Financing Biomedical Ventures
Myths and Realities

Jeff Behrens

Public Thesis Defense – May 27, 2020 - EPFL

Agenda

- Introduction/Motivation
- Paper 1 – The A2VC Paradigm Fallacy
- Paper 2 – Is Biotech VC Dead?
- Paper 3 – Impact of Corporate VC
- Conclusions

Why/How a PhD at 52???

- MBA/MS in 2007 & Antoinette Schoar
- An “ongoing gnawing interest”
- Opportunity – visits to Lausanne, Chris Tucci
- EPFL & External PhD Program


INVESTMENT PERFORMANCE OF LIFE-SCIENCE VENTURE CAPITAL INVESTMENT FUNDS, PERSISTENCE, AND SUBSECTOR ANALYSIS

Empirical Motivation - Three Stories

- Siamab
- AbBio
- Casma

→ Significant market failures?

Curious Observations → Methodology

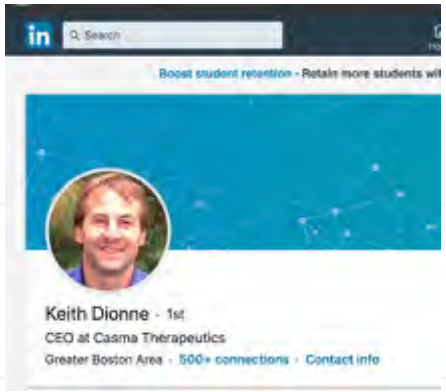
Casma is led by CEO Keith Dionne – a serial entrepreneur with over 20 years of experience in biotechnology including leading three other biotech companies. Leon Murphy, Casma's senior vice president, biology is an expert in the field of autophagy and drug discovery, most recently at Novartis Institutes for BioMedical Research. Frank Gentile, the interim COO, brings nearly 25 years of experience working with biopharma companies, including more than a decade with Tekla Capital Management. Bob Tepper, the interim CSO, is a co-founder of Third Rock Ventures and previous president of R&D at Millennium Pharmaceuticals. Cary Pfeffer, the interim CBO, is a partner at Third Rock Ventures and has assumed leadership roles in multiple portfolio companies, including Rheos Medicines, Neon Therapeutics and Tango Therapeutics.

Experience

CEO
Casma Therapeutics
Apr 2018 – Present · 1 yr 3 mos
38 Sydney St, Cambridge MA

Entrepreneur In Residence
Third Rock Ventures
Jan 2017 – Apr 2018 · 1 yr 4 mos
Greater Boston Area

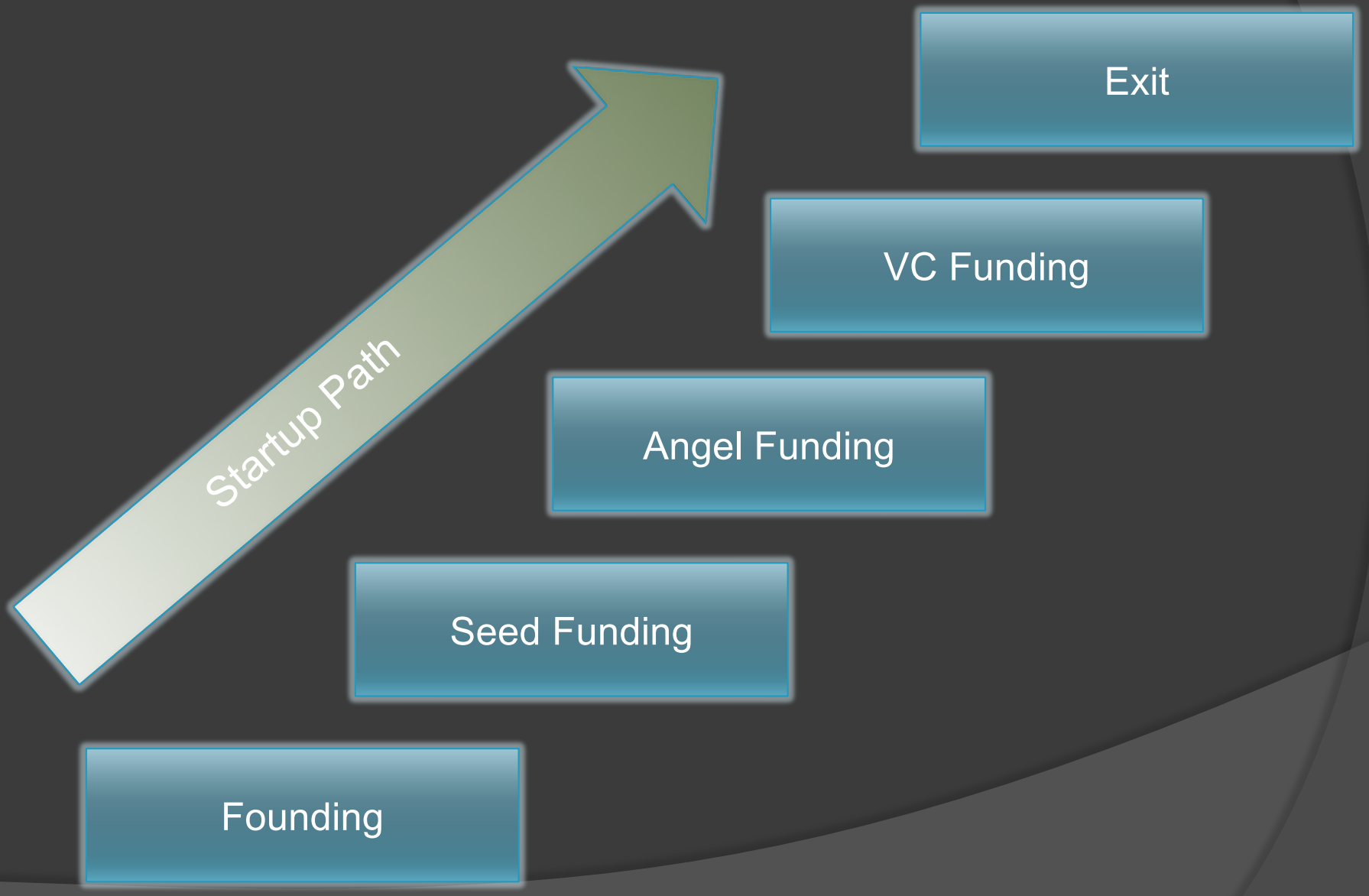
President and CEO
Constellation Pharmaceuticals
2012 – 2016 · 4 yrs
215 First Street, Cambridge, MA 02142
Constellation Pharmaceuticals is the leading biopharmaceutical company dedicated to the development of novel therapeutics in the emerging field of epigenetics.



https://www.casmatx.com/third-rock-ventures-launches-casma-therapeutics-with-58-point-5-million-dollar-investment/
https://www.linkedin.com/in/keithdionne/

The A2VC Paradigm

Underpins Many Startup Business Plans



Research Questions

- How often do startups follow this supposedly traditional path of angel to venture funding?
- Can we better understand these results by exploring various industry patterns that vary dramatically in their capital intensity?
- What can we learn from this novel process of new venture creation that some biotech VCs are now following?
- Are there measurable differences in outcomes associated with differences in various types of venture funding?

