Bone Marrow Mismatch: How compensating bone marrow donors can end the transplant shortage and save lives
By Samuel Hammond

EXECUTIVE SUMMARY

The most common goal of bone marrow donation is to harvest hematopoietic (blood-forming) stem cells (HSC) for transplant in patients with life-threatening diseases like leukemia and anemia. For decades, the main method of HSC extraction was aspiration: a painful procedure wherein a needle is inserted directly into the donor’s bone, extracting the soft, spongy tissue from its source. Today, over 70% of HSC donations are instead extracted indirectly from the bloodstream through a safe, non-invasive technique known as apheresis, after which the cells quickly regenerate.

Nearly 2% of the U.S. population is a registered bone marrow donor. However, research has found a 65% gap in the demand and supply of HSC transplants despite donation becoming medically easier. And while the volunteer donor registry has grown in recent years, it remains beset by low follow-through rates. Using the best available data, this paper estimates that the gap between the actual and optimal size of the bone marrow registry leads to 1318 fewer transplants and 275 deaths per year. This impact is felt disproportionately by racial minorities, for whom finding a close genetic match is most difficult. This report argues that legalizing compensation for HSC donors would help to close that gap by increasing registry size among target populations while improving follow-through rates of those who are called upon to donate.

In 2011, a federal court ruled compensating donors of HSC by apheresis to be legal due to the procedure’s comparability to plasma and whole blood donation. Nonetheless, the Health Resources and Services Administration (HRSA) has proposed a rule change to redefine HSCs as an organ regardless of the source of extraction, making compensation to all HSC donors
illegal under the National Organ Transplant Act. HRSA has until December 18th to move forward on its rule.

HRSA is concerned that legal compensation could cause exploitation, devalue the human body, and/or reduce the altruistic motivation of donors. In a September 7, 2016, open letter to HRSA, twenty-two of the country’s most prominent ethicists argued that each of these objections are fundamentally flawed. In that time the list of signatories has grown to thirty-seven.

This report goes deeper into disputing HRSA’s weak ethical objections, and outlines the strong positive case for compensation. The Niskanen Center thus joins the signatories of the letter found at DonationEthics.com in demanding that this rule not be enacted. At stake are thousands of leukemia and anemia patients that face preventable death due to a self-inflicted shortage of bone marrow donor matches.

BACKGROUND

In 1984 the National Organ Transplant Act (NOTA) made it a felony to compensate organ donors through any form of “valuable consideration,” including payments and other indirect incentives. Yet donors in the United States are routinely compensated for blood and plasma because these are not regarded as organs.

But what counts as an organ is not always so simple. Our blood stream contains peripheral stem cells, the same hematopoietic stem cells (HSC) that are contained in bone marrow, and which are used as transplants to treat cancers and a variety of blood and immune disorders. Should these cells be treated as an organ like bone marrow, or should the law allow for peripheral blood stem cell compensation as it does for blood?

The 2011 landmark decision in Flynn v. Holder before the Ninth Circuit Court of Appeals established that compensation for peripheral blood stem cells was not contrary to the NOTA because to interpret the law otherwise would require prohibiting compensation for whole blood donations, as well. Plaintiffs included parents of children sick with leukemia and a rare type of anemia that can be fatal without bone marrow transplants, as well as a physician who testified that one in five of his patients dies because no matching bone marrow donor can be found. They argued that compensating blood stem cell donors would stand to increase overall supply as well as donor diversity—an important factor for increasing matches within minority populations.

NOTA was originally passed in 1984 in response to fears of an emerging commercial market in kidneys. It established a national protocol for voluntary organ donation that included bone marrow as an organ. At the time, the most common method of bone marrow extraction was

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1 The list of signatories, and their affiliations (although they make clear that they are not speaking on
3 Throughout this paper reference to HSC transplantation are specifically referring to *allogeneic*
   hematopoietic cell transplantation wherein HSCs are from a donor. When the HSCs are the patient’s own
   it is known as an *autologous* hematopoietic cell transplantation.
4 Flynn v. Holder, 684 F. 3d 852 - (9th Cir. 2012)
5 (Cohen and Glenn Cohen 2012)
aspiration. This involves extracting liquid marrow directly from the bone using a long needle, from which HSCs are harvested. Today, aspiration has largely been replaced with a non-invasive procedure called peripheral blood stem cell (PBSC) apheresis. A limited number of HSCs are also harvested from umbilical cord blood (Figure 1).

