Current State and Future Trends to Optimize the Care of African Americans with End-Stage Renal Disease

Kimberly Harding\textsuperscript{a}  Tesfaye B. Mersha\textsuperscript{b}  Fern J. Webb\textsuperscript{c}  Joseph A. Vassalotti\textsuperscript{d,e}  Susanne B. Nicholas\textsuperscript{f}

\textsuperscript{a}Monarch Innovation Partners, Rockville, MD,  \textsuperscript{b}Department of Pediatrics, Cincinnati Children’s Hospital Medical Center, University of Cincinnati, Cincinnati, OH;  \textsuperscript{c}Department of Community Health and Family Medicine, University of Florida College of Medicine, Jacksonville, FL;  \textsuperscript{d}National Kidney Foundation, and  \textsuperscript{e}Division of Nephrology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, and  \textsuperscript{f}Divisions of Nephrology and Endocrinology, Department of Medicine, David Geffen School of Medicine at University of California, Los Angeles, CA, USA

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Abstract
Background: Chronic kidney disease is a progressive disease, which terminates in end-stage renal diseases (ESRD) that requires either dialysis or kidney transplantation for the patient to survive. There is an alarming trend in the disparities of ESRD in African Americans (AAs). Currently, AAs represent more than 30% of incident ESRD cases, yet they constitute 15% of the overall US population. Despite the reductions in mortality, increases in access to patient-centered home dialysis and preemptive kidney transplantation for the overall US ESRD population over the last decade, disparities in the care of AAs with ESRD remain largely unaffected. Summary: This review discusses patient-, community-, and practitioner-related factors that contribute to disparities in ESRD care for AAs. In particular, the review addresses issues related to end-of-life support, the importance of Apolipoprotein-1 gene variants, and the advent of pharmacogenomics toward achieving precision care. The need for accessible clinical intelligence for the ESRD population is discussed. Several interventions and a call to action to address the disparities are presented. Key Messages: Significant disparities in ESRD care exist for AAs. Strategies to enhance patient engagement, education, accountable partnerships, and clinical intelligence may reduce these disparities.

Introduction

There is a growing burden with regard to chronic kidney disease (CKD) in the United States, accounting for up to 13.6% or \textasciitilde26 million adults with an associated growing prevalence of individuals with end-stage renal disease (ESRD) [1]. CKD poses a major societal and economic burden. According to the US Renal Data System, more than 661,000 adults have ESRD of which 468,000 individuals receive dialysis therapy [2]. In 2013, the Medicare cost alone for ESRD had increased to USD 31 billion, which represented \textasciitilde7% of paid fee-for-service claims [1]. Further, having advanced CKD or ESRD im-
parts a significant increased risk for morbidity and premature mortality. For example, the 1-year mortality for myocardial infarction is 51% for populations with CKD stages 3–5, compared to 36% for populations without CKD [3]. Kidney disease is the 9th leading cause of death and accounts for more deaths annually than breast or prostate cancer [4]. Importantly, African Americans (AAs) suffer disproportionately from both CKD and ESRD with a prevalent ESRD rate 3.7 times higher than their Caucasian American (CA) counterparts [1]. Although ESRD mortality rates have improved in recent years, the annual rate is still unacceptably high. For example, while the mortality risk for AAs, or Blacks, was equal or higher at all levels of estimated glomerular filtration rates than CAs, the risk was highest for Blacks with estimated glomerular filtration rates 45–95 mL/min/1.73 m$^2$ (hazard ratio 1.32, 95% CI 1.27–1.26) [5–8].

The progression toward ESRD is associated with aging, but it is also aggravated and accelerated by other extra-renal factors such as high blood pressure, diabetes, and cardiovascular disease [1]. Furthermore, chemicals, drugs, and environmental pollutants can both initiate kidney disease and promote CKD progression [9]. Additionally, gene-gene and gene-environment interactions in AAs contribute to the increased risk of non-diabetic and hypertension-related ESRD [10–12]. This review discusses the factors that contribute to the disparities in care of AAs with ESRD and provides recommendations to reduce these disparities.