Methodology

- Abductive study
  - Observe and document surprising phenomena
  - Potential explanations and implications
  - Avenues for future inquiry
- Papers 1, 3
  - Crunchbase & custom coding
  - Large dataset
  - R code base
- Paper 2
  - Hand-curated dataset
  - Boston-area biotech venture investments
  - 2 time periods – 2007/2008 vs. 2017/2018

Paper #1

The A2VC Paradigm Fallacy

Path Dependency Creates Two Distinct Worlds of Biomedical Financing

Using Crunchbase to Explore Angel to VC

- Hellman studied a small, geo limited dataset (Hellman, Schure, Vo 2019)
- VentureSource and VentureOne – solid for VC, weak for angels (Kaplan, Stromberg 2002)
- Crunchbase incorporates angel rounds
- Large Crunchbase dataset - 9/20/18
- 644k companies
- Focus on US companies funded 2000-2015
- Subset by time, geography, round data = 44k

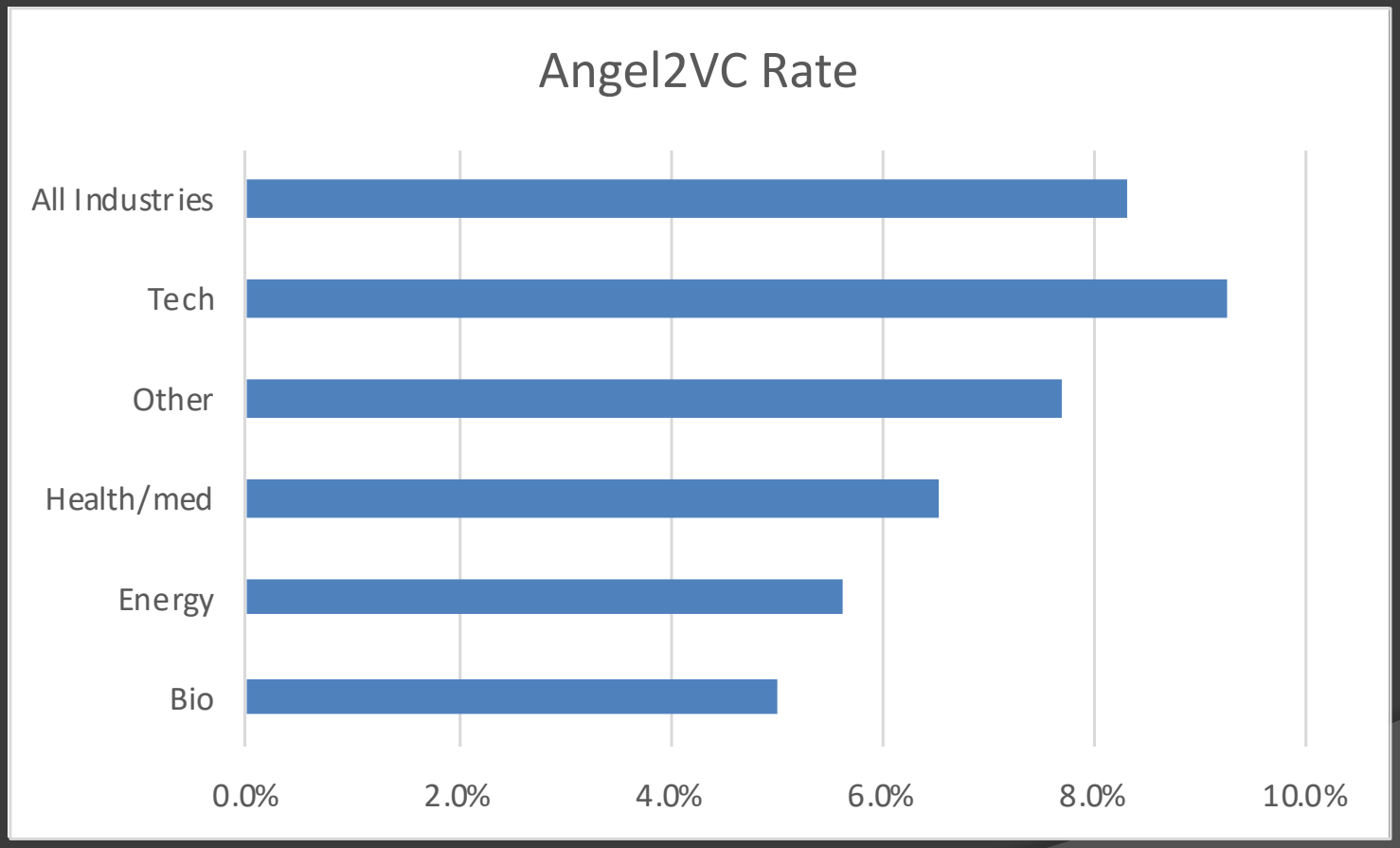
Coding Methodology

- Code each investor – Angel, VC, other
- Code each round – Angel, VC, mixed
- Code each company – round pattern
  - i.e. AAAV, VVV, AAA

