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Ensuring U.S. Biomedical Research Sustainability through Organizational Development, Quality Management, and Systems Approaches: A Review and Conceptual Framework

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Abstract

There has been a growing call for reform of the U.S. biomedical community in recent years. As a community, we face a growing list of issues including excessive waste, reproducibility, bias, inadequate training, and the absence of sustainable long-term planning that detract from the overall goal of advancing human health. In response to this debate, biomedical stakeholders have taken positive steps forward to remedy these issues. However, we must continually improve upon these steps to promote the long-term stability of the biomedical enterprise. Given the widespread interest of the scientific community in addressing these issues, there exists a unique opportunity to come together and create a new era of biomedical discovery. The completion of this exciting task requires reflection on our view and management of the system, and what the best route to sustainable change may be. Importantly, a coordinated approach that considers the collective make-up of the biomedical system and how processes and people influence collective output and create value for patients is needed. Here, these three areas and the concepts of systems theory, total quality management, and organizational development and their contribution to the management and effectiveness of biomedical discovery are discussed. Importantly recommendations are made concerning overall management strategy, process efficiency and quality research, administrative tasks, organizational cultural challenges, individual and team development, and funding strategy.

Keywords

Systems Management, Biomedical Research Policy, Organizational Development, Quality Management

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I. Introduction

U.S. Biomedical research finds itself in a period of transition where various issues including the replicability crisis [1], funding [2], workforce development [3], the need for team science [4], and improved biomedical management [5] pose significant threats to long-term sustainability and efficiency. What has become clear from these reports is the consensus that business cannot proceed as usual. The biomedical community has a unique opportunity to change the system for the better. However, system change is a complicated process that is not accomplished merely through short-term technical solutions but requires a deeper understanding of system/organizational behavior and its influence on process output and the workforce. And although the understanding of organizational behavior and development are integral to effective quality management, the topic is often excluded from the formal training of biomedical researchers and strategic planning of stakeholders. The purpose of this piece is to provide an abbreviated primer on the topic of organizational development, and its underlying concepts of systems theory and total quality management, and its applicability to the management of the biomedical enterprise. Importantly, these concepts are discussed in the context of the biomedical system, biomedical processes, and people. Overall, the aim is to provide new theoretical tools and recommendations in the pursuit of systemic positive change.

II. Biomedical Systems

Machines vs. Systems

Arguably, the most important aspect in the management of biomedical science is our view of the system and its purpose. People manage objects and solve problems based on a perception of their purpose and function (e.g. a machine vs a system). If a car has a flat tire, the tire can be replaced and the car will continue to run. However, if a human has a “flat tire”, the flat tire is often a symptom of an underlying problem (disease) and requires significant management and care to identify and treat the root cause. This difference is due to the inherent complexity and interconnectedness of living systems. Not only must we consider the function of individual “parts”, such as different organs or physiological systems, but we must consider the interaction between subsystems that produce a measurable symptom (e.g. changes in renal and endocrine function can have varying effects on the cardiovascular and nervous systems). This is part of what separates a machine from a true system in the natural world: The ability of autonomous subsystems to communicate and coordinate to produce collective function. Simply put, machine behavior is the sum of its parts, while system behavior is the holistic sum of parts and their dynamic interactions/relationships.

Systems have universal behavioral shaping characteristics that include nonlinearity, self-organization, feedback regulation, delays, history-dependence, and interaction (**Table 1**)[6,7]. In systems, cause and effect are not proportional (nonlinearity) due to the dynamic interaction among various subsystems and components (e.g. blood pressure is in constant flux due to continual change in organ system interaction). Subsystems, as individual components to a larger system, self-organize as complexity increases to maintain simplicity and order (cells→tissues→organs→body systems, or people→divisions→departments→schools→ universities). In this way, self-organization is innately decentralized and allows for subsystem autonomy and overall system robustness and promotes individual freedom while maintaining collective order. However, system sustainability is only maintained in self-organized networks when subsystem goals and needs align with, and are secondary to, collective system priorities [7-9]. For instance, the growth of cancerous tissue diminishes survival due to a dichotomy between the goals of cancerous tissue and the collective body.

The need for subsystem alignment is inherently due to the dynamic interactions between subsystems and their environments. Interactions link individual subsystem function to collective output. Interaction is often intangible and unmeasurable, but it is definable because without it

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there would be a collection of individual parts with no connection. In another sense, interactions form the highways, or networks, between subsystems. As information/action is produced from one subsystem, it travels, informs, and influences the next. For example, knowledge from academia may flow to a pharmaceutical company and influence the development of a new drug. This new drug may be beneficial for specific patient needs, leaving others unmet. Information on unmet needs then flows back to academia (feedback), where future research addresses these needs. This example also highlights the role of history-dependence and delays in system behavior. Subsystem or individual component behavior is permanently modified by previous action, feedback, and interaction. We may wish to recover money and time spent on poorly designed/wasteful experiments. Unfortunately, these actions are permanent and subsequent behavior is modified because of them. Revisiting the above example, although analysis of unmet patient needs from a new medication may take 5 years to aggregate and distribute to academia, it may take academia 10-15 years to respond (delay). Later on, after funding has been allocated and research has been conducted on unmet needs, new analyses (new feedback/interaction) may indicate these needs are trivial compared to others. As a result, research must be re-oriented and expended costs/effort cannot be reclaimed (history-dependence).

Overall, systems have unique characteristics that define their behavior. Understanding these basic principles helps clarify thinking about how the biomedical enterprise behaves on the whole, and how individual stakeholder behavior and interaction contribute to collective output. The following sections will highlight that since its inception the biomedical enterprise has been managed as a collection of individual parts and demonstrate that this unintentional management style has created and worsened current issues.

The Biomedical System

The goal of the U.S. biomedical enterprise has always been to leverage investigative insight into innovative treatment to create value for and meet patient needs. The completion of this task requires a complex collaboration between many stakeholders—or subsystems—including academia, government agencies, funding bodies, industry, healthcare facilities, research and clinical personnel, patient/citizens, and even insurance companies, all of whom have their own specific subsystem/stakeholder structure and specific priorities and expectations. While there are varying degrees of overlap, each subsystem produces a specific output that contributes to the overarching system goal (academia produces trained individuals and knowledge, industry produces therapy, government/funding agencies produce policy and funding, healthcare facilities provide care, etc.). And like the dynamic interaction between organ systems, which promote survival and behavior, the production of innovative therapies depends upon both individual stakeholder performance and stakeholder interaction. Thus, the biomedical enterprise is reflective of a system or network. In recent years, the scientific community has been challenged with a host of issues including declines in funding for young investigators [3], replicability issues [1,10], diminishing returns [11], and monetary waste [1] that have appeared to manifest all at once. Whether it be coincidence or a trend, the case can be made that these problems exist, and will continue to persist, because the biomedical enterprise is currently managed as a system of individual parts (i.e. mechanistic management). That is, the enterprise is managed to meet the goals of the stakeholders, not the needs of the patient—which has ultimately led to a culture of differing stakeholder goals, self-protection, superficial objectives and suboptimization (**Fig 1A** and **1B**) [5,12-14]. Thus, the ability of the biomedical enterprise to leverage insight into innovation has slowly diminished over time.

Mechanistic thinking and problem solving[a]—referred to as single-loop or first-order problem solving—is not surprising when considering that we, as scientists, are trained to think

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mechanistically and create simplicity and understanding from complexity. In fact, this form of decision making is instinctive, stems from newtonian principles and has been pervasive throughout all types of organizations in the modern age [15-20]. Unfortunately, this approach fails to consider subsystem/variable interdependency, feedback loops, and delays in creating output [6,21,22]. In other words, reductionist/mechanistic thinking is ineffective in managing a system like the biomedical enterprise because it assumes linear relationships between points, treats symptoms instead of problems, and fails to account for spatial and temporal nonlinearity in system behavior.