**Figure 1:** The majority of HSC transplants use peripheral blood stem cells

Apheresis machines are used for separating out a particular constituent of the blood using centrifugal forces. Plasma donation is also done using an apheresis machine through a procedure known as plasmapheresis. In the case of PBSC apheresis, donors take drugs that mobilize HSCs in the bloodstream several days in advance. Blood is then circulated through an apheresis machine to separate out the desired PBSCs before returning the blood to the patient. Apheresis has been employed for more than two decades, and is widely considered safe. Indeed, while unique complications exist, according to Mayo Clinic research the “frequency of reactions to apheresis donation is less than that seen in whole blood donation.”

The court’s opinion in Flynn v. Holder was based solely on a statutory analysis of NOTA, which permits compensation for blood. The court rejected the government’s argument that HSCs in

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6 (“Blood-Forming Stem Cell Transplants” 2016)
8 (Winters 2016)
the bloodstream represent a “subpart” of the bone marrow, pointing out that regular blood cells also originate within bone marrow, but are nonetheless considered a subpart of the blood. Thus the court argued that once HSCs are in the blood they too become a subpart of the blood.

This interpretation made good sense, especially given Congress’s intent. Nonetheless, the regulator that oversees blood stem cell transplantation, the Health Resources and Services Administration (HRSA) within the Department of Health and Human Services (HHS), disagreed with the court’s opinion, and in 2013 proposed a rule to change the definition of bone marrow to include “other hematopoietic stem/progenitor cells without regard to the method of their collection.” Following an outpouring of public comments opposing the rule change the proposal appeared to stop moving forward, until 2015 when Congress directed HRSA to issue a final rule within one year. The December 18th 2016 deadline is quickly approaching, and recent private communication has confirmed their intent to meet the deadline.

If HRSA goes forward with the rule it will represent a clear case of regulatory overreach, with the agency going contrary to NOTA’s statutory intent. As such, it will likely face a legal challenge. More importantly, the regulation will cause needless death and suffering while denying patients and donors their fundamental liberty.

THE STRONG CASE FOR COMPENSATION

According to MixedMarrow.com, every year 30,000 people in the U.S. are diagnosed with a life threatening blood diseases like leukemia, of whom only 30% find a match within their family. For the remaining 70% who must find an unrelated donor, finding a match is a matter of life and death. Currently matches are facilitated through a national bone marrow donor registry called BeTheMatch. The registry has taken strides in recent years to expand donor registration and diversity, however less than 2% of the United States is on the registry, and a significant number are either unable or unwilling to fulfill their donation when contacted. This creates a substantial gap between supply and demand.

According to one estimate, in 2012 the unmet demand for HSC transplants across the United States was 10,276 adults, out of a total demand of 16,096 for the same population. In children the unmet need was 3,213 out of a total demand of 4,561. Together, that implies an overall shortfall in demand of 65%. The demand for HSC transplants has accelerated as the population has aged, with adults ages 51 to 64 receiving 32 percent of all transplants (Figure 2). This suggests the demand shortfall will only widen if no further action is taken.

The volunteer system is clearly falling short—far shorter than can be made up through awareness campaigns alone. In contrast, legalized compensation would allow clinics to set and advertise a “market clearing rate” that would close the supply gap by both growing the national registry and increasing the follow-through rate once a match is identified. Internal market research by the healthcare company Hemeos indicates a payment of $2000 is sufficient to

9 Change to the Definition of “Human Organ” Under Section 301 of the National Organ Transplant Act of 1984, 78 Fed Reg 60810 (proposed February 10, 2013) (to be codified at 42 C.F.R. 121)
10 Stem Cell Therapeutic and Research Reauthorization Act of 2015 § 4
11 See: http://mixedmarrow.org/statistics-and-information
12 See Table 2: (Gragert et al. 2014)
13 (Besse et al. 2015)
increase the follow-through rate of pledged donors to 90%.\textsuperscript{14} Among volunteer donors, minority groups like African Americans have a markedly lower follow-through rate compared to white Europeans, presumably in part due to different socioeconomic constraints. That suggests ample low hanging fruit for even modest compensation to raise follow-through by relieving the high opportunity cost of donation experienced by less advantaged groups.