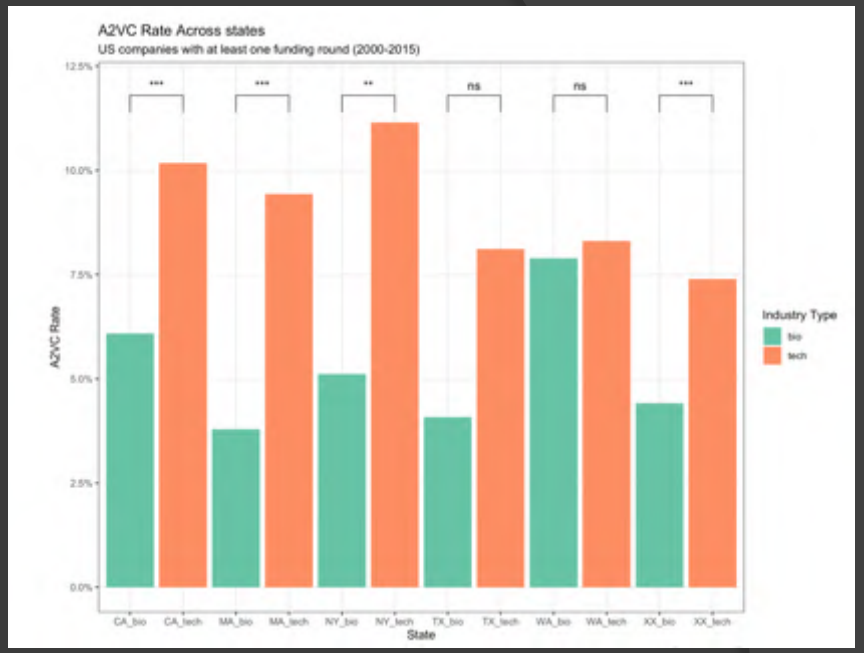
Round Category Trend	N
v	6,980
a	3,965
vv	2,653
vvv	1,492
vvvv	799
uv	775
vu	733
av	665
aa	568
au	448
vvvvv	388
uvv	352
avv	313
ua	306
vvu	274
va	271
uuv	218
vuv	213
vvvvvv	188
uvu	167
uvvv	165
vuu	160
vvvu	145

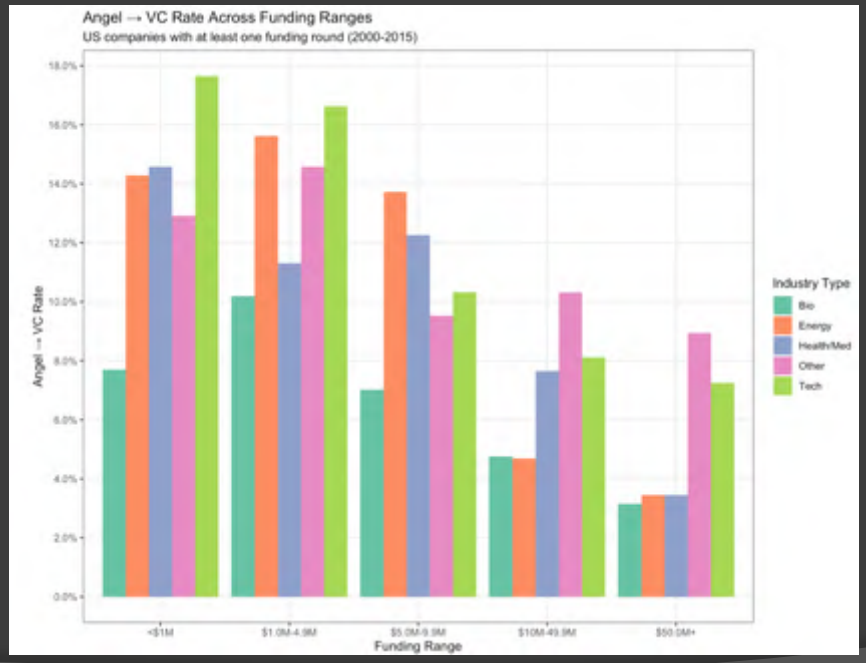
* Pure “u” rounds excluded

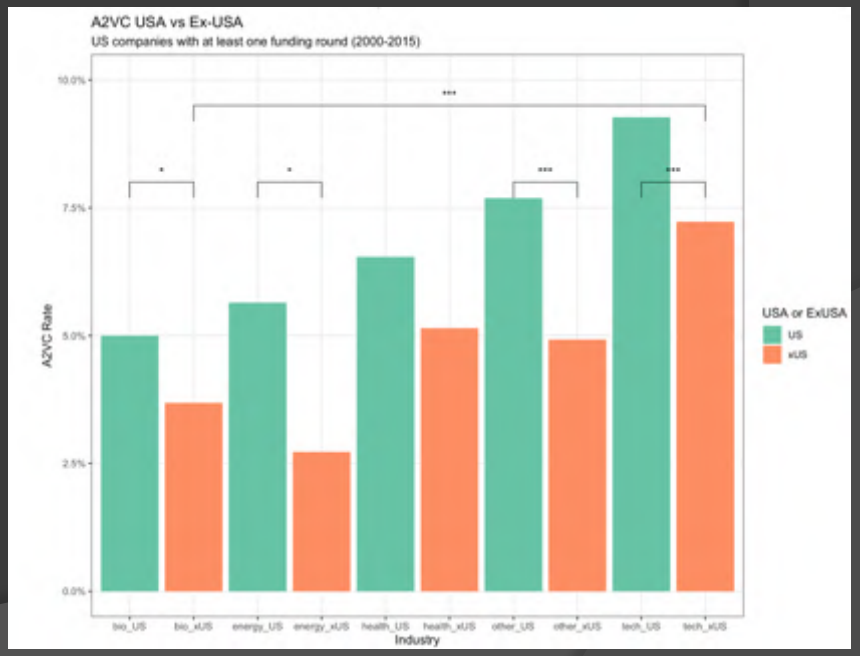
The Angel to VC Transition is Rare
Biotech Significantly Lower than Tech