Factors Contributing to Disparities in Care of AAs with ESRD

AA Patient and AA Community-Related Factors

Multidimensional factors associated with disparities in ESRD care impact outcomes in AAs. Patient-related factors include psychosocial, demographic, environmental, cultural-behavioral, socioeconomic status (SES), and equal access to ESRD care [13, 14]. Related factors also span the AA ESRD community understanding of the impact of healthcare policies including medical eligibility to ESRD care. The identification and targeting of several of these factors have the potential to significantly reduce disparities in ESRD care of AAs.

Medicare coverage has successfully reduced many disparities associated with the care of patients with ESRD such as access to dialysis services, delivery of adequate dialysis dose, use of bicarbonate dialysate, and improved management of other dialysis complications [15], but numerous sources of disparities in ESRD unique to the AA community still remain, such as unequal access to higher education, inequitable income level, low awareness of the effects of social determinants of health, low knowledge of their genetic predisposition to ESRD, poor access to education on advanced care planning (ACP), end-of-life (EOL) support and hospice care, as well as unequal access to, and participation in clinical trials.

Equal access to education is an important social determinant that affects AAs with ESRD. In fact, education and income levels have been shown to contribute to excess ESRD rates in AAs [16]. In particular, the Multiple Risk Factor Intervention Trial demonstrated that SES, in terms of lower income, correlated well with excess risk of ESRD in AA men compared to CA men (3.20–1.87, 95% CI 1.47–2.39) [17]. More recent studies also demonstrated that having low SES significantly influences the incidence of ESRD in AAs compared to CAs [18–20]. Increasing awareness of the effects of social determinants of health may potentially lead to improved clinical outcomes in AAs with ESRD.

The diagnosis of ESRD presents significant challenges to quality of life that are independent of achieving optimum dialysis and care coordination. In general, ESRD patients are confronted with deteriorating health status, struggles with complex dietary restrictions, polypharmacy and complex care coordination for ESRD, and other comorbidities, particularly in the context of common cognitive impairment and frequent depression [21]. For in-center hemodialysis, the chronic dependence on nurses, social workers, nutritionists, technicians, vascular surgeons, and nephrologists for 3–4 h, 3 times a week, or more frequent dialysis sessions for this life-saving procedure limits quality of life, particularly for an aging population. Unlike their CA counterparts, AAs are deeply concerned about disparities in terms of lack of education, awareness of their risks of comorbidities, and fear of healthcare systems [22–24]. Thus, achieving a reasonable quality of life is a challenge. Awareness of ACP and EOL issues represent an important aspect for the AA ESRD patient that may also need added attention.

EOL Decision Support and Palliative Care for AAs with ESRD

EOL issues including ACP, palliative care and hospice care have been widely explored in the ESRD population. However, in AA and other ethnic minority communities, where low SES is prevalent, discussion about EOL issues...
is typically overshadowed by activities of day-to-day existence and making ends meet [25]. On the other hand, the concerns of estate planning, the transition of one’s legacy, and appropriate EOL care may receive higher priority in high SES populations [25]. This disparity may significantly impact one’s response to life stressors and perception of mortality. It has been shown that AAs and other ethnic minorities routinely underuse palliative and hospice care, even when there is access to this type of care [23]. Peer mentoring as a culturally sensitive approach to inform AAs on ACP may be particularly effective [26]. Other factors contributing to the underutilization of hospice care among AAs include fears of unfair treatment, withholding potentially life-saving measures, and the predominance of CAs among healthcare practitioners [27, 28].