\textbf{Figure 2:} Demand for HSC transplants is growing due to an aging population

The benefits of legal HSC compensation (and therefore the human cost of the prohibition) have to date not been directly estimated. However, an estimate can be inferred by combining two elements: the number of additional transplants and lives saved for a given increase in registry size; and an estimate of the optimal registry size given the marginal cost and benefit of registering a new donor. Fortunately, the authors of an economics paper titled \textit{One Chance in a Million} have made both these estimates using donor registry statistics circa 2006.\textsuperscript{15}

To illustrate, the 2006 estimates indicate an additional 0.16 transplants and 0.035 lives saved for every 1000 newly registered African American donors. In 2006 there were only 485,791 African Americans on the registry when an optimal registry size would have had 4.7 million registered African American donors. Multiplying the gap between the actual and optimal number of registrants with the expected additional transplants and lives saved suggests an annual shortfall of 706 transplants resulting in 149 deaths. In total, across all racial groups, the

\textsuperscript{14} Doug Grant (CEO of Hemeos), email message to author, September 27, 2016.
\textsuperscript{15} (Bergstrom, Garratt, and Damien 2009)
existence of a gap between actual and optimal number of registered donors indicates 1318 fewer transplants and 275 fewer lives saved each year.\textsuperscript{16}

How one ought to value a human life for the purpose of public policy is a contentious question to say the least. However, with official government values ranging from $6 to $10 million (depending on the stage of life one is in, among other factors) it is reasonable to believe that saving 275 lives a year easily produces an annual economic benefit in excess of $100 million. This is the line beyond which a regulatory action is considered “significant,” and therefore subject to interagency review. In HRSA’s proposed rule they simply assert that banning compensation for HSCs is economically insignificant. At the very least, these rough estimates call that assertion into question.

Table 1: Overall follow-through rates are lowest for the highest need racial populations (2010)\textsuperscript{17}

<table>
<thead>
<tr>
<th>Donors Available for a DNA Match Confirmation</th>
<th>Overall Availability</th>
</tr>
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<tbody>
<tr>
<td>White</td>
<td>62</td>
</tr>
<tr>
<td>African American</td>
<td>36</td>
</tr>
<tr>
<td>Asian American</td>
<td>42</td>
</tr>
<tr>
<td>Hispanic</td>
<td>44</td>
</tr>
<tr>
<td>Native American</td>
<td>45</td>
</tr>
</tbody>
</table>

According to One Chance in a Million, achieving a socially optimal registry size requires growing the current registry by more than two-and-a-half times, and would “include approximately one-fourth of all eligible African Americans and Asian Americans, 14 percent of eligible Hispanics, and 7 percent of eligible whites.” This will be a formidable challenge for a purely voluntary registry.

Markets, on the other hand, exist as the preeminent tool for aligning individual incentives in order to approximate an optimal allocation of resources. While the exact compensatory model for closing the gap in supply and demand remains an open question, if HRSA proceeds to reclassify all HSCs as an organ regardless of the method of extraction it will also rule out the mere possibility of testing different compensatory models through pilot projects.

If HRSA allows the 9th circuit’s decision to stand and take effect nationwide, in the most likely scenario clinics would begin to advertise compensation to target groups, testing different compensation models along the way. For example, as the authors of One Chance in a Million note, meeting optimality would likely require offering differential rates of compensation in order to attract donations from specific genetic sub-groups that are in short supply.\textsuperscript{18}

\textsuperscript{16} This is derived using 2006 data and a previously conducted cost-benefit analysis with many technical background assumptions. It should therefore be treated as highly suggestive of a large, unrealized net social benefit, rather than a precise estimate.

\textsuperscript{17} (Gragert et al. 2014)

\textsuperscript{18} It should be noted that HRSA’s Ethical Principles in the Allocation of Human Organs states: “…even if there is empirical evidence that survival rates of one race, gender, or socioeconomic group exceed those of another, these factors should be excluded from utility models used to justify allocation decisions.” Thus
Importantly, using compensation to attract new registrants and ensure they follow-through once matched does not need to displace the existing volunteer registry. It is possible that HRSA’s regulatory action is in part motivated by a desire to maintain the integrity of the existing volunteer registry, which could, in some scenarios, be undermined by parallel registries that offer money to participants. This fear points to a more nuanced regulatory action than de facto prohibition. Indeed, HRSA has legitimate jurisdiction to regulate a compensatory regime in all sorts of ways, including creating rules to protect the volunteer registry from displacement. This could include guidelines on when compensation is permitted, how clinics discuss compensation with prospective donors, or a requirement to demonstrate the efficacy of compensation in an experimental setting. HRSA’s proposed rule, conversely, would immediately rule out these and all other inclusive regulatory approaches.