Take, for example, the issue of quality and reproducibility. Although, newly instituted journal/NIH guidelines for reproducibility have been helpful in conducting research projects thus far, their perceived effectiveness assumes that problems of reproducibility and quality derive from the investigator. However, the ability of an investigator to build quality into their research is limited by underlying factors that include variability of training in research design, technique, statistics, lack of clinical input and coordination, and a culture that incentivizes competition, risk aversion, publication, and procurement of research funds **(Figure 1C**). From a systems perspective, the current culture promotes a reinforcing feedback loop of this behavior [23-26], the result of which is delayed (quality and reproducibility problems are not evident for years). A sustainable solution will only come about when the system is considered. That is, we challenge our pre-conceived mental models of how subsystems operate and reflect on their contribution to current issues (also known as double-loop learning) [27,28]. Without alteration to system behavior, similar issues will continually repeat themselves [12]. A similar feedback loop is also evident in the problem of workforce underinvestment, which is discussed in the following sections.

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Systems Management Recommendations

The concepts presented throughout are applicable to all fields and stakeholders of biomedical investigation and patient care; however, recommendations were developed from the perspective of biomedical research and its stakeholders.

Communication

Poor communication between and within stakeholders remains an issue and is the top priority. Think of common issues within organizations. How often does lack of communication contribute to these issues? Systems, like humans, crave communication instinctually because it forges and supports relationships among stakeholders. It creates interconnectedness and holism. Without it, conflicts arise due to competing interests and system stability is diminished. It is recommended that stakeholders create platforms for communication (web-based, forums, in person, etc.) and establish committees between and within stakeholders. This is especially true for the NIH and academic institutions. Too often are policies developed/implemented with little input from all those affected. In addition, committee rosters should consist of varying levels of job status (front-line worker to leadership positions). Bottom to top communication promotes conscientious decision-making. Management and leadership are often too far removed from front-line processes to adequately assess specific process-related problems. The inclusion and valuing of workforce input also begets their buy-in to new policies [29].

Organizational Development

The concept of organizational development (OD) is relatively new to the biomedical enterprise, especially biomedical research. OD is the multi-dispensary theory and practice of improving organizational performance through the continual evolution of culture, processes, people, and their interconnectedness in a world of constant change [30]. Importantly, OD does not provide set solutions to given problems because solutions vary depending upon overall system makeup and behavior. Instead, OD focuses on teaching individuals how to frame problems and discover solutions. In this way, OD promotes worker investment and a culture of continual improvement.

It is recommended that more personnel in biomedicine be trained in OD and science-specific OD programs be established. OD programs should include best practices in team/leadership development and change and knowledge management that will aid leaders in instituting new initiatives and instilling knowledge dissemination/organizational learning. Organizational performance metrics should also be developed that enable assessment of how well the entire system, as well as individual stakeholders are meeting collective and individual objectives. For institutions that receive public funding for research, objectives would ideally be developed and implemented by joint panels that consisted of members from government, funding agencies, research institutions, national academies, and related associations (AHA, APS, AAAS, etc.). The goal would be to encourage consensus decision-making to create collective objectives and metrics that prioritize patient impact and individual stakeholder objectives/metrics that contribute to collective goals. As an example, if collective objectives include collaboration, workforce development, and research quality (defined by reproducibility, transparency, data sharing, etc.), research institution performance could be assessed by metrics that included employee engagement/turnover, career tracking, collaboration, monetary waste reduction, and indices of research quality. Similar to a shared vision, goal setting for performance metrics provides an aligned objective for all to work toward. The consensus setting of goals inherently motivates [31,32].

The largest challenge to a comprehensive reform such as this is buy-in, especially when considering that this type of change requires the biomedical community to re-define how research is conducted. That is, the focus would shift from the individual stakeholder mindset of growth and survival to a mindset of accountability and collaboration. Not only would this impact job functions, processes, and individual behavior, but it would also change the collective identity of institutions

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themselves and how they work. Because of this, getting stakeholder buy-in will be difficult. It will be incumbent upon funding agencies and government bodies to hold institutions accountable to buying in. Moreover, OD programs could be effective in smoothing this transition.

Data

Data is vital for strategic decision making because it provides insight into how correlated and seemingly disparate variables relate and influence one another in overall system behavior. However, not enough of it is collected or made available to the scientific workforce/public. It is recommended that more consistent data on the scientific workforce including age, race, gender, field of training, employment status and area, individual submitted/funded applications, etc., be collected. In addition, taxpayer funded research is often delayed in public dissemination due to lengthy peer-review and journal practices in accessibility, which have come under increasing fire in recent years due to a lack of apparent value [33]. For NIH and publicly funded research, policies should be instituted that incentivize/require the use of pre-print servers—whether currently existing, or managed by the NIH—in conjunction with journal submission [34]. Open accessibility of data is a cornerstone of transparency and should not be delayed due to a peer-review process that is subjective in nature nor journal policies that promote exclusivity.

Vision

System stakeholders, individually and collectively, need to create a new shared vision that encompasses the needs and goals of the individual members and overall system. The new era o biomedical research needs a vision that motivates the workforce, encourages continual improvement, and seeks to solve present and future healthcare challenges. By aligning and motivating members to achieve an overarching vision in which they are invested, a long-term focus will be instilled into the biomedical culture.

Despite current issues within the biomedical enterprise, the community has made tremendous strides in improving healthcare. By adopting and instituting organizational policies that manage biomedicine as a collective system, it will be in a better position to address problems and provide greater patient value. It should be noted that adoption of a systems form of organizational management does not guarantee correct decision making by instituting a set of principles. Instead, systems management facilitates a deeper and contextual understanding of a given problem—thereby increasing the likelihood that decisions will positively benefit the organization as a whole. However, various actions can be taken to start the transition towards a new form of management, as noted above and in **Table 2**. The ease of instituting and value of recommendations made throughout this manuscript will vary depending upon field of study and stakeholder in which they target; however, they are formed using rationale that applies to all fields and organizations. Likewise, some recommendations may seem more controversial than others, which is attributable to a patient-focused view of the system. Taxpayers are the largest funders of research and addressing/predicting their needs is the system's top priority.

III. Biomedical Processes, Waste, and Quality

Efficient and effective processes are critical to producing products and services that meet the needs/goals of individual subsystems and the collective system in which they operate. However, if subsystem priorities shift to favoring individual priorities, then processes adjust to meet those goals [12,35]. In other words, a changing of goals due to system/subsystem culture and behavior induces feedback that influences future interaction and output through task modification, whether consciously or subconsciously. This effect can be observed throughout the biomedical enterprise. For instance, the academic health research subsystem could be described as prioritizing its own needs over patient needs by promoting a culture of competition and incentives, where performance and job security are weighted towards publication prestige, acquisition of funds, and individual awards [36]. Collectively, this influences individual researchers to prioritize novelty over quality [37], be less apt to share resources and information [38], be more willing to take shortcuts [39], and continually fight for grant funding [40], all of which produce significant amounts of waste when considering their non-patient-oriented focus.

Quality Management

A culture that incentives superficial performance metrics and competition invariably leads to shortcuts, individualism, inefficient training, and subpar methods that diminish the value of biomedical discovery and generate hundreds of billions of dollars in waste [1,41,42]. More importantly, diminished research quality only hurts the patient in the long-run. From an OD approach, the most effective route to increasing the quality of work is to understand from where in the system issues arise and institute principles of quality management. Quality management (QM) is an organizational approach to creating a culture of continual improvement. Born out of statistical theory, QM is an asset to systems management and promotes customer-oriented goal setting, process thinking, data-driven decisions, employee engagement and commitment, and a culture of communication, stopping to fix problems and continual learning [35,43-45]. The institution of QM tools in the biomedical community would enhance the ability of individuals to identify waste and eliminate non-value-added work from processes. Specific recommendations related to quality are discussed below.

Process Management Recommendations

<u>Standardization</u>

As noted previously [46], it is recommended that biomedical research standardize experimental techniques. Currently, there are too many ways to conduct similar experiments with little consensus on operational definitions. Standardized approaches reduce intra-method variability, maximize repeatability and quality, and reduce re-work [12,35]. In addition, advances in technology can continually be tested and implemented into standards through consensus, thereby instilling

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learning into process behavior and making standardization enabling rather than conforming. As an example, the benefit of standardization can be witnessed in standardized PCR analysis for fusion gene transcripts—a landmark event for minimal residual disease determination [47]. However, the rest of the research community has been slower in adopting standardization. Stakeholders need to work together and slowly implement standardized techniques into basic biomedical research.