Studies have reported barriers to AAs using hospice services, including philosophical differences; cultural mistrust; the influence of culture, family, and spirituality; and inadequate health insurance [27, 29–34]. Reese et al. [28] describe a fundamental difference between AAs and the European culture of care of the terminally ill, as the AA culture emphasizes living and prolonging life, whereas the traditional European approach favors helping people plan for and cope with eventual death. Hospice programs stress the acceptance of death during the terminal phases of life and palliative care, whereas AAs value aggressive life-sustaining treatments [28, 33, 35]. In a survey of 200 respondents, Blackhall et al. [29] found that AAs were more likely to request life support in the face of terminal illness. In fact, AAs are more hesitant to: agree to withdraw life-prolonging therapies; consent to tissue and organ donations; and participate in palliative care programs [29]. Haber describes AAs as having an expectation of long life and embracing a religious belief of “not giving up” [36]. Cykert et al. [37] found that AAs had a significantly higher health utility score, meaning a greater preference to remain alive despite severe disability. As a corollary to their reluctance to withhold or withdraw aggressive treatment during terminal illness, AAs are least likely to discuss advance directives [31]. Caralis et al. [38] found that AAs believed that they might be treated differently or cared for less well if they had a living will.

The underutilization of palliative care and hospice services must be better understood and initiatives undertaken if the American healthcare system is expected to meet the goals of eliminating race-based health disparities, increasing accessibility to healthcare services, and providing culturally competent care. In contrast to previous reports that AAs were less likely to utilize hospice services [39], a recent study by Colon and Lyke [40] compared hospice utilization by 2,430 AAs (12.55% population studied) to their prevalence in the general population (7.06%) and showed encouraging results. The study showed that between 2004 and 2010, AAs in southern New Jersey were more likely than European Americans, Latinos or Asians to utilize hospice services. As the National Hospice and Palliative Care Organization continues its efforts to increase awareness about hospice, it is hoped that the disparities in EOL support and palliative care for AAs with ESRD will diminish.

Practitioner-Related Factors
Practitioner-related issues that contribute to disparities in ESRD care for AAs include inadequate communications, treatment misconceptions, and lack of appropriate and timely care [41]. AAs also experience health disparities associated with poor access to timely health education from practitioners, health educators, knowledge of advanced CKD/ESRD awareness programs, and reduced access to clinical research [42].

AAs have higher rates of ESRD compared to individuals of European Americans with a lifetime risk of ESRD for AAs residing in the United States of 7.5% compared to 2.1% among European Americans [40]. While many factors have been associated with the higher risk of kidney disease in AAs, no clear genetic link between kidney disease and AAs was established until studies linked non-diabetic kidney disease with 2 distinct alleles within a 60 kb region of chromosome 22 [10]. Earlier studies in 2008 suggested a genetic factor associated with renal disease, connecting variants of the MYH9 gene to an increased risk of CKD and ESRD in AAs [43]. Subsequent studies clarified this association to variants of the Apolipoprotein-1 gene (APOL-1) that explained a large fraction of risk factors in AAs [44, 45]. Increasing knowledge of the influence of this genetic risk may lead to advanced research and pharmacogenomics testing toward achieving personalized care for AAs with ESRD.

APOL1 Variants and Pharmacogenomics for Precision Medicine for AAs with ESRD
Apolipoprotein-1 is expressed in the lung, placenta, pancreas, liver, and kidney [46]. However, long before APOL1 had a known role in kidney disease, it was known as the trypanolytic factor of human serum, protecting humans and other primates against African try-
describing genomic variation-based precision medicine. Thus, increasing attention is being given to the impact the disparities in ESRD and its clinical outcomes. Therapies to precisely target AAs and subsequently improve the outcome of kidney disease in AAs provides the foundation to explore and discover novel clinical targets for precision medicine. This new knowledge of the impact of APOL1-risk variants on kidney disease in AAs and their lifetime risk of CKD is approximately 15%.

The association between APOL-1 variants and progression to ESRD has been reported to vary based upon the CKD etiology with strong associations between APOL-1 variants and focal and segmental glomerulosclerosis, human immunodeficiency virus, hypertensive, and sickle cell nephropathy. This new knowledge of the impact of APOL1-risk variants on kidney disease in AAs provides the foundation to explore and discover novel therapies to precisely target AAs and subsequently impact the disparities in ESRD and its clinical outcomes. Thus, increasing attention is being given to the implications of self-reported race and ethnicity and ancestry in describing genomic variation-based precision medicine.

