Moving urologic disparities research from evidence synthesis to translational research: a dynamic, multidisciplinary approach to tackling inequalities in urology

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Disparities in urology are well-documented but less is known about the role of translational research within existing interventional models to address inequalities. In this narrative review, we utilize an accepted framework of the process of translational research in mitigating disparities to investigate current translational and interventional urologic programs that bridge the gap. Three established, disparity-focused urologic interventional programs were identified and are highlighted in depth. Finally, we extrapolate from these findings to provide 10 policy relevant implications to help move urologic disparities research from evidence synthesis to translational research.

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UROLOGIC DISPARITIES

For decades, urologic disparities research has highlighted the differential access, quality of care, treatment and outcomes experienced by minorities, women, and those of low socioeconomic status (SES). For years, urologists have worked toward bridging the gap. Nonetheless, inequalities in urologic care persist. Hispanic men are more likely to present with high-risk (≥T1G3) penile squamous cell carcinoma (SCC) and undergo penectomy rather than penile-sparing surgery for equal stage SCC compared to Caucasians. African American (AA) men are more likely to present with higher stage prostate cancer but are less likely to receive definitive treatment and pelvic lymph node dissection and suffer worse survival. Women with bladder cancer present with more advanced disease and have higher mortality compared to men. Low-income patients do not receive complete guideline-concordant care for a variety of urologic conditions. Yet, clinical trials continue to underrepresent minorities, women, and low SES populations. Data demonstrate that Black, Hispanic, female, and poor patients have and continue to receive disproportionately worse urologic care with higher morbidity and mortality.

Disparities research has three generations: (1) describing relevant inequities, (2) evidence synthesis and identifying targets for intervening on underlying causes of a disparity and (3) implementing and studying interventions to bridge the gap. At present, the work of describing and documenting disparities in urology is over-represented in the literature. The next step, from evidence synthesis to disparity eradicating endeavors, requires translational research as an important tool for achieving health and health care parity.

TRANSLATIONAL RESEARCH

Translational research is no longer synonymous with “bench-to-bedside.” In 2003, the Institute of Medicine recognized two “translational blocks,” T1 and T2. T1 involves the transfer of new understandings from biomedical science to the first testing in humans; T2 is the translation of results from T1 into everyday clinical practice and health decision making. Since then, the definition has evolved to split T2 into two more parts, T3 and T4: T3 describes the implementation and dissemination process and T4 is concerned with outcomes and effectiveness research. The goals of each block are different. All are necessary. The unequal inter-group effects of medical treatments on morbidity and mortality are unlikely explained by pharmacodynamics or device properties but rather can be attributed to how, when and to whom these therapies are delivered.

Here, we utilize an accepted framework of the process of translational research in mitigating disparities to contextualize a narrative review of interventional programs that are using this approach to address urologic disparities.

METHODS

Analytic Framework
We contextualized this narrative review using the Conceptual Framework for Translational Research model (Fig. 1). This
The model is oriented toward the health services approach and is meant to complement the cyclical model of three generations of health disparities research: 1) detect disparities; 2) assess underlying causes and develop interventions; 3) implement interventions and monitor outcomes specific to health disparities.10,13 The model illustrates in detail the various elements involved in the translational research process for the development and delivery of therapies and integrates the public health perspective and community-level factors that significantly affect health outcomes. This framework is anchored in three familiar settings:

1) From the Community: Public health research is used to ensure identification and root cause analysis of the disparity followed by community engagement and epidemiologic assessment before initiation of research. Collaboration through community engagement includes methods such as community-based participatory research.14 Epidemiological assessment helps investigators identify features of at-risk populations and recognize groups that are differentially affected by specific diseases or pathologies.15

2) To the Bench: Therapeutic discovery research includes the creation of diagnostic techniques and therapies. This can be accomplished without consideration of population disparities (particularly early T1) but it is important to ensure that the target population has the opportunity to provide input (e.g., blood/tissue samples) in the research process in order to minimize lack of receptiveness and help increase widespread adoption, generalizability and curb health disparities.