Quality Measures

In line with standardization, methods should be developed to assess the quality of scientific findings. These methods would depend upon the area of investigation, and would require input from various stakeholders; however, these measures would support and contribute to a central aim of focusing on patient needs. Importantly, quantitative measurements of quality are needed for analysis and predictions of system and process behavior. This is important for basic biomedical research, as research methods and mechanistic insight yield more qualitative than quantitative findings [40]. Likewise, constructive conversations on the definition of quality are needed. The term "quality" is abstract, and its definition is subjective. Is quality defined by patient needs? By positive and negative controls (do these vary by assay, by method, can they be quantified)? By what mouse line is used? By what manufacturer? By cell-line? By agonist? By defining and developing tools to measure quality, processes will be more in line with addressing patient needs. It is also important to make sure standards of quality are instituted across the board and there is some form of oversight to ensure they are being followed. Similar to the implementation of OD programs, the oversight of quality would require collaboration among numerous groups; especially considering the amount of specialization and technical expertise needed to accomplish this task. To this end, the creation of a biomedical quality consortium, run by the NIH and research stakeholders, would aid in coordination and communication. The consortium would be an open community where scientists develop and agree upon continually evolving standards of practice and operational guidelines for scientific techniques and investigation. Much of this work could be accomplished through a multi-user online community platform. Moreover, journals, funding agencies, and research institutions should require guideline use for publications, grant proposals, and protocol approvals.

Value vs Non-value

A key aspect to process thinking is understanding where waste occurs. What steps in a process contribute to the end product (value adding) and which do not (non-value adding)? After this determination, focus is placed on removing non-value-added steps. With this approach, quality is maintained, efficiency improved, and cost saved. An example of this is shown in **Figure 2**.

Overwork

There is a hefty price tag that comes along with worker overload. Not only are there significant health consequences to individuals in work environments of overburden (the CDC has a website dedicated to this topic), but there are severe ramifications to productivity and work quality. Increases in work overload—defined as hours worked, stress, number of tasks—is correlated with decreased productivity and quality of work [48-51]. This is critically important on the clinical side, where healthcare professional work overload remains an issue that has significant ramifications for both employees and their patients [52-55]. On the side of academia, organizational and work demands of educational/research environments have been shown to influence the development of psychiatric disorders in PhD students [56], and create environments of job dissatisfaction and low morale in faculty [57]; factors that undermine quality. Although counterintuitive (most system solutions are!), organizations should find ways to reduce personnel work load to enhance quality and productivity of scientific findings.

Administrative Waste

Even though much of the scientific community despises the administrative portion of science, when effective, administrative processes facilitate cutting-edge research. They keep the lights on, infrastructure up to date, help scientists submit grants, and help ensure investigation is being conducted safely. However, there is waste within science administration in the form of increasing regulations, exorbitant paperwork, and increasing amounts of tasks and responsibilities of science and administrative personnel [5,58], all of which require significant amounts of time to complete—which further increases monetary waste.

To highlight this point, an estimate for total administrative cost of junior and senior investigators submitting a new R01-equivalent grant can be calculated using data from a recent study [59]. Using estimated hours per application (120 for junior and 70 for senior)[b] and NSF 2015[c] salary data, the administrative cost of a new R01 application would be $6,574 and $3,824 for a junior and senior investigator, respectively. Extrapolating application costs to the 18,171 new R01-equivalent applications received by the NIH in 2015 would result in a total administrative cost accruement of $119.5 and $69.5 million for junior and senior investigators, respectively. Note, these values are meant to convey magnitude and not exact values. When considering all other NIH applications for a given year, administrative cost of support staff, and delay in economic return from keeping scientists away from the bench, the opportunity cost may well reach into the billions. Streamlining regulations and reducing administrative burden of investigators and administrative personnel could free up a significant amount of money that can be used for research purposes. The topic of re-structuring grant applications is further discussed in section IV.

Standardized Training in Graduate Education Curriculum

As mentioned in section II, issues of replicability and quality in science are not solely born out of purposeful negligence by the worker, but by underlying factors including variability in training and

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education. Training and education in basic practice are often provided by the laboratory in which trainees work and are subject to personal and environmental bias. To this end, the institution of standardized formal training may be a pertinent avenue to explore. A well-developed core curriculum based on standardized training in the areas of statistics, study design, decision-making, safety, basic laboratory technique, etc., would provide a uniform base for all scientists to build upon. Similar to process standardization, standardized basic training could help reduce variability and bolster quality in biomedical output. In addition, competency-based training could be implemented into a curriculum such as this [60]. The creation and implementation of a program of this scale would require communication, debate and consensus decision-making between all stakeholders. To ensure continued learning, programs would need to be reassessed every few years and modified based upon current consensus of present and future needs. Moreover, a program such as this could be implemented into the NIH accreditation system and would be similar to the process used for accrediting MD programs. Continuing education training in best practices for active investigators should also be considered [61].

Overall, the implementation of methods and practices focused on quality will have an immediate and long-term positive impact on biomedical discovery and therapy creation. Moreover, it is important for us to recognize the influence that overall system culture has on subsystem process behavior and to actively root out ineffective cultural practices to maximize quality. This concept is explored in section IV.

IV. People and Organizations

As the founding members of every stakeholder/subsystem, people shape the biomedical system. They run laboratories, teach students, treat patients, run government organizations, and set policies. Collectively, they build structure and shape system culture and output through action, autonomy, human spirit, and communication. Thus, people are the catalysts of change and the

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critical piece to solving biomedical challenges. However, like any other system component, people are susceptible to system feedback.

Culture and Behavior

Studies suggest that attitudes, work performance, behavior towards others, determination of knowledge importance, and problem-solving ability are all partly influenced by the collective behavior and culture of an organization/system [26,62-64]. From a general and behavioral perspective, there is no standard definition of "culture". It is subjective. And from the perspective of organizational psychology, organizations are thought to "have" or "are" culture [65]. Regardless of view, organizational culture is considered to be observable at three levels: (1) artifacts, (2) values, and (3) underlying assumptions [66,67]. Artifacts are the physical manifestations of culture that are readily observable: facilities, laboratory layout, awards, publications, how people interact, etc. All artifacts hold significance for the individuals of an organization, but they fail to convey why they hold significance [65]. Espoused values are behavioral norms, codes of conduct, and ideologies explicitly expressed by the organization—usually by those in management and leadership positions. Espoused values are not inclusive to enacted values and thus may not reflect reality to individual members. An organization may espouse teamwork, integrity, and quality, but enacted values promote individualism, misconduct, and short-cuts. Lastly, underlying basic assumptions are the ingrained subconscious beliefs that create behavior and perception within an organization. They are seldom discussed and are the source of resistance to organizational change and contradiction between espoused and enacted values [63]. In biomedicine, we recognize the importance of teamwork and quality to progress scientific discovery, but we sometimes engage in contradictory behavior. Is this behavior purposeful, or a result of ingrained subconscious assumptions? Due to enacted values, artifact systems, and the behavior/beliefs of individuals, biomedical research can be observed to act on a few underlying assumptions. These include, but are not limited to: (1) innovation comes from the individual; (2) the best ideas come from continual

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competition between individuals; (3) success is measured by the accumulation of artifacts; (4) novelty is more important than quality; and (5) decisions of best practices and science only come from experience. The self-interest fulfilling incentives that arise from these assumptions can be seen as guiding the "invisible hand" whereby self-interested actions result in societal benefit. However, if self-interested incentives undermine the moral values that drive common good—organizational/individual performance can falter [68]. For example, continual competition for funding between scientists has resulted in declines in funding for young investigators, which has spurred their exodus from academic research. Although many would argue that humans are not rational agents concerning traditional economic theory [69,70], their behavior is rational in the context of a macro biomedical culture that favors experience and research that fits within a pre-defined subconscious boundary. Therefore, the exclusion of new or risky ideas outside the cultural norm is far more likely than their inclusion.

Culture plays a significant role in shaping individual behavior because it instills belief systems that influence output. The following sections will further explore the role of organizational practices in the behavior of people.

