

A Last Gift

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Audience Ponder

- Would you consider participating in a research study that would potentially help others but not yourself if you thought you had less than 6 months to live because of a terminal illness?
- Would you participate if it might decrease your lifespan further, and if so, by how long?
- What physical discomforts would you ever consider enduring for participation?
- Would you participate if it exposed you to an infectious agent that might cause you to become infected with this agent?

HIV Reservoirs

- Main barrier for HIV eradication
- Established during primary HIV infection
 - In peripheral blood cells
 - In all tissues and compartments
- Only one person has been cured from HIV so far



Timothy Ray Brown (The Berlin Patient)

HIV Cure Research Approaches

- In vitro models
- Animal models
 - Mice, Rabbits, Macaques are not humans.
- Clinical Research with otherwise healthy HIV-infected volunteers
 - On peripheral blood or limited sampling in accessible compartments (e.g. shallow LN, small gut biopsies, CSF, genital secretion).
 - Risks
- **All current methods have limitations**
- **Many questions remain open...**

Some Open Questions

- What impacts the size, distribution and activity of HIV reservoirs throughout the body?
- How do accessible HIV reservoirs (blood) relate to deeper HIV reservoirs (tissues)?
- How cellular subsets and tissue reservoirs (other than blood) are repopulated during viral rebound?
- How to analyze diverse data types to best characterize HIV persistence and rebound throughout the body?

Our Proposed Solution

- Altruistic HIV-infected individuals who have a terminal illness, usually from a non-AIDS related condition.
 - Solid organ cancer, cardiovascular disease, etc.
- Interested in participating to HIV Cure Research.
 - No benefits for themselves.
 - Advance HIV cure research and help others.

“Last Gift Cohort”

- HIV-infected people who are diagnosed with a terminal illness (<6 months to live) and who wish contribute to end-of-life HIV cure research will provide.
- **STEP 1 (Observational)**
 - Detailed reports on social and clinical factors until time of death.
 - Access to previously collected biological samples.
 - Limited blood collections while they are alive.
 - Their entire bodies after they die (rapid autopsy).
- **STEP 2 (Intervention)**
 - Test early stage Interventions (for safety, penetration in tissues)
 - For example, immune-modulatory drugs, neutralizing antibodies

Rapid Autopsy

- Within 6 hours from death
- Goal: preserve RNA quality and proteins
- Extensively used in cancer research



Rapid Autopsy

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The Legacy Gift Rapid Autopsy program arranges and performs autopsies on an urgent basis to collect tumor and other tissues for researchers in many different areas. Specimens collected at autopsy have been used to grow living cell lines which can be used to evaluate for genetic mutations and test new chemotherapies. Samples can also undergo genetic sequencing and RNA expression analysis, as well as immunohistochemical and proteomic studies.

Why RapidAutopsy



“There’s horrible poetry to the idea that your tumor lives longer than you do, but that’s what happens.” (Dr. Jody Hooper, John Hopkins University)

HAS THIS BEEN DONE BEFORE?

Our Hypothesis

“PEOPLE ARE NATURALLY ALTRUISTIC AND WOULD WELCOME THE OPPORTUNITY TO PARTICIPATE IN SCIENTIFIC RESEARCH AT THE END OF LIFE EVEN IF IT PROVIDED NO BENEFIT TO THEMSELVES”.

Willingness to participate in End-of life Research

2 surveys were administered

HIV NEGATIVES

- 377 Individuals
- Recruited online via “Amazon’s Mechanical Turk”