3) To the Bedside: Clinical research is composed of traditional clinical trials and practical clinical trials. Traditional trials are randomized clinical trials (RCTs) which are considered the gold standard for learning the independent effects of specific therapies on health outcomes. Practical clinical trials differ from RCTs in that they are designed to assess effectiveness of interventions that can be implemented in real-world settings with a focus on recruitment of diverse study populations from a variety of settings; results can be used to inform evidence-based practice.16,17

4) Back to the Community: Public health research can help identify systemic obstacles to treatment utilization through the process of intervention evaluation by way of established frameworks like RE-AIM (reach, efficacy/effectiveness, adoption, implementation, maintenance).18 Public health research is also applied to perform an ecological assessment, known as a community diagnosis19 prior to intervention initiation which is important for identifying environmental, social and psychosocial factors associated with disease in a target population; biomedical and clinical treatments can be maximally effective for populations if the secondary and tertiary determinants of disease are also addressed. Finally, this model incorporates community-level intervention as a means to most efficiently address identified barriers to therapies. Community-level approaches include advocacy, resource support, community capacity building, information dissemination, and community engagement.

Literature Review
We conducted a literature review using a PubMed MEDLINE search through the National Library of Medicine database (http://www.pubmed.gov) and included all English language articles from inception until February 10, 2021. Medical Subject Heading (MeSH) terms pertinent to our topic subject were used along with free-text, truncated, related, derivative, and exploded terms. All entries included “urolog*” with the following
combinations: healthcare disparities, implementation science, translational medical research, biomedical research, clinical trials as topic, clinical trial publication type, biomedical research, health services research, telemedicine, outcome assessment (health care), outcome*, intervention*, medically underserved area, safety-net, social determinants of health, health equity, disparity, disparities, diversity, minority*, race. We expanded the formal literature search via manual search engine queries in Google to find documents and definitions of the non-urologic health concepts discussed in this review. We iteratively reviewed and selected the final sources for inclusion.

RESULTS

Our search revealed three established interventional programs which either sought to directly tackle urologic disparities or have directly improved care for underserved populations in urology (Table 1).

Improving Access, Counseling and Treatment for Californians with Prostate Cancer (IMPACT)

IMPACT is a public assistance program initiated in 2001 to address the underlying causes for differential health care utilization (i.e., realized access to care) among low-income patients with prostate cancer. Investigators adopted the Behavioral Model of Health Services Utilization with the premise that racial/ethnic minority status is a predisposing characteristic associated with less-frequent receipt of necessary health services and with adverse health outcomes. The program provides free and comprehensive prostate cancer care to uninsured men with biopsy-proven prostate cancer and with incomes under 200% of the Federal Poverty Level. The multidisciplinary approach provides enrollees with insurance benefits, an assigned local primary care provider, a clinical case manager, and social service resources including: counseling and interpreter services; culturally-dependent, literacy-sensitive educational materials; transportation assistance; food security; and housing referrals. The authors postulated that racial/ethnic disparities would be attenuated in this population. Primary aims were extent of racial/ethnic disparities in health services utilization and patient-experience outcomes (i.e., patient satisfaction and confidence in care) while adjusting for other predisposing, enabling and need factors in order to identify modifiable variables that might explain any observed racial/ethnic disparities. Study measures included the following variables: race/ethnicity, age, alcohol use, educational attainment, language preference, partnership status, number of dependents, self-efficacy, spirituality, prostate cancer knowledge. In an analytic sample of 357 enrollees from 2001-2005, 55% were Hispanic, 17% African-American, and 22% non-Hispanic White. Two-thirds were ≤65 years old at enrollment; two-thirds had PSA values <10 ng/mL; half had Gleason scores ≤6; and half had clinically-localized cancers. Median duration of program enrollment was 18.7 months (range 3.7–42.9 months). The key finding revealed equitable prostate cancer health services utilization across the diverse racial and ethnic groups served by IMPACT. Bivariate associations revealed more favorable patient-experience outcomes (satisfaction and confidence in care) for racial/ethnic minorities compared to non-Hispanic Whites (P < 0.05). A higher percentage of Hispanic men reported complete satisfaction with health care received in IMPACT vs. White men, 84% vs. 67% respectively (adjusted OR = 5.15, 95% CI 1.17–22.6, P = 0.11). Language preference and self-efficacy emerged as potentially-modifiable explanatory variables for the associations between race/ethnicity and patient-experience outcomes: higher levels of satisfaction among Hispanic men were consistent across language preference categories and, conversely, the higher levels of confidence among Hispanic men were from those who preferred Spanish. This community health program uses resource support and culturally-sensitive information dissemination to turn the T1 invention of PSA screening test and the T2 results that inform clinical practice into parity in realized access to care.