**THE WEAK ETHICAL CASE AGAINST COMPENSATION**

HRSA’s objection to HSC donor compensation, as expressed in the proposed rule, appears to be based on three core ethical assertions. Referring to the congressional intent underlying the statutory ban on organ sales, HRSA maintains that compensation for HSC will:

- Lead to exploitation of the poor or desperate;
- Commoditize and therefore devalue the human body;
- Undermine the intrinsic or altruistic motivation for donation.

In a September 2016 open letter to the HRSA published at DonationEthics.com, thirty-seven of the country's most prominent medical, business and normative ethicists convincingly argue that each of these objections are fundamentally flawed.19 “Furthermore,” they argue, “there is a strong moral presumption against standing in the way of a model that would avoid preventable deaths. We conclude that the Rule is unethical, and should not be enacted.” The Niskanen Center wholly agrees, and expands on the arguments within the open letter below.

Exploitation

The charge of exploitation stems from the notion that organ sales may take unfair advantage of individuals struggling to support their basic needs. The paradigmatic example used by philosophers involves charging $1000 for a bottle of water to a hiker lost in a desert. The intuition is that, even when such an exchange is mutually beneficial, extracting such a high price is still in some sense unjust.20

There are two sides to every exchange, and as such two potential victims of exploitation; in this case, the donor and the patient. Critics of compensation for plasma donation, for example, tend to focus on exploitation of the donors, many of whom have low incomes or urgent bills to pay. But as the water in the desert example shows, this argument from exploitation proves too much, as it does not apply uniquely to blood, plasma, or stem cell donation. Rather, the root issue is poverty and unmet basic needs. Thus prohibiting ad hoc ways the poor or unskilled can earn income is counterproductive when it is the very lack of such opportunities that makes their exploitation conceivable.

This sort of exploitation is even weaker in the case of PBSCs due to the non-trivial delay between the time one decides to be a donor and when one can expect to be compensated. Donors go through extensive preliminary screening, and may wait months or years before an appropriate match is identified. Then, unlike plasma donation, PBSC must be administered with G-CSF, the protein based medicine that mobilizes HSCs in the blood stream. Outside of some minor flu-like side effects and a small risk of allergic reaction, G-CSF is safe.21 These sources of delay plus the cap on repeat donations means PBSC donation can hardly be construed as a method of fast cash for the poor and vulnerable.

Indeed, the exploited party in HSCs compensation is usually alleged not to be donor, but rather the patient receiving the transplant—at least potentially.22 The compatibility of a donor’s stem cells depends on blood proteins known as human leukocyte antigens (HLA) which have hundreds of millions of combinations. The average probability that two unrelated persons’ stem cells are compatible is less than one in 10,000. For two randomly selected African Americans,

19 The initial number of signatories was twenty-two but quickly grew.
20 It’s important to note from the outset, however, that exploitation is distinct from coercive harm. As Zwolinski and Wertheimer write, “Coercion characteristically involves threats by which the coercer proposes to make her victim worse off unless she does as the coercer demands. Exploitation, in contrast, often involves offers by which the exploiter proposes to make her victim better off if she does as the exploiter proposes.” (Zwolinski and Wertheimer 2001)
21 (Pulsipher MA 2016) and (Bojanić I 2016)
22 As indicated in the House committee report from NOTA’s passage: “[Bone marrow donors] are very difficult to match with recipients, … [and bone marrow donations] may represent a last resort to potential recipients.” H.R. Rep. No. 98-1127, at 17 (1984)
the probability of matching is less than one in 100,000.23 According to the Institute for Justice, “if an African-American finds a match on the registry there is an 80 percent chance that the identified donor is the only match on the registry.”24

With the patient’s life at stake, some may fear this creates a powerful monopoly-like bargaining position for the donor, who may threaten to “hold out” for an extortionary rate of compensation. Yet this fundamentally confuses the way compensation would interact with donor matching. As the authors of One Chance in a Million note, “hardly anyone knows whether they have a rare or common HLA type,” and “the HLA type of registrants is not known until after they enrolled and tested”. This effectively places donors behind a veil of ignorance. Outside of within-family matches, donors are unlikely to ever know or be in contact with their match as the entire process is mediated by third parties. Once a donor is matched they would simply invited to make the donation at the level of compensation they had previously and credibly revealed was, for them, sufficient.