HIV POSITIVES

- 97 Individuals
- Recruited in person at UCSD Owen’s Clinic

Study Participants

		HIV Negative n (%)	HIV Positive n (%)	p values
Gender	Female	192 (50.9)	6 (6.3)	<0.01**
	Male	182 (48.3)	84 (88.4)	<0.01**
	Transgender	3 (0.8)	4 (4.2)	0.03**
	Genderqueer	0 (0.0)	1 (1.1)	0.20
Race/Ethnicity	Caucasian	271 (77.0)	38 (39.6)	<0.01**
	Asian	31 (8.8)	1 (1.0)	<0.01**
	Hispanic	23 (6.5)	27 (28.1)	<0.01**
	African American	16 (4.5)	18 (18.8)	<0.01**
	Other	11 (3.2)	12 (12.5)	<0.01**
Age	18-24	61 (16.2)	1 (1.0)	<0.01**
	25-44	217 (57.6)	30 (31.3)	<0.01**
	45-64	85 (22.5)	54 (56.3)	<0.01**
	Over 65	14 (3.7)	11 (11.6)	0.01**
Education	Less Than HS	2 (0.6)	3 (3.2)	0.07
	HS/GED	38 (10.8)	21 (22.1)	<0.01**
	College	230 (65.2)	65 (68.4)	0.62
	Advanced Degree	83 (23.5)	6 (6.3)	<0.01**
Annual Income	\$0 - \$25,000	106 (30.0)	67 (70.5)	<0.01**
	\$25,001 - \$50,000	105 (29.7)	18 (18.9)	0.04**
	\$50,001 - \$75,000	75 (21.2)	5 (5.3)	<0.01**
	\$75,001 - \$100,000	25 (7.1)	3 (3.2)	0.23
	>100,001	42 (11.9)	2 (2.1)	<0.01**

Overview.

HIV-infected group:

- More male
- Racially mixed
- Older
- Less wealthy
- Less educated

Study Participants

		HIV Negative n (%)	HIV Positive n (%)	p values
Partner Status	Single	150 (42.3)	55 (57.3)	0.01**
	Married w/o children	44 (12.4)	12 (12.5)	1.00
	Married with children	84 (23.7)	3 (3.1)	<0.01**
	Divorced	18 (5.1)	8 (8.3)	0.22
	Separated	6 (1.7)	1 (1.0)	1.00
	Widowed	3 (0.8)	3 (3.1)	0.11
Religion	Living w/partner	50 (14.1)	14 (14.6)	0.87
	Not religious	209 (55.4)	45 (47.9)	0.20
	Catholicism	39 (10.3)	28 (29.8)	<0.01**
	Protestant	50 (13.3)	7 (7.4)	0.16
Children	Other	79 (21.0)	14 (14.9)	0.25
	No Child	228 (65.5)	74 (77.1)	0.04**
	1 Child	41 (11.8)	4 (4.2)	0.03**
	2 Children	40 (11.5)	10 (10.4)	0.86
	>/= 3 Children	39 (11.2)	8 (8.3)	0.57

Overview.

HIV-infected group:

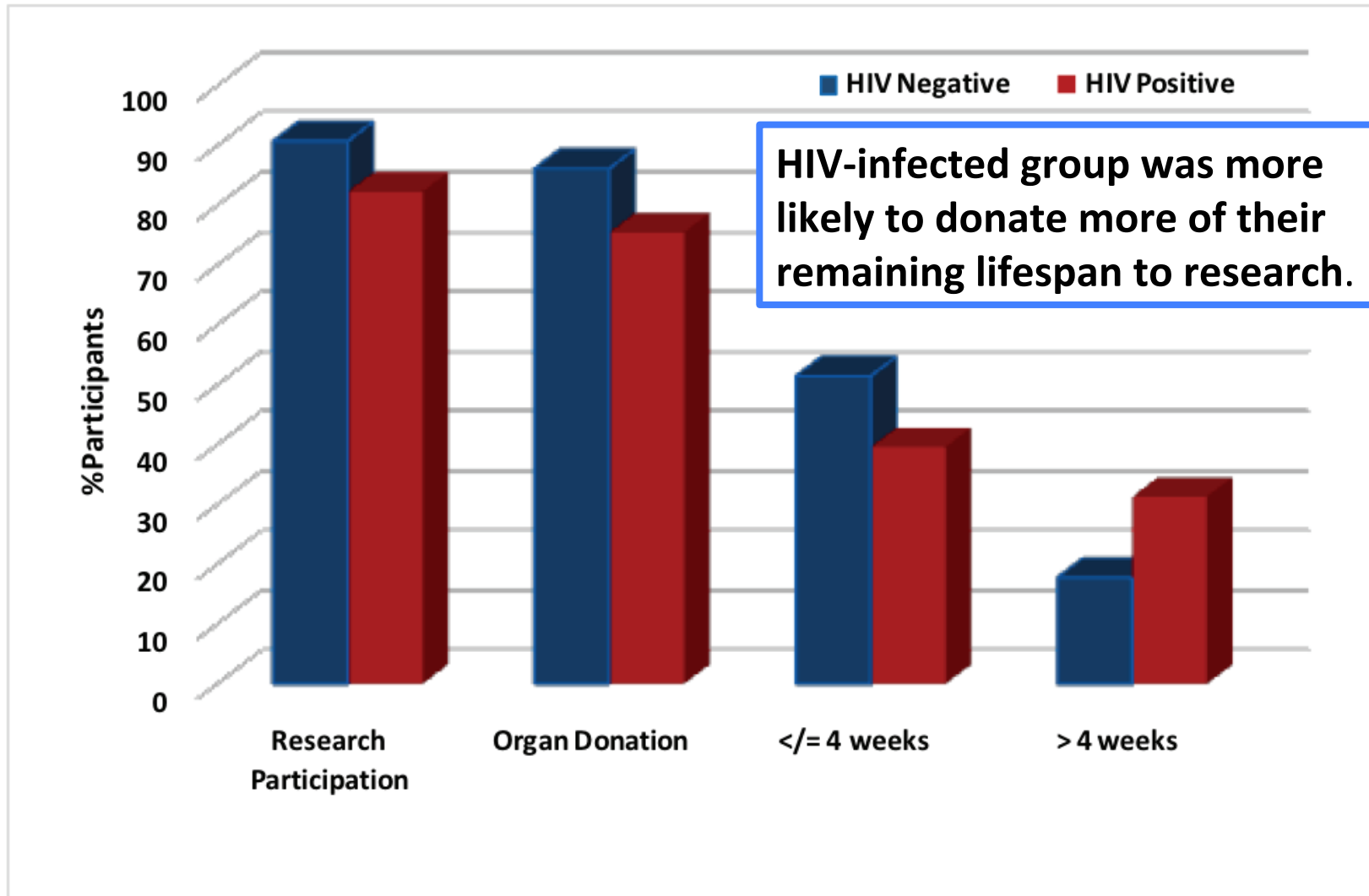
- More Catholics
- Less married
- Less with children