Autonomous vs Controlled Motivation

According to self-determination theory, self-motivation manifests from the innate psychological needs for competence, relatedness, and autonomy [71]. We continually explore and ask questions to understand (competence). We form partnerships and show care for others (relatedness). And we desire to have control over our own lives (autonomy). The fulfillment of these needs sustains self-motivation and promotes the growth and well-being of the individual. This is especially true in work environments where motivation is the driving factor of performance and productivity.

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Like all humans, scientists are self-motivated to solve puzzles. They spend most of their lives solving puzzles that are of interest to them (autonomy) in the hope of obtaining understanding (competence). And they form relationships that aid in their quest (relatedness). By the nature of their work, they strive to subconsciously fulfill the needs of self-determination. However, the fulfillment of psychological needs is also dependent upon the culture and environment of the organization, and how it utilizes internal and external reward systems in promoting either autonomous or controlled motivation.

In relation to organizational culture, autonomous motivation is instilled by leveraging the internal motivation of the individual and coupling it with organizational external factors that are deemed valuable to the individual [72]. Autonomous is not synonymous with independence and involves volitional action coupled with a sense of choice. Action may be shaped by outside sources including person-to-person interaction, teamwork, or internalized external goals; however, the person acting has a sense of control in the matter. On the other hand, independence refers to being alone in action, and not involving input from others. Opposite of autonomous motivation, controlled motivation is driven by the introjection of external incentives whose values are in contradiction with those of the individual [72]. In these environments, organizations place little emphasis on fulfilling innate needs and rely on enforcing conformity onto its workforce. This is a common theme of mechanistic management. A false sense of autonomy is also common in these organizations, as independence is given so long as individuals meet specific performance goals—which may be of little value to the individual. Thus, these organizations promote independence, but not autonomy. The type of motivation instilled by organizations plays a significant role in work performance, as autonomous motivation is associated with less burnout and emotional exhaustion and greater job satisfaction, self-reported work performance, knowledge sharing, work commitment, and organizational performance [73-76].

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In the case of academia, institutions provide laboratory space to investigators, which provides a sense of independence to conduct scientific investigation. The discrepancy between independence and autonomy in this setting arises from the introjection of external motivating factors (publications, grants, etc.) that are poor indicators of quality. However, Introjected regulations and requirements persist due to the implied reward for their completion (promotion, tenure, job-security) and the structuring of salary contributions (hard-money vs soft-money). This results in a continual systems feedback loop where the same external incentives are both the drivers of success and job-security, and an environment of controlled independence (external incentives control perceived autonomy). It would serve research institutions well to re-shape their organizational culture to support autonomous motivation and create external incentives that align with workforce values. Although counterintuitive, empirical evidence supports the validity of this approach in promoting long-term organizational success [73].

Development of People and Teams

In line with re-shaping organizational practices to ensure sustainability, programs that focus on developing individual skills and group collaboration fulfill innate needs for competence and relatedness. Individuals use acquired skills to complete and improve upon work tasks, and teams participate in knowledge sharing and brainstorming—which results in higher creativity and performance [77].

Biomedical investigation has shown an increasing appreciation for team-based science in recent years [78]. This is due to myriad factors including a general appreciation for team-based solutions and constraining factors of diminishing resources and greater publication criteria. In addition, academic institutions have taken an active role in creating career development programs for new investigators to aid them in starting a research team and navigating the promotion landscape. Both the appreciation for teamwork and career development programs have been beneficial to

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scientific investigators, and additional programs should be implemented to maximize individual and team performance.

(1) Scientists must be trained in more than just science. Specifically, scientists should be trained in business, management, and administration skills [79]. The inclusion of this training would equip scientists with a broader knowledge base and differing perspectives that would aid them in various job functions/career paths. This is especially important considering the need to train scientists for careers outside of academia [80]. Like standardized research training, this training could be incorporated into the formal education of graduate students.

(2) Programs should be developed that teach scientific investigators how to work in teams, both internal and external to their organizations and scientific disciplines. The formal education of scientists does not typically include training in the soft-skills of teamwork, which can result in challenges and conflict when building a team [81]. Managing and participating in a well-functioning team requires an understanding of how to create a shared vision, mesh differing personalities and points of view, deal with conflict, promote individual/group accountability, and share knowledge/communicate effectively [82]. Productive teams require constant work, and the skills that promote team efficiency require dedicated training. In addition to teaching teamwork skills, the biomedical culture needs to fully embrace teamwork—in policy, funding, and investigation—to maximize its effectiveness. There has been an uptick in multi-PI grant funding in recent years, suggesting a slow inching towards this objective. However, single-PI funding still predominates in basic research (**figure 3**). Given the complexity of disease “systems”, and continuous calls and need for collaborative research, funding institutions should prioritize collaborative research.

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Additional Organizational Culture and People Recommendations

Funding and Grants

The issue of funding has been discussed before, but given its importance and lack of sustainable solutions, it bears repeating. The biomedical research community is experiencing a growing trend of disparity in the funding of early and new investigators that is similar to income inequality and socioeconomic disparities within the US [3,83]. Updated funding trends between 1980-2017 show significant decreases in funding allocated to younger researchers with parallel increases in funding to older investigators, although younger researchers comprise a larger percentage of funded investigators (**Figure 4A** and **4B**). Concurrently, there has been a consistent decline in funded investigators 40 years of age or less, as well as no increase in number of awards for these investigators (**Figure 4C**). The increased share of funding going to the smaller percentage of older investigators may be partly attributable to the significantly larger award sizes for these investigators compared to their younger counterparts (**Figure 4D**). Although further data regarding career stage of these individuals would be of great use, the continued trend of underinvestment in younger investigators is alarming.

The trend of diminishing resources for early/new investigators is perpetuated by a growing list of causes including inherent bias in peer-review [33,84], the competitive exclusion principle [85], constant infrastructure spending [86], inconsistent funding allotment by government agencies, and a growing base of biomedical workers, to name a few. In a way, these causes are a feedback loop of the system and culture. As government funding increases, biomedical stakeholders try to capture resources for the sake of continual growth. They build new institutions and facilities, recruit new investigators who apply for more grants, and expand graduate training. Ultimately, growth surpasses resource support capacity, further driving competition and declines in grant success (**Figure 4E** and **4F**). Thus, initiatives—such as the NGRI—that increase funding and provide benefit to a single group in the short-term, may exacerbate problems in the long-term because they fail to address systems problems. The creation of sustainable solutions will most-likely require significant modification or complete overhaul of pre-existing funding policies. In addition, research institutions that depend on government funding need to think about the long-term consequences of continual expansion with finite resources. There are limits to growth [87].

(1) Prioritize funding for **team grants** and incentivize diversity in team-member career status (early through established investigators). This approach encourages team-based problem solving of health challenges and provides less-experienced investigators with funds to conduct independent/group work and an opportunity to receive guidance and mentorship from experienced investigators.

(2) Restructure funding mechanisms to mitigate unequal competition. Even with a 10% bump, the inexperience of early and new-investigators creates a competitive advantage for established investigators in grant funding. A potential solution could be to **separate grant funding competition by career status**. Early/new investigators compete against one another, early-established compete against one another, and so on. Upon acquisition of a specified number of grants (and other metrics), investigators are bumped into the next career stage bracket until they reach the level of established investigator. In addition, modification of the current career stage scheme may be needed to further separate out experience. Funding allotment to specific career stage groups should also be reflective of population distribution.

(3) As mentioned in (2), there is a competitive advantage for experienced investigators in NIH grant funding, which is partly evident in the higher funding scores for this group [88]. Higher funding scores coupled with a large population of experienced investigators creates disproportionate funding that negatively affects early stage investigators (ESI) and new investigators (Non-ESI New). For example, 69% of R01-equivalent applications discussed between 2010 and 2013

belonged to experienced/established investigators. However, this group was successful in acquiring 75% of funded awards, which led to smaller percentage funding to both ESI and Non-ESI New investigators (15% and 10%, respectively) [88]. It is unclear from the study if funding statistics include the 10% payline bump for ESIs. Regardless, higher impact scores for experienced investigators skew the scoring distribution whereby this group acquires a larger percentage of funding than their representative makeup (**Figure 5A**). Thus, a payline bump for ESIs does not overcome this skew and provides no benefit to Non-ESI New investigators. A potential workaround to this problem is the **application of a continually updating scaling factor after initial scoring** of all applications. Upon scoring, an overall scoring mean (assuming distribution normality) and career group means are calculated and ratios between group mean and overall mean are generated. All individual scores within a given group are then scaled by these ratios, which alleviates skewed distributions (**Figure 5B**). Using previous scoring data [88], 4 simulations were performed using the standard or scaled methods of grant scoring (**Figure 5A** and **5B**, respectively). The standard way (including a 10% ESI bump) conformed to current output. However, the scaled method (including a 5% ESI bump) resulted in a more equitable distribution of funding by career stage.