The Cleveland Clinic Glickman Urological and Kidney Institute “Minority Men’s Health Center”

In 2004 the Cleveland Clinic established the Glickman Urological and Kidney Institute’s Minority Men’s Health Center (MMHC) with the central mission to reduce and eliminate health disparities by specifically addressing the range of health conditions known to disproportionately affect minority men. The MMHC combines urologic care, streamlined preventative health screenings, primary care, referrals for specialized care including kidney transplants, weight loss surgery, colorectal cancer and digestive diseases, shared medical appointments, prescription assistance and spiritual care. The program, at a local level, also supports exposure of minority youth to health professions careers. This academic-community health program uses a number of public health strategies to ensure that minority men benefit from the T1 breakthroughs in health screening tests and treatments.

The Los Angeles County Department of Health Services (LAC DHS) clinical integration program

The Los Angeles County Department of Health Services (LAC DHS) is the second-largest U.S. public health care system and serves primarily minority and uninsured patients. In an effort to maximize resources, increase access and improve care through clinical integration, the LAC DHS initiated an innovative program in 2012 by combining three interventions: first was empowerment where each PCP is assigned a primary care patient; next was implementation of electronic specialty referral system (eConsult; Safety Net Connect); and lastly, was the creation of jointly defined clinical algorithms (expected practices) for managing common diagnoses between PCPs and physician specialists. This program has led to a dramatic decrease in time to complete hematuria workup from an average of 404 days before eReferral to 192 days after eReferral (median 239 vs. 170; 2-sample median P = .0013). Patients have also benefitted from a significant decrease in inefficient urologic care (i.e., patients who did not need specialty care or who received insufficient workup prior to the urology clinic visit) and decreased wait times to see the urologist. Incontinence patients too are getting better care due to clinical integration methods. In a recent review on the impact of eConsult, mostly Medicaid and minority patients in this LAC safety-net had higher quality of incontinence care compared to Medicare, HMO, or PPO insurance patients at a local academic tertiary care center. The county system PCPs were more likely to provide recommendations regarding pelvic floor exercises (37% vs. 22%, P = 0.03) and to adhere to general incontinence quality indicators compared to their academic
<table>
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<th>Program</th>
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<td>IMPACT (Improving Access, Counseling and Treatment for Californians with Prostate Cancer)</td>
<td>Public assistance program</td>
<td>Uninsured, Californian prostate cancer patients with incomes below 200% of the Federal Poverty Level</td>
<td>Reduce disparities by addressing financial and non-financial obstacles to utilizing prostate cancer care</td>
<td>Racial/ethnic disparities in access to care may be attenuated among IMPACT participants</td>
<td>Behavioral Model of Health Services Utilization</td>
<td>Free and comprehensive prostate cancer treatment; assigned local primary care provider and clinical care coordinator; counseling and interpreter services; culturally-competent, literacy-sensitive educational materials; transportation assistance; food security; and housing referrals</td>
<td>No racial/ethnic disparities in health services utilization among 357 (55% Hispanic, 17% African-American, 28% White/other) men. Hispanic men reported greater satisfaction and confidence in IMPACT providers compared to Whites.</td>
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<tr>
<td>The Cleveland Clinic Glickman Urological and Kidney Institute Minority Men's Health Center</td>
<td>Academic tertiary care program</td>
<td>Minority men in the local community</td>
<td>Reduce disparities through a multidisciplinary and multifaceted approach targeted at providing comprehensive health care for minority patients</td>
<td>Health disparities will be reduced and eliminated by specifically addressing the range of health conditions known to disproportionately affect minority patients</td>
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<td>Cleveland Clinic Glickman Urological and Kidney Institute Minority Men's Health Center and various community settings</td>
<td>Minority Men's Health Fair 2016: attendance = 1,700 (53% AA, 17% Hispanic/Latinx). Organ Donation Outreach Program: increase of 3.4% donations/registry in the 28 BMV locations (one BMV with mostly AAs clientele had increase of 6.425%; P &lt; .05). COVID-19 Community Health Response: 18,000 referrals for emotional support and food bank assistance; established five testing sites in dense AA neighborhoods, screened 376 individuals (74% AA) in 6 weeks.</td>
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<td>Los Angeles County Department of Health Services</td>
<td>Safety-net health system throughout Los Angeles County</td>
<td>Primarily uninsured and minority patients</td>
<td>Integrate care and optimize the specialty referral process through a web-based referral system (eConsult)</td>
<td>Through empanelment and optimization of the specialty referral process, access and care for safety-net patients can be improved</td>
<td>Policy enactment: PCP empanelment and clinical care integration through the use of technology (eConsult)</td>
<td>Patient empanelment to PCP throughout the LAC DHS safety net and web-based eConsult implementation with required eConsult for ambulatory PCP-specialty referral</td>
<td>Decreased time to complete hematuria workup (average of 404 days to 192 days), decreased wait times by 5 days to see urologist, decreased inefficient urologic care (73% vs. 22%, p = 0.001) after eConsult. Higher quality incontinence care from PCPs compared to a local academic tertiary center care.</td>
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DISCUSSION