The real hold-out risk stems not from rapacious donors seeking to extort their lone match, but volunteer donors who, without malicious intent, are simply unable or unwilling to honor their commitment. As One Chance in a Million puts it, “the biology of stem cell donations poses an unusual free-rider problem. Some who would willingly incur the costs of a donation if there were no other way to save the patient’s life might prefer to let someone else bear this cost if another donor is available.”25 Donor compensation solves the free rider problem, and in turn eliminates far more hold-out risk than it could ever possibly create.

In lieu of legal compensation through a registry, patients desperate to find a matching donor are increasingly turning to less regulated systems, including online message boards and social networks.26 While the scale of abuse is unknown, this opens up genuine opportunities for a prospective patient to come into contact with their donor and risk being exploited, if not simply scammed. Legal compensation would pull these transactions into the public eye and allow certified intermediaries to institute the well-established best practice of blinding donors to their patients.

For all these reasons, the open letter’s authors are clearly right to point out that the HRSA has a burden of proof, and so far “provided no evidence that either the level of compensation or the expected poverty or desperation of the donating population provide grounds for concern about wrongful exploitation.”

Commoditization

By proposing to define HSCs as an organ, even when extracted from blood, HRSA claims to be following Congress’s intent under NOTA to prevent the commodification of organs. Something is said to be commodified when it becomes bought or sold within the context of market norms. Opponents of compensation for organ donation argue that commodification devalues human life by instrumentalizing aspects of a person—that is, treating a human as a means to an end.

23 (Bergstrom, Garratt, and Damien 2009)
24 See: http://ij.org/bonemarrowstatistics/
25 (Bergstrom, Garratt, and Damien 2009)
26 (Kabbur 2016)
This should not be confused with being commoditized which instead corresponds to the economic definition of a commodity, i.e. a relatively homogenous primary good like wheat or oil. Indeed, it would be wonderful were HSCs commoditized like blood and plasma have in many ways become, as it would imply a surfeit in supply.

Confusion between the meaning of commoditize and commodify is common. Unfortunately, it is not the only way the concept is frequently misused. In their book *Markets Without Limits*, authors Peter Jaworski and Jason Brennan explain that critics of commodification often fail to distinguish between “commodities” and “mere commodities”.

If something is bought and sold, it follows trivially—as a matter of definition—that it is regarded as a commodity. However, it is an interesting, substantive thesis to say that a person buying and selling something regards the object as a mere commodity. From the fact that someone treats something as a commodity, we cannot automatically infer that she views it as a mere commodity. We know something is a commodity in the neutral sense if that thing is for sale. But to know that people regard something as a mere commodity, we would need to conduct additional psychological research into their attitudes and beliefs.

As Jaworski and Brennan go on to point out, there are many objects that are bought and sold that are not normally treated as mere commodities, and that continue to matter intrinsically and non-instrumentally, including pets, fine arts, religious objects like rosaries or devotionals, and so forth. Likewise, humans routinely exchange money for their services, to participate in clinical trials, for their hair, sperm and eggs, and even to be a surrogate mother—all without becoming considered a mere commodity.

For a human to be treated as a mere commodity would mean something else entirely. Human trafficking would surely qualify, as would a farm of humans grown solely for the procurement and distribution of their organs. While this latter scenario may seem fantastical, a prison in China became infamous for reportedly harvesting organs from executed prisoners on a massive scale. Of course, nothing of the sort comes close to describing compensation for peripheral blood stem cells, which regenerate much like plasma, blood, hair, or sperm. It also goes without saying that every apheresis clinic waiting to offer compensation for HSCs would practice informed consent, and treat donors with the dignity and respect required of a fully autonomous person.