As with any solution, there are potential pitfalls to the scaling method that would need to be worked through. One limitation is the lack of data on non-discussed applications. The current model was run using data from discussed applications, and so normality was assumed based on sample size reported. Inclusion of all scoring data would bolster accuracy and validity of this approach. Likewise, data transformation methods may be suitable to overcome distributional skewness or differences. Regardless, the strength of a scaling method with continually updated group coefficients lies in its ability to alleviate disparity in grant scoring—which is a problem that no current initiative addresses adequately. This method is also effective in increasing competition within career groups while reducing competition between them. Moreover, specific scaling coefficients may also be suitable for boosting scores for those in need of funding, and slightly reducing scores for those who have an excess of funding. Although some investigators oppose what could be considered a "progressive tax" on their scoring after a given number of grants, resources are becoming scarce and the problem of funding inequality is a threat to the sustainability of science. When effectively instituted and regulated, the statistical merit of a progressive tax comes from its ability to markedly increase the purchasing power of those less fortunate while minimally reducing the purchasing power of those with greater wealth [89].

(4) Keeping in line with a new grant scheme, NIH applications should be streamlined to minimize time spent writing/reviewing and administrative waste. Writing lengthy approaches with exorbitant data may convey ability in research design, critical thinking and feasibility, but science is unpredictable. The likelihood of an investigator following through on every research item is exceedingly small. Yet, scientists spend increasing amounts of time crafting a "perfect" grant. A more effective and time-efficient approach would be to reduce the length of the research strategy section and convey ability through the review of selected applicant publications. In addition, novelty and innovation have become buzzwords in science, and—in this author's opinion—are a detriment to quality research. Innovation has a place in biomedical discovery, but it is meaningless if the methods and techniques used are not of significant quality. A greater emphasis should be placed on quality in grant review. NIH reviewers should also be required to give more constructive feedback that will aid applicants in future research and grant applications similar to other funding agencies [90].

Careers in Academia

(1) As highlighted, the current culture of superficial incentives is not adequate to ensure long-term health of the biomedical enterprise, nor does it reflect the values of most scientists. Soft-money positions and minimal institutional salary contributions are becoming the norm, making it

increasingly common that job security is tied to grant success and publication prestige. It is recommended that academic institutions adopt policies that give more weight to an investigators' contribution to his/her scientific community (peer-review, professional organization activity), the quality of their scientific research (metrics must be developed), and their contribution to their organization. Some of these metrics are already employed in promotion schemes, but they are not weighted as heavily as funding and publications. Institutions should also take on more risk by increasing salary contributions to investigators. Institutional practices including constant infrastructure spending with debt service calculated into indirect costs coupled with increased graduate training, faculty hiring, and reduced investigator salary contributions have significantly contributed to enterprise instability [2,91]. Institutions should bear more responsibility for fixing the system. The NIH should also reduce debt service inclusion into overhead calculations and limit individual salary contributions from research grants to a specified percentage that cannot exceed a given amount. Institutions should also consider the nonlinearity of NIH funding in future spending plans for strategic initiatives.

(2) Universities and academic training institutions should provide more opportunities for career development to trainees and take better care of their well-being, especially postdoctoral researchers. It has become a cultural norm within academia to hire postdoctoral researchers to "temporary full-time training positions"—which now last an average of 4.5 years—that offer low salaries and no retirement benefits from the hosting institution [92,93]. In this way, academic institutions hire skilled labor for low-cost and minimal risk to promote the institution's continued growth and success at the detriment of the worker. Combining graduate training and academia postdoctoral training, most doctorate-trained researchers cannot effectively save for retirement or earn livable wages—considering inflation and the increasing student debt—until their early to mid-30's. Likewise, because they are not considered full-fledged employees or

departmental/divisional employees, postdocs are often excluded from faculty/staff training programs, meetings, and institutional career development programs.

Organizational structure and culture play significant roles in shaping workforce behavior. Despite having a culture that is built upon ineffective assumptions and enacted values, the scientific workforce has made miraculous discoveries and contributions to the betterment of people's lives. It's time organizational culture and practices provide an environment in which scientists can thrive.

V. Where do we go from here?

Change Management

Overall, the structure of systems instills within them a resistance to change because they operate as intended. Changing how a system functions requires enormous effort, modification of perceptions, coordination, communication between all stakeholders and members, and consistent and intentional action. The biomedical enterprise needs both leadership buy-in and supportive policies, and a motivated workforce that embraces the new direction to ensure long-term success. Of the numerous recommendations that have been discussed, the most important in creating meaningful change is communication. The individualistic and bureaucratic nature of many biomedical institutions has enabled communication silos that inhibit knowledge sharing, debate, and planning between biomedical stakeholders. Barriers to communication need to be disassembled and transparency and discussion need to become common practices. The institution of organizational development and behavior policies discussed throughout would help in this approach.

The areas discussed in this piece contribute to the shape and output of the biomedical system. The problems that persist in these areas are not easily solved because in many ways they are interconnected and continually evolving. We can no longer solve adaptive problems with technical

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solutions. By instituting changes in how we view the system, carry out processes and develop people, we will slowly change the system.

Concluding remarks

The current need to transform our biomedical system is reflective of our constant need to continually progress, build upon what we know, and learn from our mistakes. While causes and solutions have been suggested here, solving the problems of biomedical research requires input from all parties involved, consistent and sustained action, and internalization of ideals into the fabric of biomedicine. We've spent decades discovering solutions to biomedical challenges with minimal consideration for how systems and organizational structure influence collective output. In other words, we've been fighting disease with one arm tied behind our backs. By implementing practical policies that redefine how our system behaves and focus on creating value for the patient, we will be in a better position to solve health challenges. Thus, true innovation in the coming decades may be defined not by the solutions themselves, but by the organizational practices that lead to solutions.

Disclosures

None

Notes:

[a] Mechanistic is also referred to as analytic thinking, which consists of (1) simplifying a problem into parts or variables, (2) explaining the behavior of parts separately, and (3) aggregating the behavior of parts into an explanation of the whole.[20] While this is an effective approach, it assumes no connection between variables.

[b] The study estimated 120 person hours per junior investigator and 70 person hours per senior investigator are needed to submit a new R01.[59]

[c] According to the 2015 NSF survey of earned doctorates, the median yearly salary for a full-time employee (all faculty ranks, assuming 52 weeks) was $88,000 with a fringe rate of 29.5% (US-BLS, Education and health services, 2015).

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Tables and Figures

Figure 1. Schematic of the biomedical scientific system.

(A) illustrates the current system objectives where focus is diverted from the long-term goal of quality care to primarily focusing on publications and funding. External pressure and emphasis on these objectives only exacerbate the cycle. (B) illustrates an optimal biomedical scientific system where primary objectives are influenced by a system purpose of helping the patient. A patient first approach facilitates long and short-term decision making that focuses on producing value for the patient. In this optimized system, dissemination of findings and funding are by-products that stem from the primary objective. (C) Illustrates external and internal feedback loops of quality and their influence on the investigator. External interventions such as guidelines help investigators perform higher-quality research; however, they don't address the underlying factors that influence quality such as investigator training and culture.

Figure 2. Value and Non-Value.