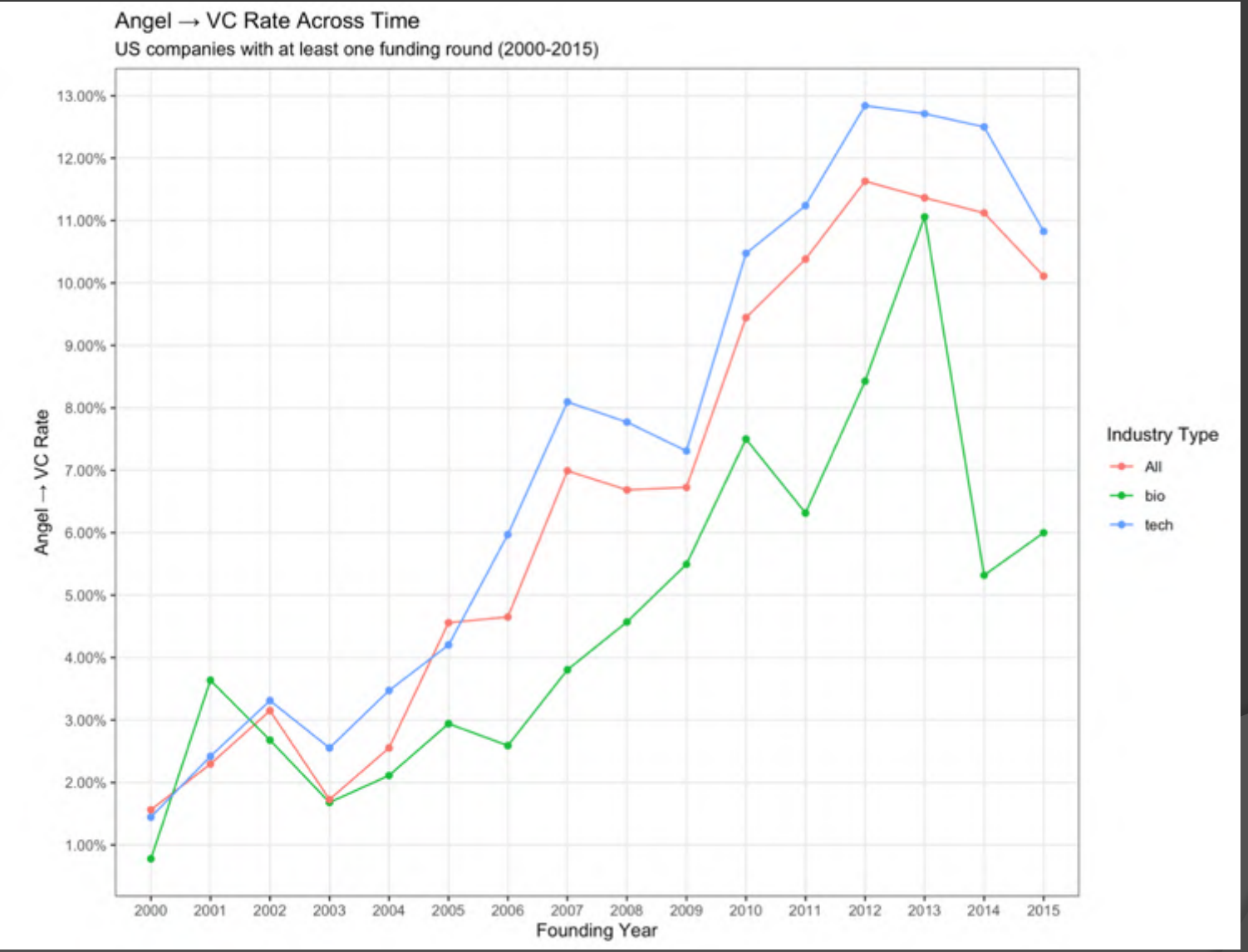
A2VC by Funding Level, Geography, VC Hub States



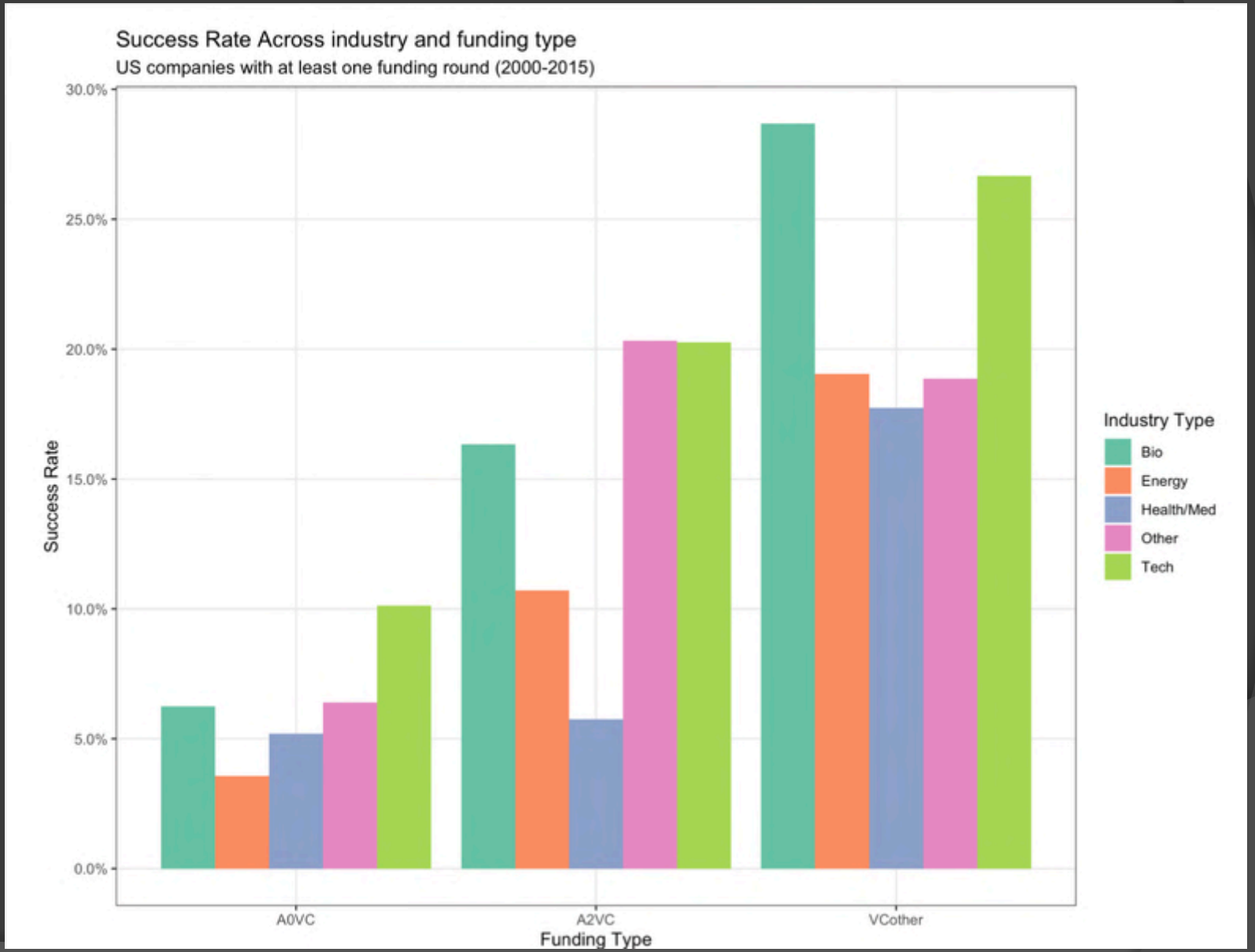




A2VC Rates Increase Over Time



Funding Pattern Impacts Success



Key Empirical Findings

1. A2VC rates are low - 8.3%
2. A2VC rates much lower for biotech firms
3. A2VC rates increase over time
4. MA biotech A2VC << than CA (VC founders?)
5. Angel-funded firms have significantly lower success rates

Potential Explanations - Building Hypotheses

- Selection effects – do VCs pick better? (Gompers & Lerner, 2001; Kaplan & Lerner, 2010)
- Signaling and herding (Scharfstein & Stein, 1990; Connelly et al 2011)
- Network effect/syndication patterns (Sorenson & Stuart, 2001; Fritsch & Schilder, 2006)
- Novel VC behavior?(Kaplan & Lerner, 2010)
- Capital intensivity?
- Is this a market failure?