Survey Questions

Would you “consider participating in a research study that would **potentially help others** but not yourself if you thought you had **less than 6 months to live** because of a terminal illness?”

Would you participate if it“...might **decrease your lifespan** further, and if so, **by how long?**”

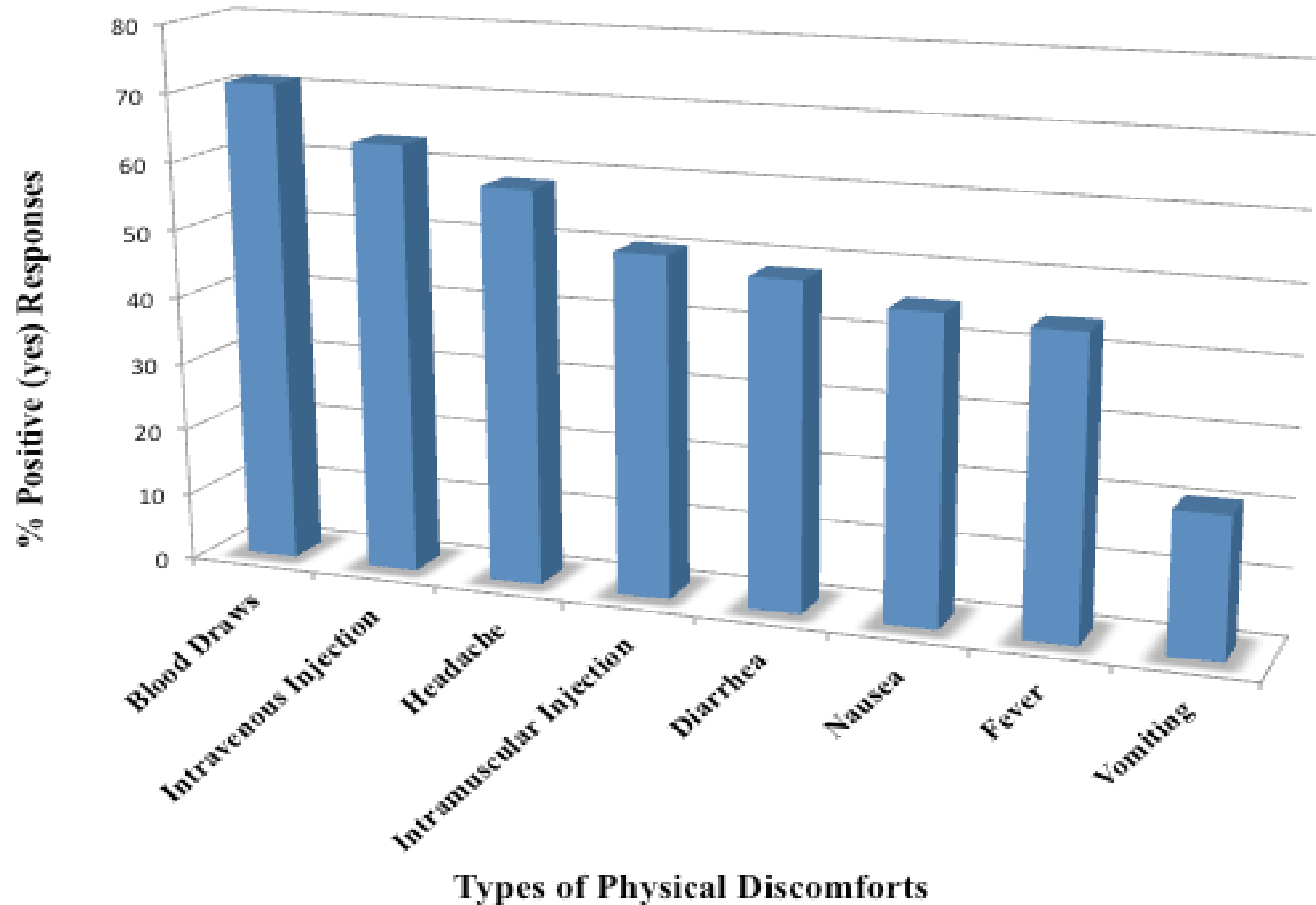
Willingness To Engage In End of Life Research