We identified an accepted framework for the role of translational research in ameliorating health care disparities and discovered three urologic interventional programs that are using this interdisciplinary approach in a targeted effort to reduce disparities and improve care for disadvantaged populations. This review underscores a dearth of disparity-focused interventions in urology. The IMPACT program, ongoing for over 20 years, shows that when controlling for financial and non-financial factors, healthcare utilization (i.e., realized access) is equal across race/ethnicity.\(^2\) It also demonstrates that when patients receive equal treatment and quality of care, health care outcomes for minorities are comparable to Whites. The lack of a control group and possible omitted-variable biases in the IMPACT program does limit conclusions about racial disparities in utilization and self-reported outcomes among disadvantaged prostate cancer patients outside of IMPACT. However, this equality in realized access and outcomes among IMPACT participants is reinforced by findings within the equal-access Veterans Health Administration (VA) including recent data from Dess et al.\(^{25}\)showing no association between black race and inferior stage-for-stage prostate cancer-specific mortality (PCSM) from a pool of four randomized clinical trials in an equal-access setting with standardized treatment; although, conversely, they found that Black men had higher PCSM in the population-based SEER registry, and higher other-cause mortality in both the SEER and RCT cohorts.\(^{25}\) McNamara et al.\(^{25}\)retrospectively reviewed 2,123 White men and 787 AA men with chemotherapy-naive metastatic castration-resistant prostate cancer (mCRPC) within the VA health system. AA men treated with abiraterone acetate or enzalutamide had significantly better overall survival than White patients with the same hormonal therapy.\(^{26}\) These data suggest that race-defining biological differences do not explain differential prostate cancer health outcomes. Equal access, insurance, and supplemental social services including a usual source of care, case management, educational resources, and transportation can prove critical to remove barriers to care and help address social determinants of health for low income and minority patients. It is not enough to invent new screening, diagnostic or treatment tools — the work of T1 — we also need to confront the secondary and tertiary influences across populations that lead to differential utilization and outcomes. Of note, we must also recognize that registries are increasingly being used in urology to analyze population data and inform evidence-based practice.\(^{27,28}\)

Policy implication: Increase funding for programs that integrate social services and health care.