Paper #2

The A2VC Paradigm Fallacy:
The Curious Case of Massachusetts Biotech VC

Authors
Jeff Behrens
Joshua Krieger

What Does the Literature Say VCs Do?

- ”VCs spend a large amount of time and resources screening and selecting deals” (Kaplan & Lerner, 2010)
- VCs use specific tools (Gompers & Lerner, 2001; Hall & Lerner, 2010)
  - Pre-deal diligence
  - Ongoing monitoring of the deal
  - Tranching investments
  - Syndication
  - BOD seats
  - Compensation arrangements
- “Staged capital infusion is the most potent control mechanism a venture capitalist can employ” (Gompers and Lerner, 2001)
- Novel “founder” model challenges this role/description

The Data: A Deep Dive

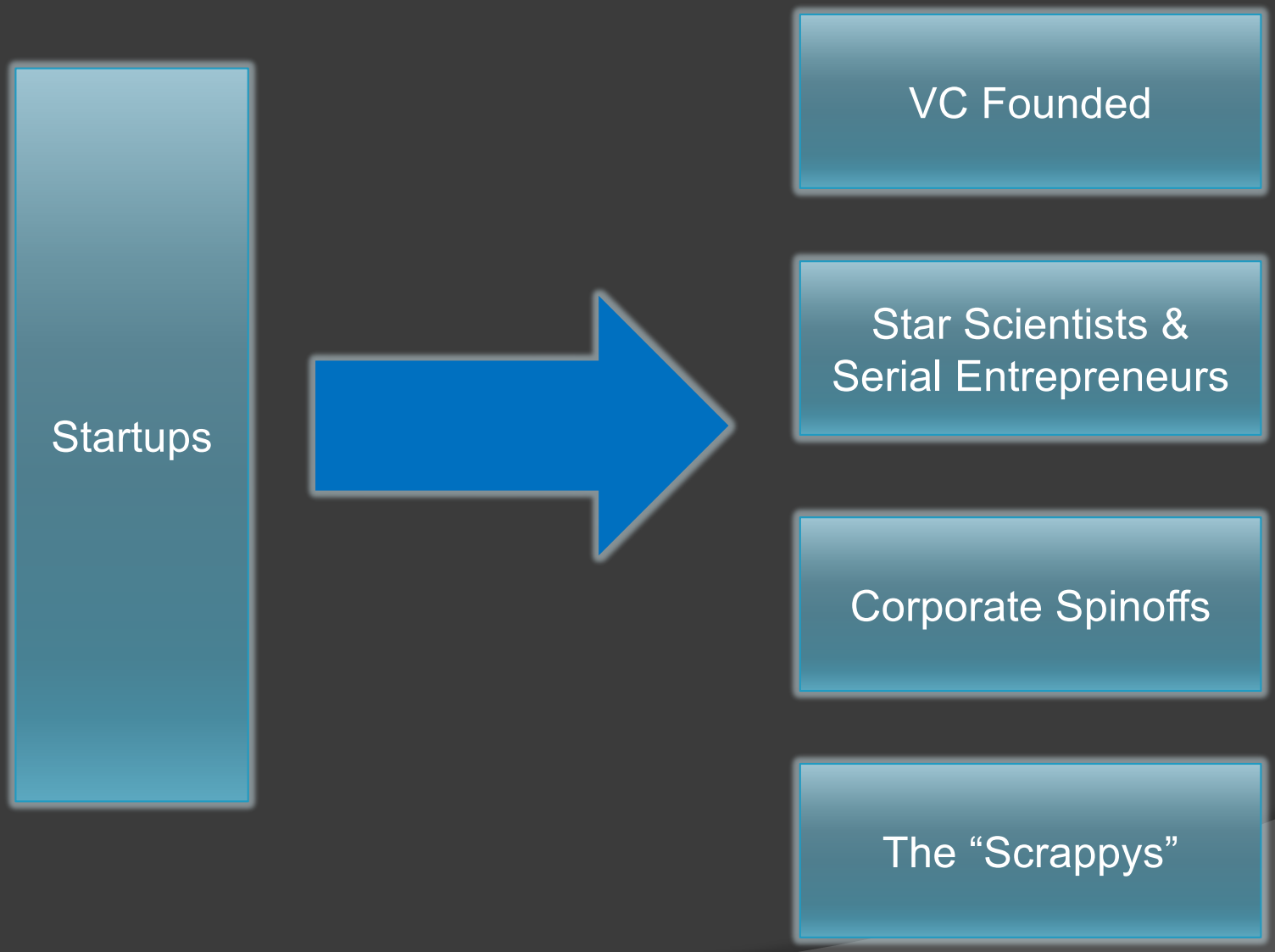
- All Massachusetts biotech VC A-rounds in two time periods
  - 2007-2008 (right before the crash)
  - 2017-2018
- Manually coded for ”VC Founded?”

Leading Mass VCs are Founding Companies – Not Funding Them

VC Firm	# deals 2017-18	# founded
Third Rock Ventures	10	9
Atlas	11	10
Flagship Pioneering	15	13
Polaris	9	6

Are these Firms Investors or Entrepreneurs?