A scientist is aliquoting a stock into 1.5 mL Eppendorf tubes that include the steps: (1) pickup pipette tip from rack→(2) move to stock tube→(3) take up stock with pipette→(4) move to Eppendorf tube→(5) dispense stock→(6) move to waste container→(7) dispense tip→(8) move to tip rack→repeat. In this scenario, steps 1, 3, and 5 are the only value-added work because they contribute to the end goal of putting stock in a tube. All other steps are either movement or elimination steps. To understand the cost benefit of removing non-value-added steps, imagine steps 2, 4, and 6 take 1 second to perform, and step 8 takes 2 seconds. For 100 aliquots, total time spent is 8.3 minutes. If the employee performing the work makes a salary of $65,000 per year (including benefits, 52 weeks per year, 40 hours per week), the salary cost of performing this task is $4.32. When accounting for the cost of pipette tips ($.13 per tip X 100 tips used), the total cost increases to $17.32. Assuming sterile technique is used, an efficient step to eliminate non-value-added work would be to minimize pipette tip use (use one tip for all aliquots). Thus, reducing

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resources and non-value-added movement. The steps would then follow: (1) pickup pipette tip from rack→(2) move to stock solution→(3) take up stock solution→(4) move to Eppendorf tube→(5) dispense stock→(6)→ move back to stock→ repeat (3) through (6) 99 times→(7) move to waster container→(8) dispense tip. Using this improved method, total work time is reduced to 3.24 minutes, and total cost (including tip cost) to $1.82; an 89% reduction. At no point were value-added steps reduced. The new method keeps quality and saves time and cost. This simplistic example is adaptable to every biomedical process.

Figure 3. Single vs. Multi-PI Projects

(A) Total dollar amount allocated to single and multi-PI awards (2000-2017). (B) Total number of funded projects between single and multi-PI projects (2000-2017). All data were collected from the NIH RePORT database. www.projectreporter.nih.gov/reporter.cfm

Figure 4. Research Funding Trends

(A) Percent funding distribution for research grants separated by age category (1980-2017). (B) Age distribution of funded investigators. (C) Number of funded awards, (D) average dollar amount per award, and average median dollar amount per award (single-PI grants only). (E) Comparison of yearly NIH budget (1990-2017) and rate of change per year (bottom), number of applications, awarded applications, and success rate (middle), and comparison of academic research space and faculty/trainee number (top). Range colored gray depicts the NIH doubling period and the American Recovery and Reinvestment Act of 2009 (ARRA). (F) Schematic representation of the positive influence scientific capital has on various components of the scientific system. Each process is depicted as having an inflow that increases a stock (capital, grants, scientists, infrastructure) and an outflow that decreases the same stock. Feedback signals are depicted as dashed lines. Data for (A-E) were collected as part of an NIH FOIA request for funding information on R, P, M, S, K, U (except U6), DP1, DP2, DP3, DP4, DP5, D42, and G12 grants. (D) shows

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inflation adjusted dollar amounts using consumer price index-urban values from 1980-2017 (Bureau of Labor Statistics). Data used in (F) were collected from the NIH RePORT database (www.report.nih.gov), and the WebCASPAR Resource Data System (www.ncsesdata.nsf.gov/webcaspar/).

Figure 5. Scaling Method for Grant Funding

Data for grant scoring were acquired from previously reported data.[88] Distributions were created using random number generators and reported mean and standard deviation. Given lack of data, normality was assumed based upon large reported sample sizes for each group. Estimated proportions of funded grants from 1,000 applications were determined using 15% general and 25% ESI paylines (standard method) or by the use of overall mean scaling for each group with 15% general and 20% ESI paylines (scaling method). For score scaling, an overall mean and individual mean scores for each career stage were calculated. Career stage-specific coefficients were generated by dividing the overall mean score by individual career stage means. Individual grants scores were then multiplied by their respective career stage coefficients resulting in final scaled scores. 4 separate simulations of 1000 randomly generated grant scores were conducted.

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Table 1. Characteristics of Systems

Characteristic	Description
Adaptability	Capabilities and decision rules fluctuate over time. Systems re-organize and remodel
Continual Change	Growth is an inherent part of the natural world. Systems continually grow and increase complexity
Counterintuitive	Cause and effect are far apart in space and time. Effective leverage points for intervention are often not obvious
Feedback Regulation	Actions produced by individual components and interactions influence subsequent action
History-Dependent	System choices permanently affect system behavior
Interaction	Subsystems continually interact with one-another and the world around them. Everything is connected
Non-linear	Cause and effect are not always proportional, and relationships in one subsystem may not apply in another. Non-linearity ensues from multiple subsystem interaction
Self-organizing	Internal structure arises out of spontaneous local and distant interactions. Naturally form hierarchies that reduce complexity and increase robustness
Policy Resistant	Complex nature of systems makes them difficult to understand, which leads to policy decisions that have little influence on system behavior
Delays	Time delays in feedback between subsystems cause differences between long and short-term responses

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Table 2. Organizational Recommendations

Issue	Recommendation	Rationale/Benefit
Lack of communication	• Create platforms for communication (web-based, forums, in person, etc.) • Establish committees between and within stakeholders (multi-university, university and industry, university and healthcare, etc.) • Committee rosters should consist of varying levels of job status (front-line worker up to leadership positions)	• Continual communication within and between subsystems is integral to system sustainability • Bottom to top communication promotes conscientious decision making • Management and leadership personnel are far removed from front-line processes and cannot adequately assess specific process-related problems • Workforce buy-in occurs when input is valued
Organizational Development (OD)	• Train personnel in and establish OD programs • Develop change management programs • Develop knowledge management programs (the sharing and spreading of subsystem information throughout the entire organization) • Develop organizational performance metrics (non-financial unless they measure resource utilization). Create accountability to meet metrics	• Increased appreciation for the role of organizational structure and culture in influencing employee performance and organizational growth • OD provides people with tools on how to view and solve problems themselves instead of providing set solutions (heuristic vs algorithmic). Promotes investment in workers and creates culture of continual improvement • Recording and sharing of knowledge facilitate organizational learning • Understanding how people respond to change and how to manage it is vital to any successful initiative • Goals provide objective to work towards. Consensus goals inherently motivate.[36,37]
Data	• Collect and report more on science workforce that includes age, race, gender, field of training, employment status and area, number of submitted and funded applications, etc.	• Will provide valuable information that will help in the assessment of current and future needs.
Vision	• Create a shared vision	• New era of biomedical research needs a vision that motivates the workforce, encourages continual improvement and seeks to solve complex health problems • Long-term over short-term