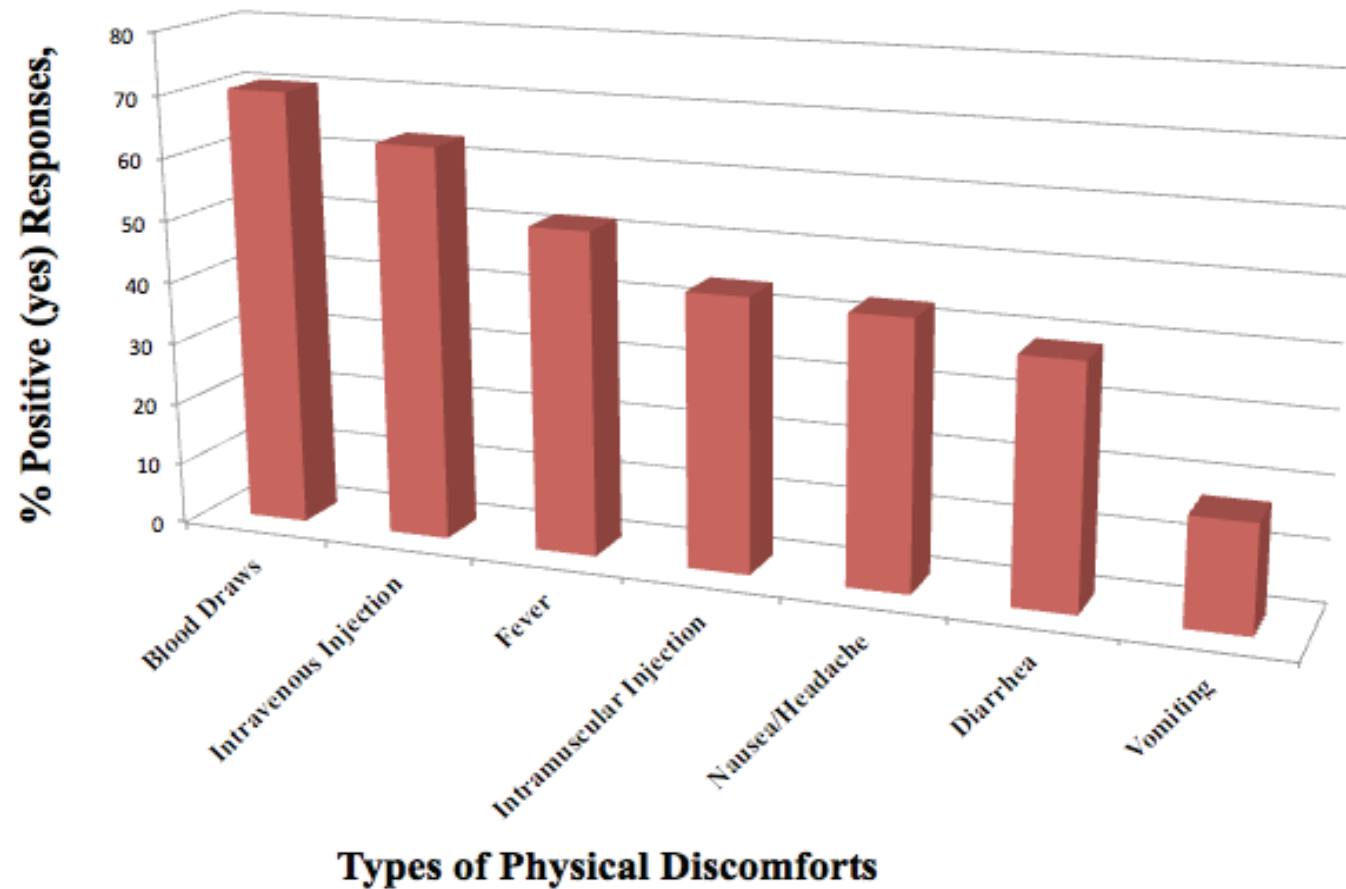
Survey Questions

“...Which of these physical discomforts would you ever consider enduring?”

Willingness To Endure Physical Discomforts (HIV Negative Group)



Willingness To Endure Physical Discomforts (HIV Positive Group)

