Category	Factor	Percentage Change in Cost
<i>Time</i>	Pre-human Phase	-4.9%
	Clinical Phase	0.2%
	Regulatory Review	-3.0%
	Overall Development Timeline	-5.6%
<i>Cost of Capital</i>	Discount Rate	-3.1%

* Factor impact on current study cost relative to prior study cost (\$1,044 million in 2013 dollars)

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Summary

- “ **Total capitalized cost per approved new compound grew at an 8.5% compound annual rate; out-of-pocket cost per approved new compound grew at a 9.3% annual rate.**
- “ **Clinical approval success rates have declined significantly.**
- “ **Increases in the cash outlays used to conduct clinical development and higher drug failure rates during clinical testing have contributed most to the estimated increase in R&D costs.**
- “ **Changes in the time to develop and get new drugs approved and in the cost of capital had modest moderating effects on the increase in total R&D cost.**

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