A variant of the commodification objection is based on the invocation of human dignity, usually with reference to Immanuel Kant’s formulation that we must “treat humanity … always as an end and not as a means only.” These arguments invariably commit the identical conceptual mistake discussed above. Note, for example, how the word “only” anticipates the same nuanced, though critical, distinction between commodities and mere commodities. Indeed, without that distinction Kant’s moral framework immediately falls apart, as any undergraduate philosophy student

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27 (“Commodified vs. Commodified - Rushkoff” 2005)
28 (Brennan and Jaworski 2015, 53)
realizes when pondering whether holding the door for a friend (and thereby becoming a means to the friend’s seamless passage into the next room) ought to count as an affront to their dignity. The answer is that it does not because, though in the moment they may be a means to the friend’s end, they are not only a means, but also continue to be an end in themselves. Yet the bastardized version of Kant’s concept of dignity continues to be used and abused in biomedical discourse, leading to similar non-sequiturs, up to and including the notion that remuneration for HSCs will devalue human life.30

On the contrary, using the concept of dignity to restrict a person’s freedom to buy and sell their peripheral blood stem cells runs precisely counter to human dignity. Kant, after all, argued that individual autonomy serves as “the basis of the dignity of human and of every rational nature.”31 In other words, dignity is upheld wherever autonomy is preserved.32 Thus restricting an individual’s autonomy to donate their HSCs in an uncoerced fashion and in exchange for remuneration itself undermines human dignity.

In his 2008 essay, “The Stupidity of Dignity,” the psychologist Steven Pinker takes this elementary point to its logical conclusion,33 writing that when bioethical arguments lean on the misuse of “dignity,” it flaunts a callousness toward the billions of non-geriatric people, born and unborn, whose lives or health could be saved by biomedical advances. Even if progress were delayed a mere decade by moratoria, red tape, and funding taboos (to say nothing of the threat of criminal prosecution), millions of people with degenerative diseases and failing organs would needlessly suffer and die. And that would be the biggest affront to human dignity of all.

Altruism and Quality

Our culture celebrates altruistic behavior, and rightly so. A healthy concern for the interests of others is a bedrock virtue of civilization. And yet a just society cannot be organized on altruism alone. Rather, institutions must be designed with a realistic, rather than idealistic, model of how and why humans act. This is equally true of the institutions for collecting and matching HSC donations. It would be wonderful if every patient found a matching donor on the basis of altruism alone, but this is not the world we live in.

HRSA nonetheless contends that monetary compensation for HSCs, regardless of their source of extraction, undermines the altruistic motivation for donation sufficiently to warrant NOTA’s statutory scrutiny. Indeed, protecting altruism as the central motivation for organ donation is of such centrality to NOTA that its prohibition on “valuable consideration” covers not merely monetary compensation, but any emotional or symbolic reward as well. In lieu of any dispositive

30 This elementary error is present in the World Marrow Donor Association 2011 perspective opposing PBSC remuneration. They further argue (without evidence) that remuneration for PBSC creates a slippery slope to the sale of body parts. (Boo et al. 2011)
31 (Reath and Andrews 2006)
32 This point is echoed in a famous essay by medical ethicist, Ruth Macklin, titled “Dignity is a useless concept,” which argued that dignity “means no more than respect for persons or their autonomy,” and that it “can be eliminated [from medical ethics] without any loss of content.” (Macklin 2003)
33 (Republic 2008)
evidence that compensation harms donor motivation in aggregate, altruism has become, in Richard Epstein’s words, “the watchword of the transplantation establishment.”

While there is ample evidence that a “motivation crowd-out” effect exists, it is by far the exception to the rule. The evidence is particularly mixed in the realm of blood donation. The reason appears to be due to the nonlinear impact of monetary payment. That is, a very small monetary payment may be sufficient to undermine the altruistic motivation of blood donors without inducing an offsetting increase in supply, while if even modestly larger payments are considered the relative price effect swamps the weak behavioral effect. As the economists Uri Gneezy and Aldo Rustichini succinctly put it, “Pay enough for don’t pay at all.”