The National Institute of Health (NIH) National Institute on Minority Health and Health Disparities launched a new health disparities research program exploring the potential for precision medicine to promote health equity and advance the science of minority health and health disparities for all populations. Precision medicine is the study of how a person’s genetic makeup influences his or her response to drugs and is one of the cornerstones of personalized medicine in which drugs and drug combinations may be tailored to a patient’s genetic profile. Precision medicine can also provide tools for personalized medication regimens and information about potential drug interactions.

Pharmacogenomic testing has been increasingly used to optimize drug regimens that have the potential to promote research in precision medicine for CKD and ESRD. In addition, National Institute on Minority Health and Health Disparities is developing guidelines for pharmacogenomic and precision medicine tools to identify critical biomarkers for disease progression and drug responses in diverse populations and translate pharmacogenomic discoveries into clinical practice, including effective treatments. The randomized controlled study on Genetic testing to Understand and Address Renal Disease Disparities will provide meaningful information on the possible incorporation of genetic testing in clinical practice on renal surveillance that will target AAs with hypertension. Thus, genomic discovery for kidney disease in AAs provides a platform for the potential success of these tools to address genetic-based health disparities in AA patients with ESRD.

Interventions to Address the Disparities in ESRD Care of AAs

Interventions that the practitioner can support include increasing timely nephrology referral, equal access to care, and education about ESRD therapies (particularly home dialysis). The use of informatics at the point of care, and improved continuity of care may also address disparities in the care of AAs with ESRD. A retrospective cohort study of the clinical database of the department of defense medical system of beneficiaries with CKD stages 3–5 indicated that over the period of 12 months, compliance with the National Kidney Disease Outcomes Quality Initiatives clinical and biochemical targets was essentially identical for both AAs and CAs, or in a number of cases, higher for AAs than for CAs. The equity in achieved clinical and biochemical targets was attributed to the positive influence of equal access to care, early referral, and compliance with Kidney Disease Outcomes Quality Initiatives targets related to identification of disease progression and treatment.

Peritoneal dialysis and in-home hemodialysis are patient-centric treatment modalities that should be offered to all ESRD individuals. Data from 2014 show that AAs compared to CAs are underrepresented in the in-home dialysis population (6.4 vs. 9.2%) [1]. This racial disparity may be inaccurately ascribed to the entire nation, since considerable regional and inter-state variability exist. The intervention thought to most likely attenuate the racial disparities of in-home dialysis and access to kidney transplantation is improved education [59], and particularly education of potential donors, recipients and clinicians [60, 61]. The first step in the process would be early diagnosis and referral to a nephrologist for the patient with advanced CKD to allow more time for education. Notably, Medicare covers up to 6 sessions of education services for advanced CKD (stage IV) patients to learn about kidney disease [62].
low for more timely preparation that would facilitate the possibility of preemptive kidney transplant and home dialysis therapies. Sequence and time of educational interventions are important to emphasize for a population that has multiple challenges as outlined in this paper. Simple education delivery to patients may be the most scalable for dissemination, and should include education for dialysis clinic staff as well as nephrologists. Effective strategies for providing education may include patient navigators [8], and dedicated patient educators who visit dialysis clinics and/or visit patients in their social environment [63], and the use of live donor champions [64].

Although hemodialysis patients have an overall higher mortality rate relative to the general population, for many years a paradoxical 45% lower mortality in AAs vs. CAs has been observed in the hemodialysis setting [65]. The reasons for this are not entirely clear but likely include younger age (<50 years) at dialysis initiation and higher body mass index despite other factors such as higher use of catheters that would increase mortality [66]. This reverse disparity results in bias among clinicians to not refer AA hemodialysis patients for transplantation, since some have suggested that dialysis should be the preferred therapy for ESRD in Black patients [67]. However, US Renal Data System data indicate that the advantages of transplantation over dialysis, including significant prolongation of life expectancy, are enjoyed by AAs as well as all other races or ethnic backgrounds [4].