Biotech Founder Taxonomy

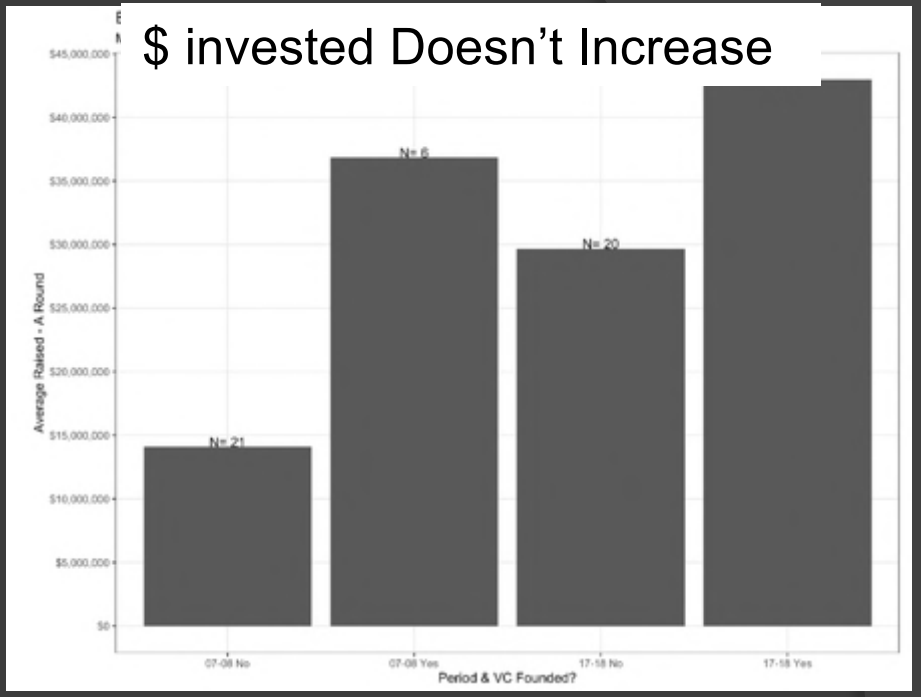


Mass-based Biotechs Funded in 2017-2018

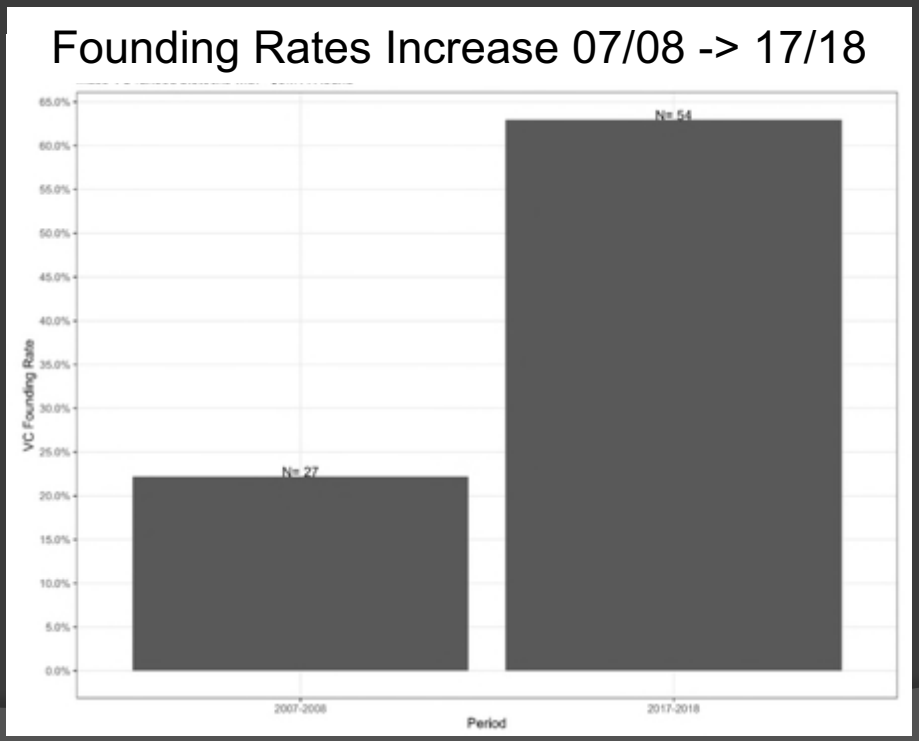
	# companies	% of total companies	Median A round	Total A round raised	% of capital invested
VC founded	35	59.3%	$41m	$ 1,463,662,183	71.4%
Not VC founded	24	41%	$24m	$ 586,740,942	28.6%
Star academic	8	13.6%	$31m	$ 255,100,000	12.4%
Serial entrepreneur	2	3.4%	$54m	$ 109,000,000	5.3%
Spinout	5	8.4%	$31m	$ 155,540,942	7.6%
Scrappy	9	15.3%	$8m	$ 67,100,000	3.3%
	59	**100.0%**		**$ 2,050,403,125**	**100.0%**

Key Findings

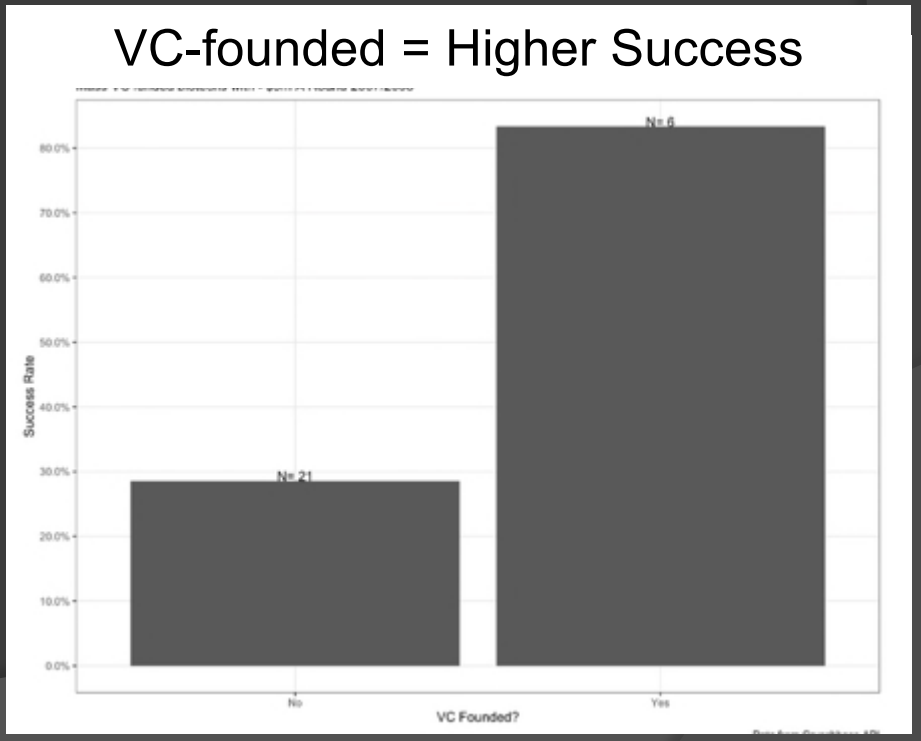
$ invested Doesn't Increase



Founding Rates Increase 07/08 -> 17/18



VC-founded = Higher Success



Questions and Potential Explanations
Building Hypotheses

- Why are Biotech VCs Founding Companies?
  - Enhancing Control & Return? (Gompers et al 2020; Da Rin et all 2013; Chesbrough 2002)
- How is performance compared to traditional selector/funder-VCs?
- Can we see evidence of this phenomena in other industries?
  - VC – outside of biotech?
  - Film/Movies? (Ravid 1999; Goettler & Leslie, 2005; Palia et al 2008; McMahon 2013)
- Is this creating a funding market failure for angel-funded biotechs?