With the understanding that certain conditions disproportionately affect communities of color, and to help minority patients better address these health conditions, the Cleveland Clinic established the Glickman Urological and Kidney Institute “Minority Men’s Health Center” nearly 16 years ago.\(^1\) This program uniquely applies an interdisciplinary approach to help urologist providers and their patients also consider and manage non-urologic diseases — via a patient-centered system consisting of clinical care integration with streamlined preventative health screenings, primary care, and referrals for certain specialty care, among other things.\(^{21}\) While we could find no data evaluating the direct effect that the establishment of MMHC has had on patient urologic health outcomes, there are a number of studies from MMHC urologist leaders highlighting their multidisciplinary approaches to reducing disparities. Zaramo and Modlin et al\(^{29}\) developed a culturally sensitive, collaborative, educational outreach program to promote organ donation rates among AAs in the community through implementation in 28 venues of Ohio’s Bureau of Motor Vehicles (BMV) and saw a rise in the number of AAs willing to register. The recurring MMHC health fair provides researchers with the opportunity to study minority health behaviors, beliefs and practices ranging from areas of cancer communications between minority males and their relatives\(^{30}\) to health literacy and health related quality of life among minority men.\(^{31}\) This type of community research is an important aspect of the Fleming et al model because these understandings can help to identify systemic obstacles to treatment utilization.\(^{13}\) Cleveland Clinic teams have even continued collaborative, multidisciplinary interventions to address COVID-19 health disparities through development of a regional community health response focused on connecting and communicating with local officials, faith-based organizations, key community stakeholders, and providing direct service to vulnerable community members through reaching out to prior participants of the Cleveland Clinic’s Minority Men’s Health Fair and partnering with the Ohio Minority Strike Force to fulfill unmet health needs and provide COVID-19 testing.\(^{16}\) Our search revealed another more recent program taking a similar, multidisciplinary approach to caring for men: the Thomas Jefferson University Men’s Health Program focuses on comprehensive care emphasizing Urology, Cardiology, Endocrinology, Primary Care, Sports Medicine, and Sleep Medicine that was started by first developing a business model and then incorporating resources such as patient navigators and electronic medical record integration.\(^{33}\)

Policy implication: Fund public health focused health care-community based collaboratives aimed to specifically address disparities through multidisciplinary efforts.
Finally, our search showed that the LAC DHS has implemented clinical integration strategies for the past 9 years to successfully increase access and improve care for urologic patients. Their approach heavily relies on technology for remote patient co-management through PCP-specialist eConsult use and clinical care algorithms. After implementation, patients with hematuria had faster complete hematuria workup, more efficient urologic care and shorter wait times for an in-person visit to see a urologist. eConsult use was also associated with better quality of incontinence care for these uninsured patients compared to Medicare, HMO, or PPO insurance patients at a local academic tertiary care center. This is likely attributed to the fact that an eConsult is a required first-step for initiation of ambulatory specialty referral within LAC DHS and this policy, together with established clinical care algorithms, allows for education and improved co-management through urologist triage and iterative provider-provider communication. Although the Fleming et al model does not explicitly incorporate technology into the translational research process, they do highlight the role of technology as an important component for high quality translational research as it allows for the collection, integration and sharing of large volumes of data types across diverse laboratory, clinical and community settings allowing for efficiency and ability to confirm effectiveness of treatments.

Policy implication: Increase funding for patient-centered technology based programs in underserved settings.

Policy implication: Incentivize providers for working in underserved settings with higher incentives for those adhering to evidence-based practice.