Consider the difference in work effort between an event organizer who volunteers and someone offered a single dollar. By offering the dollar the latter person psychologically construes the work as a paid employment relationship and thus reduces effort to reflect the miserly pay, assuming they don’t simply walk off insulted. Yet the mere existence of what social psychologists call “the hidden cost of reward” does mean we therefore organize our economy on a voluntary basis. The pool of volunteers is simply too small. Instead, there is some wage at which the paid organizer will work harder than if they volunteered, and which, importantly, also induces a positive supply response. There is no reason to suspect HSC donation would work any differently. With compensation in the $2000-$3000 range, a net decline in donor registrations is simply an unfathomable outcome.

A natural field experiment involving nearly 100,000 donors to the American Red Cross confirmed this in the case of blood, and with much smaller dollar amounts. The researchers found that not only were subjects more likely to donate when offered rewards of $5, $10 and $15 gift cards, but they were more also more likely to attract others to donate. Offering a lottery ticket or a paid day off work has found similar results in Switzerland and Italy, respectively.

If the argument from altruism is so weak, why does it persist? Blame the influential 1970 book, The Gift Relationship: From Human Blood to Social Policy, by Richard Titmuss. In it, Titmuss compared the British voluntary system of blood donation with the U.S. market system, and concluded that the British blood supply was of both higher quantity and quality. Incentives, he argued, crowded-out the high quality altruistic donors in favor of lower quality donors, causing the blood supply to become contaminated with viruses like hepatitis.

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34 (Satel 2008, 79)
35 (Deci, Koestner, and Ryan 1999)
36 “According to researchers ample evidence exists that behavior is usually in line with incentives, and research on motivation crowding out is looking for the exceptions. Although increasing numbers of studies uncover such exceptions, the conditions under which they occur are currently not well understood.” (Promberger and Marteau 2013)
37 (Niza et al. 2013)
38 (Gneezy, Uri, and Aldo 2000)
39 For more on the economics of volunteer labor see: (Freeman 1997)
40 (Lacetera et al. 2014)
41 (Goette and Alois, n.d.)
42 (Lacetera and Macis, 2008)
Titmuss’s evidence for his claims was weak, consisting of anecdotes, donor questionnaires, and his own speculation. *The Gift Relationship* nonetheless had an immediate and profound influence on the public policy of blood donation. U.S. blood collection and transfusion organizations immediately released statements in favor of a voluntary system. In 1975, the World Health Assembly issued a resolution urging member states to “promote the development of national blood services based on voluntary nonremunerated donation of blood.” And in 1978 the FDA requested blood donations be labeled as either paid or volunteer.

Despite Titmuss’s immense influence, his central claims about quality and quantity could not have been more poorly timed. The 1970s saw the development of blood tests to detect hepatitis A and B, and by the mid-1980s they were used by blood banks routinely. Tests for HIV and Hepatitis C became available in the late 1980s and by the 1990s donors were being universally screened for these and other infectious diseases. And while altruism might have been sufficient to produce the supply of blood demanded circa 1970, in the years that followed demand has grown significantly faster than supply thanks to an aging population and medical innovations that require the use of transfusions. This has led to seasonal blood shortages in countries with voluntary systems, while in the U.S., which never fully jumped on the altruism bandwagon, shortages continue to be effectively mitigated through the use of incentives. Likewise, countries with voluntary systems for plasma do not come close to matching the robust U.S. supply.

Just like blood donors, HSC donors go through extensive screening for infectious diseases. That said, the rarity of finding a close match makes stem cells much less prone to adverse selection in the first place. Only 1 in 430 registered donors go on to donate their HSCs. Finding a match—any match—is simply paramount given the life or death ultimatum faced by many on the bone marrow waiting list. As such, many patients undergo HSC transplants using imperfect matches with the full knowledge that they face a high probability of serious complications. Legal compensation therefore stands to increase quality by expanding the supply of HSCs and increasingly the probability of finding a closer match.

**CONCLUSION**

Most medical texts define bone marrow as the blood-forming tissue within the bone. A minority argue that the bone and bone marrow cannot be meaningfully distinguished, and should therefore be considered the “same unique functional unit, the bone-bone marrow organ.”

In some ways the debate resembles the grain-heap problem within philosophy: at what point does adding a marginal grain of sand create a sand heap? Similarly, at what point does the marginal stem cell constitute tissue, and the marginal bit of tissue constitute an organ? Philosophers like Wittgenstein concluded that, while some things are clearly organs and some things are clearly cells, there is simply “no fact of the matter” of where or how to draw a bright line.