Paper #2: Limitations & Next Steps

- Broaden dataset: Geography, industry, time
- Qualitative case studies/surveys: motivations
- Venture outcomes: How does founding perform?
- Syndication and network effects: Who works with whom?

Paper #3

Is the Impact of Corporate Venture Capital Meaningful for Venture Outcomes?

CVC as a Funding Alternative

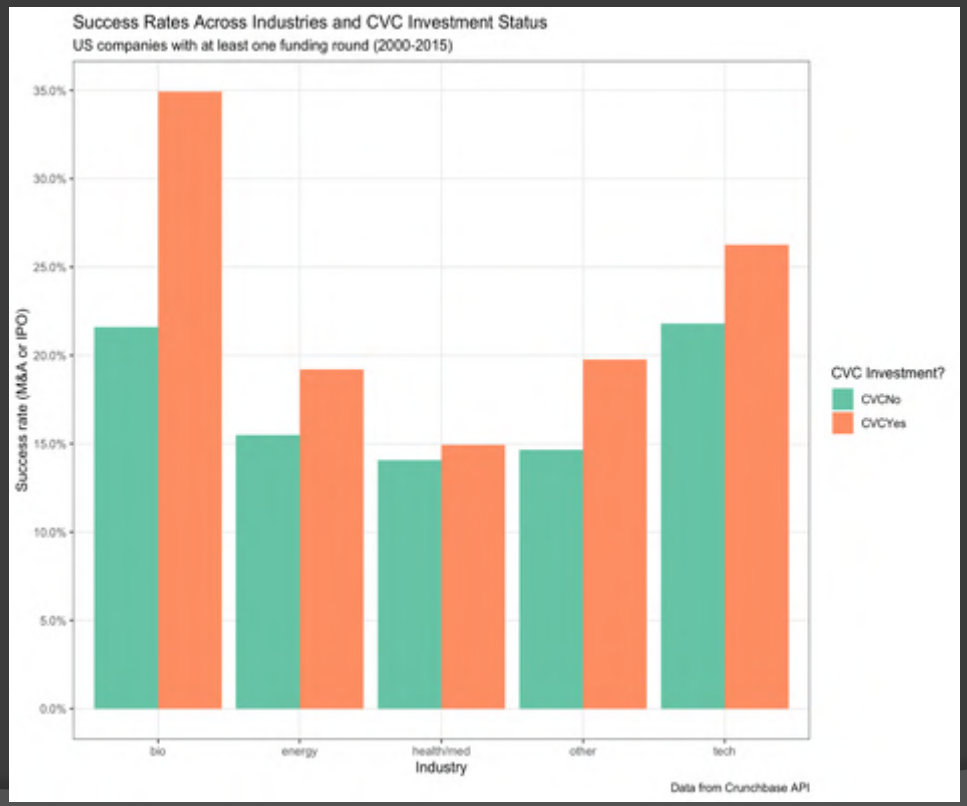
- Is it an (independent) alternative?
  (Dushnitsky 2009)
- Does CVC funding change outcomes?
  (Gompers & Lerner, 2000)
- Does CVC serve its corporate parent as external R&D? (Tucci & Chesbrough, 2005; Chesbrough 2000)

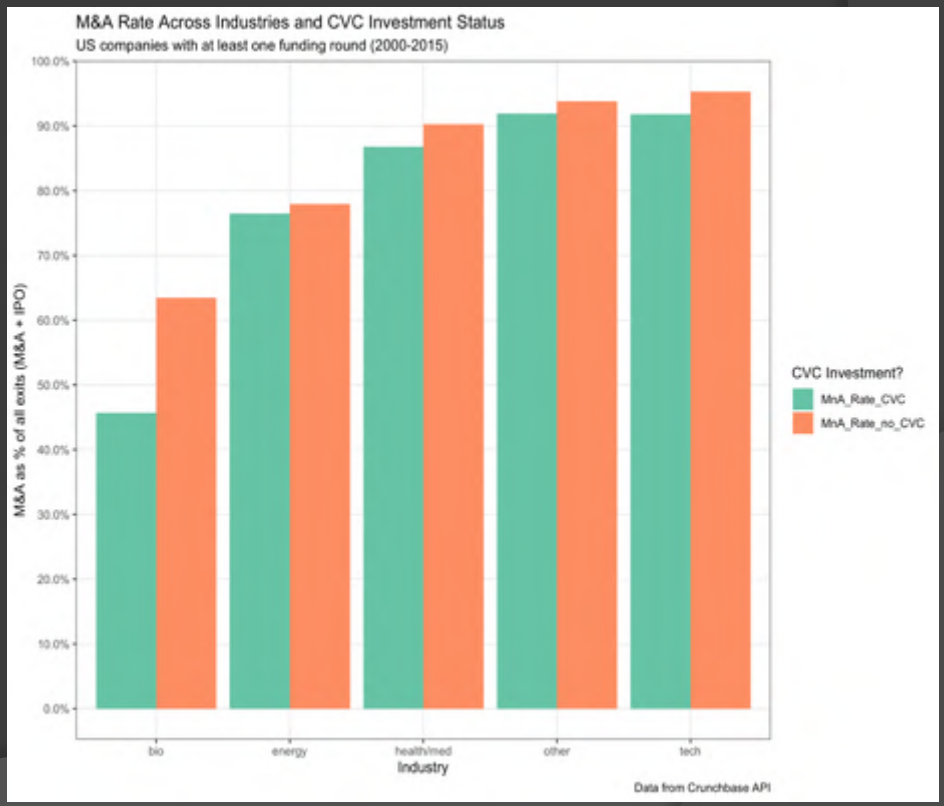
Methods

- Examine 28k US firms w/ Crunchbase dataset
- Crunchbase data
- Recoded VCs: Institutional vs. Corporate
- Examined investment round patterns