Figure 1

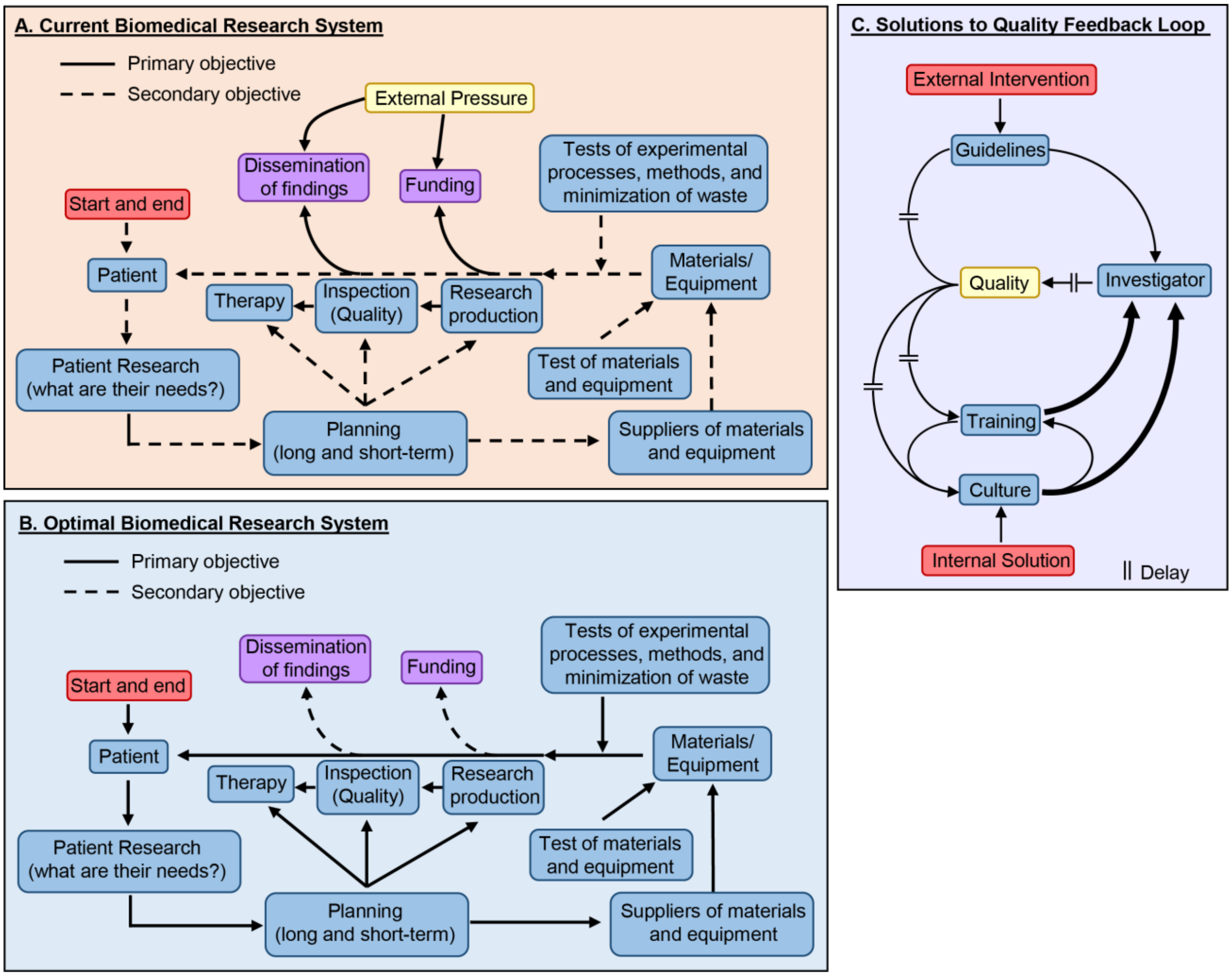
A. Current Biomedical Research System
Primary objective
Secondary objective
External Pressure
Dissemination of findings
Funding
Tests of experimental processes, methods, and minimization of waste
Start and end
Patient
Materials/ Equipment
Therapy
Inspection (Quality)
Research production
Test of materials and equipment
Patient Research (what are their needs?)
Planning (long and short-term)
Suppliers of materials and equipment
B. Optimal Biomedical Research System
Primary objective
Secondary objective
Dissemination of findings
Funding
Tests of experimental processes, methods, and minimization of waste
Start and end
Patient
Materials/ Equipment
Therapy
Inspection (Quality)
Research production
Test of materials and equipment
Patient Research (what are their needs?)
Planning (long and short-term)
Suppliers of materials and equipment
C. Solutions to Quality Feedback Loop
External Intervention
Guidelines
Quality
Investigator
Training
Culture
Internal Solution
Delay