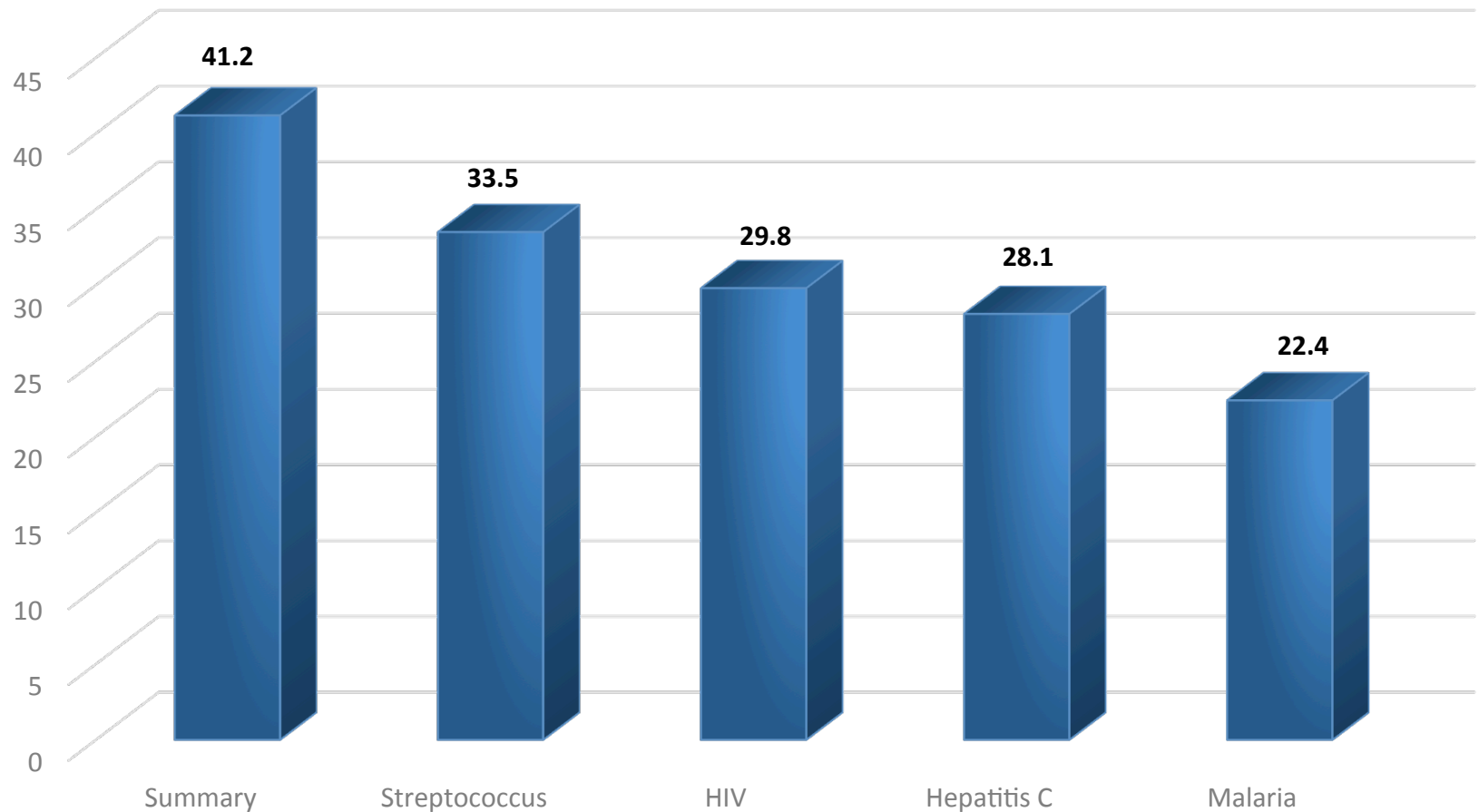


Both groups are willing to endure a wide variety of discomforts for research.

Survey Questions

Would you participate if it “...exposed you to an infectious agent...that might cause you to become infected with this agent...”

Willingness To Be Exposed To Infectious Pathogens (HIV negative only)



Potential End of Life Participants

- 12 HIV-infected people with terminal illness
- Semi-quantitative interview by Dr. Smith
 - Willingness to participate to HIV cure research
- All 12 participants expressed strong interest

Important Quotes

- *“I feel like these last few weeks are wasted.”*
- *“I hate my cancer but I hate HIV more.”*
- *“I wish I could do something else to help.”*
- *“At least I could be doing something.”*
- *“I don’t like the idea to be excluded from research just because I am dying.”*



CONCLUSION

- Animal Models are powerful but have limitations.
- More human studies are needed for scientific advancements in HIV cure.