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43 U.S. demand for blood has declined slightly in the last few years due to improved understanding of when a transfusion is and isn’t necessary.
44 See: https://bethematch.org/support-the-cause/donate-bone-marrow/join-the-marrow-registry/likelihood-you-will-donate/
45 For more on how supply affects the probability of finding a close match see: (Bergstrom, Garratt, and Damien 2009)
46 (Del Fattore, Capannolo, and Rucci 2010)
line between the two. Instead, we draw a fuzzy line for pragmatic reasons, so we can get on in
life making meaningful use of concepts in ordinary language.

The law, however, is different. It exists to settle disputes, and as such requires hard and fast
demarcations even where, strictly speaking, there are none. So when the Ninth Circuit Court of
Appeals was put the question of whether hematopoietic stem cells—the blood forming stem
cells produced within bone marrow but also found within the bloodstream—ought to be
considered an organ or a subpart of the blood, it had to make a judgment. Its logic was simple:
The National Organ Transplant Act, and a close reading of its congressional intent, reveals a
conspicuous exception made of blood and plasma as substances for which remuneration is legally
permissible; stem cells within the bloodstream, extracted with the same sort of machines
that extract plasma (and which were not in common use at the time of NOTA’s enactment), are
commonsensically a “subpart” of the blood; therefore, blood forming stem cells, extracted from
the blood, are also substances for which remuneration is legally permissible.

HRSA has proposed a rule that supersedes the courts judgment by redefining hematopoietic
stem cells as bone marrow regardless of their source of extraction. There are two possible
motivations behind this decision. Either HRSA has adopted an extremely contrived
understanding of what constitutes a “subpart,” or it feels legal compensation for HSCs is
particularly prone to the three core ethical concerns espoused by congress: exploitation,
commodification, and altruistic motivation.

As this report argues in depth, each of these concerns falls flat in the case of HSCs.

   Exploitation

Donors have large, potentially multi-year delays between registering and being called upon to
donate—if they are ever matched at all—removing the fear of the donor exploited in a moment
of desperation. Furthermore, all matching takes place between third parties that blind donors to
patients, and don’t reveal, ex ante, the rarity of a particular donor-patient match, removing the
fear of the patient exploited by the one and only donor in procession of matching stem cells.

   Commodification

Hematopoietic stem cells regenerate much like other substances for which you may be legally
compensated, such as blood, plasma, hair, eggs and sperm. There is therefore no fear of legal
compensation for HSCs fueling the creation of human organ farms, or other alarmist fantasies.
The commodification objection tends to be based on the confusion between a commodity and a
mere commodity. We buy and sell pets, fine art, and religious objects without them being
sapped of their intrinsic value. They are commodities, but not merely so.

   Altruism and Quality

Altruism is a noble motive, but has clearly failed to close the gap in HSC supply and demand.
While some behavioral studies have found compensation can reduce the altruistic motivation of
blood donors by reframing the situation as transactional, the effect is quickly swamped by the
influence of relative prices. Large field experiments have found no effect. Indeed, without
incentive schemes the U.S. blood supply would face seasonal shortages. The risk of adverse
selection reducing the quality of HSC donors is also minimal, as only 1 in 430 registered donors
are ever called upon.
These abstract ethical objections are a distraction from the strong positive case for compensating HSC donors. Every year, the unmet demand for HSC transplants is in excess of 10,000 patients, with a net-economic cost surpassing $100 million a year. According to researchers, achieving an optimal registry size will require registering "approximately one-fourth of all eligible African Americans and Asian Americans, 14 percent of eligible Hispanics, and 7 percent of eligible whites." With roughly 2% of the population registered, fewer than half of whom fully follow-through when contacted, closing the gap between supply and demand without legalizing compensation will be a formidable challenge.

HRSA has a legitimate interest in regulating the market for HSC transplants. However, a prohibition on compensation goes much too far, ruling out even the possibility of piloting different compensation models. Whether it is out of a legal contrivance, or a set of specious ethical objections, HRSA's rule needlessly threatens to harm the autonomy and lives of thousands of donors and patients each year.

REFERENCES

Gneezy, Uri, Gneezy Uri, and Rustichini Aldo. 2000. "Pay Enough or Don’t Pay at All*." The Quarterly