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Figure 2

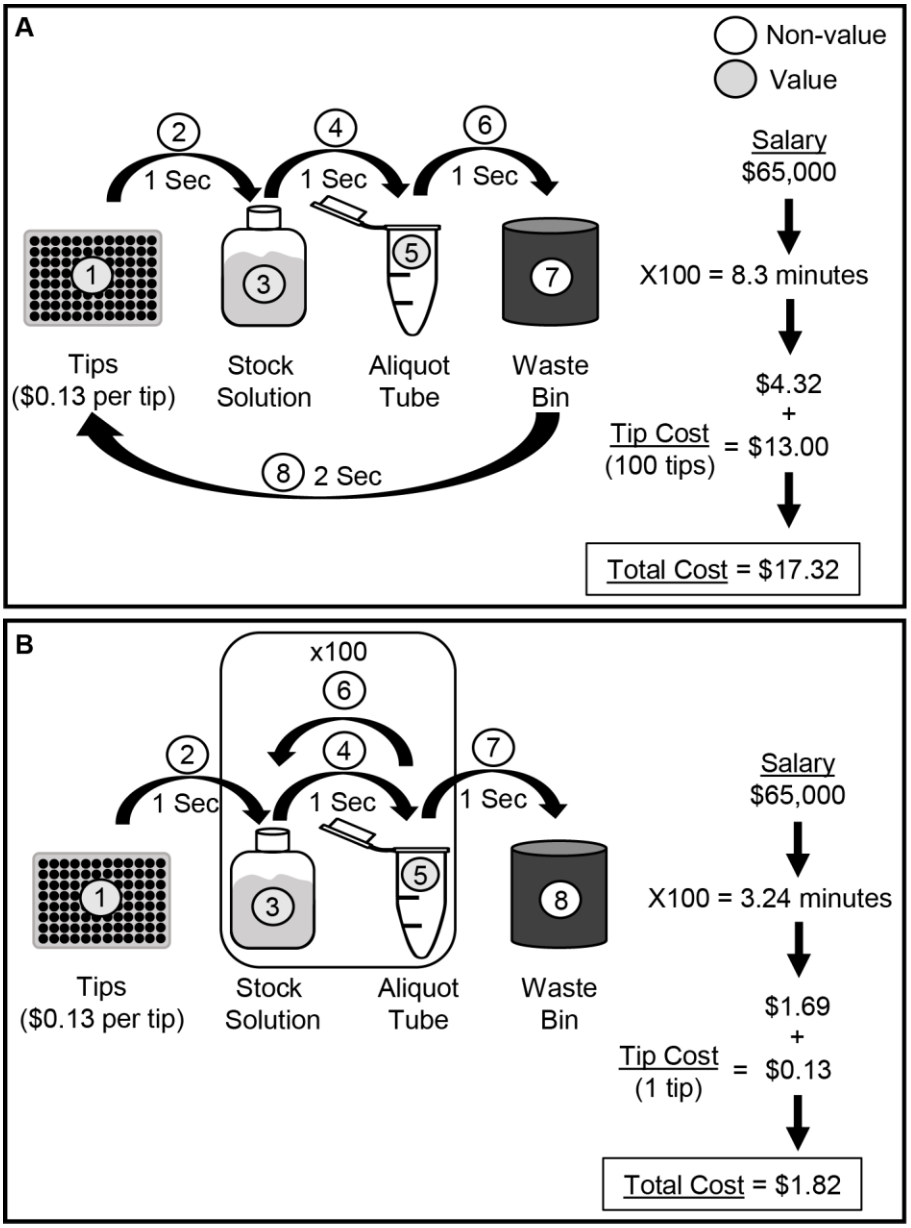

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Figure 3

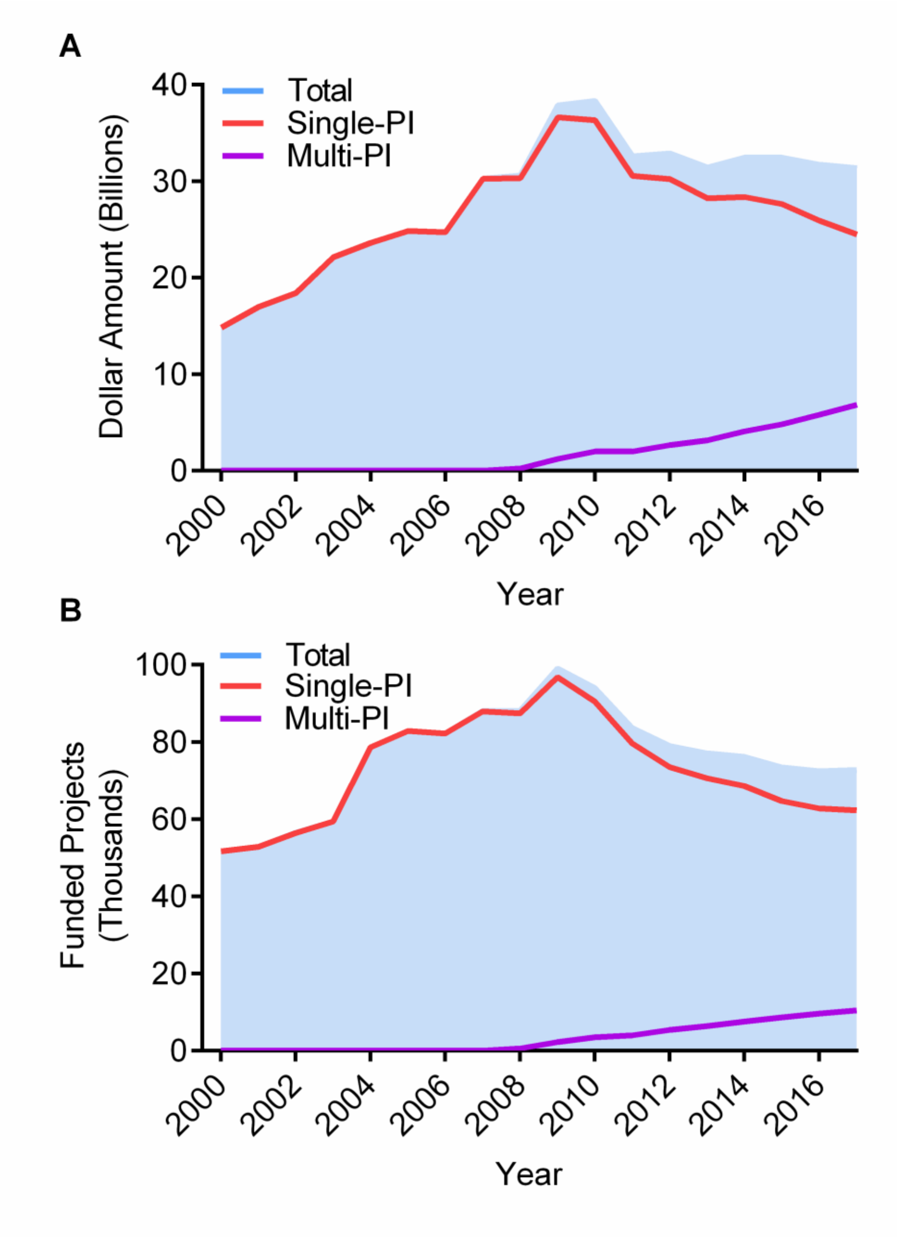

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Figure 4

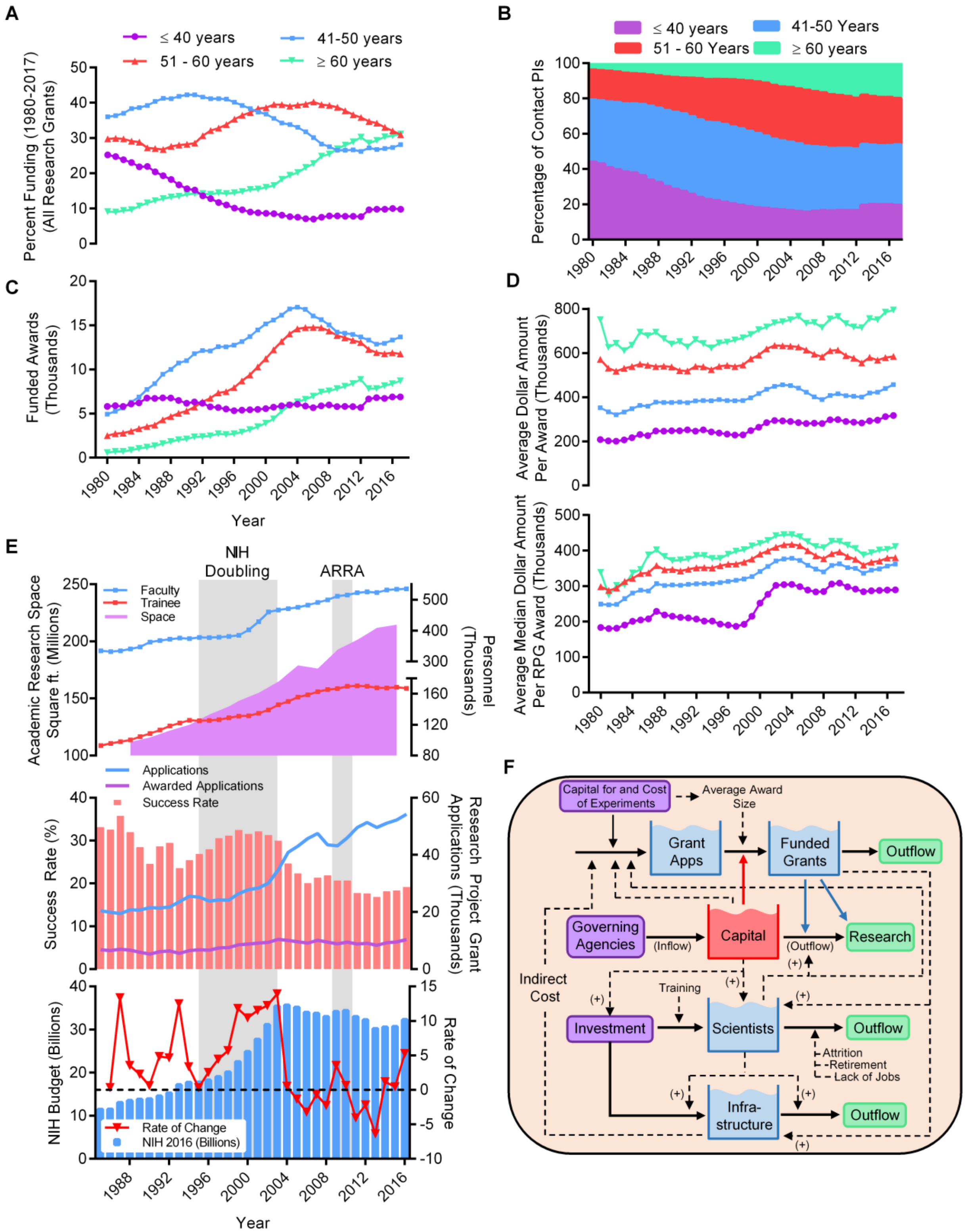
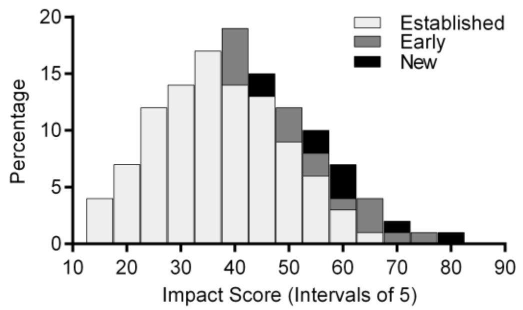


Figure 5

A

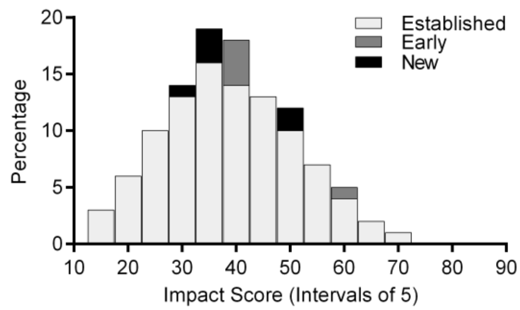
Current Funding Strategy (Impact Score)			
Level	Established	Early	New
Mean	34.53	38.75	41.51
SD	11.62	12.68	13.06



Current Funding Strategy					
Payline - 15% ESI- 25%		Number of Grants			
		Early	Established	New	Total
# Discussed Per Trial		160 (16%)	690 (69%)	150 (15%)	1000
Funded	Trial #1	30	126	10	166
	Trial #2	27	125	8	160
	Trial #3	33	117	10	160
	Trial #4	30	124	9	163
	Total Funded	120	492	37	649
	Percentage Funded	18.49%	75.81%	5.70%	

B

Revised Funding Strategy (Impact Score)			
Level	Established	Early	New
Mean	36.25	36.25	36.25
SD	12.20	11.82	11.40



Revised Funding Strategy					
Weighted to Mean Payline - 15% ESI- 20%		Number of Grants			
		Early	Established	New	Total
# Discussed Per Trial		160 (16%)	690 (69%)	150 (15%)	1000
Funded	Trial #1	30	106	22	158
	Trial #2	39	104	18	161
	Trial #3	31	101	16	148
	Trial #4	34	104	18	156
	Total Funded	134	415	74	623
	Percentage Funded	21.51%	66.61%	11.88%	