- The majority of non terminally sick HIV-uninfected and -infected individuals would be willing to participate in research at the end of life.
- HIV-infected would be more likely to donate more of their lifespan than HIV-uninfected individuals.
- Terminally sick HIV-infected individuals would be willing to participate in research at the end of life.

Points for Discussion

Would you participate in end of life research?

Do you think the community is ready for end of life research?

What are the main ethical concerns in end of life research?

THANK YOU

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Annah Lee

Persist, Resist

History of Human Experimentation



Jesse Lazear (1866-1900)



Daniel Carrion Garcia (1857-1885)



Barry Marshall (1951-)

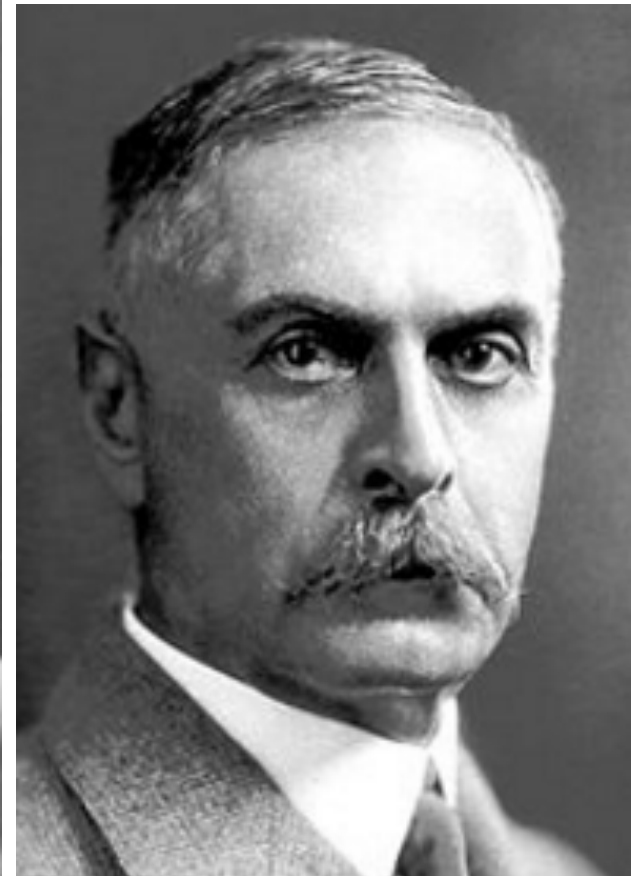
History of Human Experimentation



Nicholas Senn (1844-1908)



Werner Forssman (1904-1979)



Karl Landsteiner (1868-1943)