CVC Impact – Unexpected Findings

* Impact on Biotech startups only
* No Impact on M&A Rates





Regression Models

MODEL 1 & 2

$$\text{Success} = \beta_0 + \beta_1 \text{Angel\_founded} + \beta_2 \text{VC\_funded} + \beta_3 \text{CVC\_funded} + \beta_4 \text{Total\_funding} + \beta_5 \text{Num\_Rounds} + \beta_6 \text{VC\_Hub} + \beta_7 \text{Industry}$$

Model 1: Success = M&A or IPO

Model 2: Success = M&A

MODEL 3 & 4

$$\text{Success} = \beta_0 + \beta_1 \text{CVC\_late\_early} + \beta_2 \text{Total\_funding} + \beta_3 \text{Num\_Rounds} + \beta_4 \text{VC\_Hub} + \beta_5 \text{Industry}$$

Model 3: Success = M&A or IPO

Model 4: Success = M&A

Regressions: Models 1 & 2

Logit Regression on Success & Aquisition

	Dependent variable:	
	Successful Exit	Acquisition
	(1)	(2)
a_founded	-0.594*** (0.051)	-0.482*** (0.053)
vc_funded	0.825*** (0.062)	0.945*** (0.065)
cvc_funded1	0.015 (0.036)	0.047 (0.038)
funding_total_m_usd	0.0002* (0.0001)	-0.0005** (0.0002)
funding_rounds	0.060*** (0.008)	0.007 (0.009)
vchubvchub_yes	0.245*** (0.036)	0.234*** (0.037)
industry_typeenergy	-0.495*** (0.131)	-0.021 (0.148)
industry_typehealth/med	-0.541*** (0.089)	0.050 (0.099)
industry_typeother	-0.393*** (0.062)	0.228*** (0.071)
industry_typetech	-0.026 (0.051)	0.614*** (0.061)
Constant	-2.036*** (0.079)	-2.708*** (0.088)
Observations	23,810	23,810
Log Likelihood	-12,156.480	-11,424.840
Akaike Inf. Crit.	24,334.960	22,871.680
Note:	*p<0.1; **p<0.05; ***p<0.01	

Regressions: Models 3 & 4

Logit Regression on Syccess & Aquisition

	Dependent variable:	
	Successful Exit	Acquisition
	(1)	(2)
cvc_late_earlycvc_late	0.017 (0.065)	0.035 (0.069)
funding_total_m_usd	0.0001 (0.0001)	-0.0004 (0.0003)
funding_rounds	0.025* (0.014)	-0.042** (0.017)
vchubyes	0.212*** (0.080)	0.124 (0.084)
industry_typeenergy	-0.833*** (0.252)	0.035 (0.282)
industry_typehealth/med	-0.952*** (0.202)	-0.003 (0.219)
industry_typeother	-0.684*** (0.124)	0.274* (0.144)
industry_typetech	-0.398*** (0.095)	0.521*** (0.118)
Constant	-0.756*** (0.128).	-1.417*** (0.151)
Observations	4,649	4,649
Log Likelihood	-2,785.370	-2,566.543
Akaike Inf. Crit.	5,588.740	5,151.085
Note:	*p<0.1; **p<0.05; ***p<0.01	

Conclusions – Paper #3

- CVC+/- does not impact exit rates except for biotechs
- CVC-funded firms do not have increased M&A
- Early “treatment” by CVC -> no impact

- CVC – a true, independent financing actor?

Practical Implications

- Multiple funding paths
  - VC-founding
  - Scrappyland
- For angels
  - Beware the “data now, VC later” story
  - Path to exit cannot rely on large equity later
- For new founders (i.e. postdocs)
  - Test ideas with VC/pharma early
  - Map a credible path independent of VC

A Proposed Explanatory Framework

	Low CapX	High CapX
Short time to revenue	"Spray and pray" Software/iphone apps TRADITIONAL VCs ANGELS	Movies, manufacturing facilities
Long time to revenue	Lifestyle businesses, small scale ag, real estate ANGELS	Biotech, cleantech FOUNDER VCs

Syndication ----------? +++++++++?

Theoretical Frameworks

- Moral hazard: Avoidance of angel-funded companies/"first-in problem" & Information asymmetries

  (Goldfarb et al 2013; Elizur & Gavious, 2003; Aktekin et al, 2010)

- Selection theory
  - Are VCs "cherry picking" best deals and leaving weaker deals for angels? (Knockaert et al, 2010; Brander et al, 2002; Ding et al 2014)

- Signaling theory
  - The critical importance of first institutional investor as a quality signal
  - Future question: Does CVC provide such a signal?

  (Elizur & Gavious, 2003; Connelly et al, 2011; Conti et al, 2013)

Theoretical Implications & Future Studies

- VCs avoid angel-funded firms → How to explain market failure?
  - Investor herding behavior (signaling?) (Grinblatt et al 1995; Scharfstein & Stein, 1990)
  - Relationship to increased risk (Biotech) (Schwienbacher 2009; Van Osnabrugge 2000)
- Network analysis – syndication patterns
  - Angels and VC? (Schwienbacher 2009; Drover et al 2017)
  - CVC and IVC? (Borgatti et al, 2002; Bygrave 1987)
- Future directions
  - Temporal effect – sustained/leveling off?
  - Industry/capital intensity effects

Policy Implications

- VC pitches → low value
- Incubators, accelerators, competitions?
- “Dangerous affirmations” - A road to nowhere?
- Focus entrepreneurs on realistic paths - independent of VC

“We never take pitches”

- Dave Berry, Partner Flagship Pioneering

FierceBiotech

RESEARCH CRO MEDTECH BIOTECH

Biotech

Flagship Pioneering adds a new $824M biotech growth fund

by Amirah Al Idrus | Mar 20, 2019 11:12am

VC firm Flagship Pioneering raises $1.1b for biotech startups, despite reeling economy

The Cambridge firm’s CEO says the coronavirus crisis means such investments are more critical than ever

By Jonathan Saltzman Globe Staff, Updated April 2, 2020, 12:00 a.m.

https://www.fiercebiotech.com/biotech/flagship-pioneering-adds-a-new-824m-biotech-growth-fund
https://www.bostonglobe.com/2020/04/02/business/vc-firm-flagship-pioneering-raises-11b-biotech-startups-despite-reeling-economy/

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Questions / discussion

THANK YOU!