The Conceptual Model for Translational Research to address disparities is certainly oriented towards a health services approach, but we would be remiss to undermine the role of basic science and T1-2 clinical trials in understanding and minimizing disparities. Geographic area of origin has a stronger correlation with genetics than does self-reported race and applying precision medicine genomic biomarkers tailored to population-specific genomic and genetic information plus other known urologic cancer-specific characteristics can improve outcomes and decrease disparities. Once we understand the epidemiological assessment as highlighted by the Fleming et al model, we can create clinical trials targeted at specific diseases or pathologies that differentially affect certain groups and then study treatment effects in real-world settings. The real-world outcomes of sipuleucel-T immunotherapy in the Provenge Registry for the Observation, Collection, and Evaluation of Experience Data (PROCEED) trial confirms the importance of T1-2 translation for prolonging life in men with mCRPC and underlines the need for increased minority patient accrual to reduce disparities. PROCEED is a contemporary multicenter, open-label, observational registry that prospectively followed men treated with sipuleucel-T in real-world urology and medical oncology clinics across private practices and academic clinics. In the pivotal phase III trial Immunotherapy for Prostate Adenocarcinoma Treatment (IMPACT; NCT00065442), sipuleucel-T proved to be a breakthrough drug for reducing the risk of death among patients with mCRPC and improved median overall survival (OS) by 4.1 months but only had accrual of 6.7% AAs; it was not until the percentage of enrolled AAs was higher (11.6%) in PROCEED that we saw emergence of race as a statistically significant predictor of OS. Urology has seen remarkable medical advancements from the T1 sphere. If we hope to leverage T1 translational research to benefit the most patients, and to provide the most benefit to each patient, we need to figure out better ways to recruit underrepresented populations. Recruitment cannot only be an afferent effort, but there needs to be an efferent effort for investigators to partner with community clinics and organizations leading to improved patient-provider trust, collaboration and accrual. We can also increase the chances of minority trust and accrual by diversifying the urologic translational research enterprise workforce.

Policy implication: Incentivize basic science research in urologic disease that focuses on the genetic underpinnings of different genetic ancestry groups.

Policy implication: Require minimum minority and female accrual in clinical trials.

Policy implication: Academic research institutions should diversify their workforce and support pipeline programs for historically excluded or under-represented groups.

As T1 and T2 research yield evidence-based therapeutic interventions and guidelines, an important next step for all programs wanting to leverage translational research to improve outcomes and reduce disparities should be for investigators to apply implementation science, dissemination, outcomes and effectiveness research — T3 and T4 research. For example, implementation science uses theory-based models to promote a systematic approach to timely uptake of evidence-based guidelines into practice; currently there are over 70 validated implementation frameworks. This type of research can help the urologic community understand and employ the most effective methods for ensuring real-world delivery of, for instance, urologist-led smoking cessation treatment strategies or intravesical chemotherapy in appropriate bladder cancer patients.

There is no doubt that basic science is the sine qua non to understanding, managing and curing disease, but translating breakthrough findings into gap-closing reductions in morbidity and mortality requires harmonious integration of all phases of the translational research process. Ensuring that both young and seasoned investigators are appropriately trained to conduct T3-T4 translational research is critical in the fight against disparities.

Policy implication: Increase funding and training programs for T3-T4 research.

Policy implication: Support implementation science research aimed at improving value-based payment models to incorporate equity and deconstruct health coverage/health system-level barriers.
CONCLUSION

Urology is not colorblind; it is not gender neutral. It plays favorites. Within the context of the Conceptual Model for Translational Research to address disparities, the three interventional programs highlighted in this review show real promise in the fight for urologic equality through a multidisciplinary approach, but they are not enough. It is increasingly clear that T1 research cannot take place in a vacuum; we need T1-T4 combined with public health research and disparities research. Thus, we have proposed 10 policy relevant implications to move past evidence synthesis to translational research interventions and help those who need it most. Before we can cure disease and disparities we must first cure ourselves of our pride, face the uncomfortable knowledge of the realities that many of our most disadvantaged patients live in, and humbly embrace the challenge to understand and help even the most vulnerable patients live in, and humbly embrace the uncomfortable knowledge of the realities that many of our most interventional programs highlighted in this review show.

References