**ESRD Informatics at the Point of Care**

There is an opportunity to develop a new paradigm that identifies and defines the clinical, environment, and socioeconomic dataset that provides the most accurate indicator of health status and well-being of AAs ESRD. There is also an essential need for a core set of meta-data attributes that key clinical, financial, and administrative stakeholders can benefit from to ensure care coordination and continuity of care for the ESRD patient. In a study of CKD of unknown origin, which causes ESRD in tropical countries, Wimalawansa and Wimalawansa [68] created a multifactorial etiology model of 3 meta-data domains that could reduce the overall health outcome due to genetic or other disposition. The premise of the model was to determine the impact of hard or soft water on patients, along with clinical and sociological factors. The author showed, through longitudinal studies, that in contrast to previous dogma, there is no measurable impact of these factors on the outcome of patients with CKD [42]. In a similar way, common risk factors for progressive CKD in the United States may be incorporated into a model specific for ESRD. This would spur the development of more comprehensive clinical assessments, and expand the use of industry codes and modifiers to provide new insights into the impact of environmental toxins, such as exposure to lead, on clinical outcomes.

**Development of a Continuity of Care Data Model for ESRD**

A continuity of care data model specifically for ESRD may be developed based on a study conducted by Huang et al. [69]. A comprehensive approach was developed across the kidney disease spectrum including death. A visualization tool was created based on a Sankey diagram that represented the comorbidity and progression of kidney disease over time. The tool has the potential to help clinicians when deciding on the management of ESRD patients [69]. In terms of medical education, it can be used to assist with understanding the nature of a complex chronic disease by showing the dynamics between the comorbidities and ESRD outcomes in a temporal fashion. The author hypothesized that data visualization of comorbidities and outcomes may lead to better understanding of the disease pathogenesis [69]. Efforts in this direction will eventually aid in prediction and disease prevention, personalization of diagnosis and treatment, as well as greater participation of patients in the healthcare system.

**National Kidney Disease Education Program Health Information Technology Workgroup**

The NIH National Institute of Diabetes and Digestive and Kidney Diseases National Kidney Disease Education Program Health Information Technology Workgroup and 3 subgroups (the CKD Care Plan Working Group, the CKD Computable Phenotype Working Group, and the CKD Business Case Working Group) recently launched the Managing Chronic Disease Populations through Health Information Technology platform [70]. The workgroup consists of a multidisciplinary team of clinicians, patient advocates, and public health and health information technology specialists to guide the development of a comprehensive clinical data set that is specifically designed to enable ESRD care teams to capture essential information aligned to best practices in care management at all stages of CKD, including ESRD. In addition, the mission of the workgroup is to ensure that data specifications can be adapted to electronic health record standards supported by the Department of Health and Human Services. Incorporating a structured data set into elec-
Electronic health records will significantly improve the clinical intelligence of providers treating patients who are at risk for ESRD, especially AAs.

**Call to Action**

The development of ESRD knowledge management and patient engagement strategies that reflect evidence-based care plans focused on mitigating social determinants is essential. These types of care plans would facilitate best practices in disease management for ESRD. Based on this review, an approach may consist of the following strategies. Please see Table 1 for a summary.

**Enhance Patient Engagement**

Develop a culturally sensitive patient-engagement strategy that addresses the need to acknowledge preexisting reservation and distrust that AAs with ESRD have experienced related to his or her patient care. This includes proactively initiating provider-patient discussions regarding mutual healthcare goals, EOL choices and social determinant factors that may impede patients’ ability to achieve their goals. The current timing cannot be better, given the renewed advocacy and funding of nationally recognized efforts sponsored by the Centers for Medicare and Medicaid Services and the Centers for Disease Control and Prevention to address healthcare disparities in ESRD. These include national initiatives such as Centers for Disease Control and Prevention’s Healthy People campaign to address healthcare disparities for high-risk patient populations based on race, gender, and sexual orientation [71].

**Enhance Professional and Patient Education**

The National Kidney Foundation and the American Society of Nephrology have both been instrumental in providing guidelines and education related to the care of AAs with ESRD. Enhance patient engagement, patient education, use of patient navigators/educators, live donor champions

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<th>Concerns</th>
<th>References</th>
<th>Interventions and call to action</th>
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<td>community-related</td>
<td>Awareness of risks and progression of CKD/ESRD, fear of healthcare systems, end-of-life support, use of hospice care</td>
<td>[23–26, 30]</td>
<td>Provide equal access to education</td>
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<td>Equal access to education, socio-economic status, awareness of healthcare policies</td>
<td>[15, 16, 19–21]</td>
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<td>Practitioner-related</td>
<td>Inadequate communication, treatment misconceptions, lack of appropriate/timely care, poor access to health education, reduced access to research Access to home dialysis therapies</td>
<td>[42, 43]</td>
<td>Timely referrals for preemptive transplantation, reduce bias</td>
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<td>Enhance education, compliance with KDOQI guidelines</td>
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<td>Provide equal access to home dialysis</td>
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<td>Encourage utilization of Medicare-covered education services</td>
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<td>Genetic-risk for progressive kidney disease, pharmacogenomic testing for precision medicine</td>
<td>[44–46, 51, 54, 57]</td>
<td>Participate in NIMHD precision medicine research program to promote health equity</td>
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<td>Predominance of CAs among healthcare practitioners</td>
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<td>Enhance accountable partnerships</td>
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<td>Develop multifactorial risk-factor data model to predict health status</td>
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<td>Adapt comprehensive clinical dataset to the EHR</td>
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<td>Encourage discussion on advance care planning</td>
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Table 1. Summary of disparities in care of AAs with ESRD
patients at all stages of CKD. Recent strategies to disseminate education to primary care physicians on CKD by the National Kidney Foundation and recommendations to Centers for Medicare and Medicaid Services addressing new pathways to optimize quality of care for patients may succeed in reducing healthcare disparities of high risk AA patients with ESRD. A concerted effort by other new and established organizations committed to the care of patients with ESRD would greatly enhance these efforts.

Enhance Accountable Partnerships

Accountable Care Organizations are groups of doctors, hospitals, and other health care providers who come together voluntarily to give coordinated, high-quality care to their Medicare patients. Through the Affordable Care Act of 2010, the goals of Accountable Care Organizations were to ultimately improve the clinical outcomes of patients with CKD and ESRD. To further advance the goals of these partnerships, primary care physicians and multi-specialty practices who treat ESRD should consider the current knowledge, data management maturity, and the strategic approaches necessary to improve areas of healthcare and health disparities faced by AAs. The recommendation goes beyond incentivized efforts supported by private and federal payer initiatives. Another approach to reduce or eliminate disparities in the care of AAs with ESRD may include a complete assessment of the points of failure at all levels and implementation of accountable partnerships between the patient, the provider and the payer. The advent of sophisticated information technology provides a population health platform for accurate data collection that may facilitate coordinated care, identification and implementation of new, related policy measures, and ultimately significantly improved clinical outcomes for AAs with ESRD.

Advance the Use of Clinical Intelligence:

There should be a long-term approach to the process of evolving the practice to achieve measurable goals associated with clinical intelligence and population health management as well as clinical risk intervention and predictive analytics. The impact of nontraditional factors and clinical intelligence that are not sufficiently covered within ESRD medical training that may directly impact outcomes in the care for AAs should be investigated. This includes areas related to environmental factors in addition to sociological, behavioral, and clinical determinants that AAs with ESRD may face as barriers to consistent healthcare delivery. The goal would be to develop a care model (being developed by co-authors) that supports and leverages personalized medicine and available digital platforms, with access to industry and quality-certified CKD and ESRD databases and knowledge networks.

Conclusion

A new era of opportunity to reverse the trend of healthcare disparities within the AA ESRD patient population is within the reach of the healthcare community. It is essential to convert the significant concerns of healthcare disparities into prioritized efforts in order to achieve improved outcomes for this high-risk patient population. By the year 2050, racial and ethnic minority groups will comprise most of the US population. Thus, there is an urgent need for research studies focused on the elimination or reduction of health disparities including ESRD in AAs to reduce or eliminate potentially significant burdens on the healthcare system, and the society at large.

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Disclosure Statement

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