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A Retrospective Study of Research Data on End Stage Renal Disease

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Summary

The growing incidence of end stage renal disease (ESRD) in the United States is a cause for concern. The main objectives of this research were to study the contribution of demographic factors and medical conditions to ESRD by developing statistical models of age, gender, race, and co-morbid factors. Data analysis of the United States Renal Data System indicated that from 1980–2011 the ESRD incidence increased at a high rate of 6.23% while the US population grew at 0.99%. Results showed that the older population carried an increased ESRD burden. Males and females did not have a significant difference in incidence. People with European ancestry had the highest incidence in absolute terms while African Americans had the highest per capita rate. While diabetes and hypertension were significant contributors, glomerulonephritis was highly prevalent among the young. In absolute terms, all top ten incidence groups consisted of 70+ year old white Americans, with either diabetes or hypertension. In per capita rates however, nine of the top ten incidence groups consisted of 70+ year-old African Americans with either diabetes or hypertension. In summary, this work provides a better understanding of ESRD trends and offers mathematical models to predict ESRD incidence over time.

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Glossary

- ESRD: End Stage Renal Disease
- PMP: Per Million Population
- USRDS: United States Renal Data System
- CKD: Chronic Kidney Disease

Introduction

Kidney disease is the 8th leading cause of death [1] in the United States, and it is estimated that around 31 million Americans [2] suffer from some form of chronic kidney disease (CKD). End Stage Renal Disease (ESRD) is the terminal stage of CKD, and unless patients receive a transplant or undergo dialysis, ESRD can be terminal. Recent studies have noted that the number of patients diagnosed with ESRD is increasing at an annual rate of about 5% [3]; therefore, understanding this condition is of prime importance to medical professionals and patients. Gilbertson et al. [4], in their 2005 study, noted that by 2015, the ESRD rates would increase by 44% and the per million population (PMP) rate by 32%.

While the ESRD burden is inversely related to income level, males and older patients have a higher incidence [9, 10]. Chronic kidney disease in older adults also means that, in addition to ESRD, they would also suffer from cognitive impairment and physical decline [10, 11]. Diabetes, hypertension, and age are important predictors of ESRD [12, 13]. Several works [14, 15] have studied whether the higher hypertension rates among African Americans explained the increased ESRD incidence and concluded that even after controlling for this factor, they have a disproportionate ESRD risk when compared to white Americans. Further, ESRD incidence is inversely proportional to socio-economic status [15]. While poverty at all levels is associated with higher ESRD risk, African Americans are at a greater disadvantage [16]. Native Americans and Asians also have a higher risk of ESRD [17, 18]. In terms of gender, women are at a lower risk than males but have a higher prevalence of CKD [19]. From a disease perspective, diabetes was noted as a major cause of ESRD [20]. Further, one-fourth of all ESRD cases are attributed to hypertension [21], while glomerulonephritis is significantly prevalent among younger patients [22].

To fully understand the incidence trends over a 32-year study period and to illustrate the increasingly morbid ESRD issue, as opposed to just studying individual values, we studied ESRD incidence over time. The main objectives of this research were to study the ESRD incidence over time and to understand the contribution of underlying disease factors and the burden of ESRD by age, gender, race, and underlying medical conditions. Hence, the following hypotheses were developed: 1) As age progresses, ESRD incidence also increases in both absolute values and per million population (PMP) rates. 2) Males tend to have a higher ESRD incidence

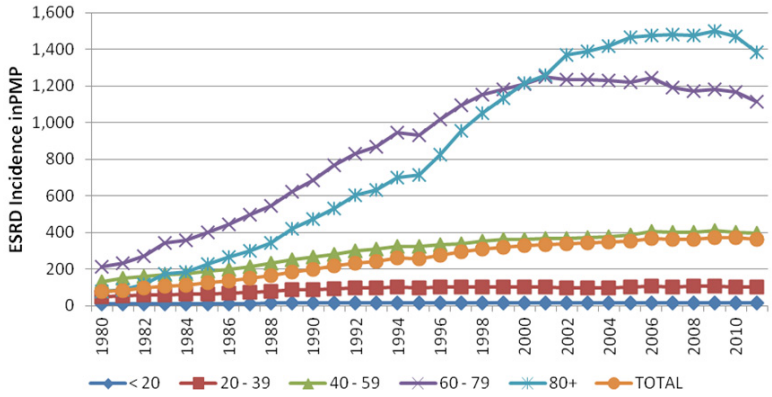

Figure 1: ESRD incidence by Age Groups in PMP. In this figure, the blue line represents under-20 year-olds, red is the 20-39 age group, green is the 40-59 year-olds, purple is the 60-79 year-olds, light blue is the 80+ year-olds and the orange line is the total incidence.

than females. 3) There will be no difference in the ESRD incidence between race groups. 4) Diabetes, hypertension, glomerulonephritis, and cystic kidney disease have varying impacts on age, gender, race, and disease factors.

While the hypotheses were established after reviewing the available literature, care was taken to ensure that previous research did not dictate or create any presumptions. In particular, hypothesis 3 was defined as such so that no presumptions were made about either the absolute or PMP values for the race groups. Previous research also did not study per capita values and so there were no concrete data that suggested that ESRD rates would differ for the races. Given the purpose and objectives of this research, a literature search was conducted to define the stated hypotheses. The United States Renal Data System (USRDS) [7] data for the 1980–2011 period were obtained and analyzed. The population data [8] were then used to normalize ESRD incidences and to calculate the PMP rates. The USRDS is supported by the National Institute of Diabetes and Digestive and Kidney Diseases. It contains extensive ESRD data including patient characteristics and treatment modalities. The data from the 'incidence' reference tables of USRDS were used.

Results

Trend Analysis

This section presents the ESRD incidence analysis by age, gender, and race.

Age

The best fit linear regression line for the total ESRD incidence, with time as the independent variable, has a near perfect coefficient of correlation ($R^2 = 0.99$) (**Figure 1**). The PMP trends for the under-20 and 20–39 year-olds were generally stable during the study period. For the 40–59 and 60–79 age groups, the gap between ESRD incidence widened, resulting in growth rates of 5.77% and 6.98%, respectively. The 80+ year olds experienced a very high growth rate of 12.44% despite having fewer cases. Between 1980 and 2002, the PMP rates for the 60+ age groups were higher than those of others, possibly due to an increase in awareness about

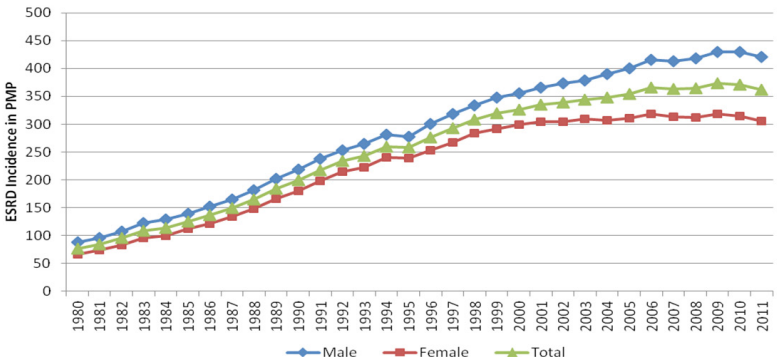

Figure 2: ESRD incidence by Gender in PMP. The blue line in this graph represent the male ESRD incidence, the red trend describes the female incidence and the green line represents the total incidence.

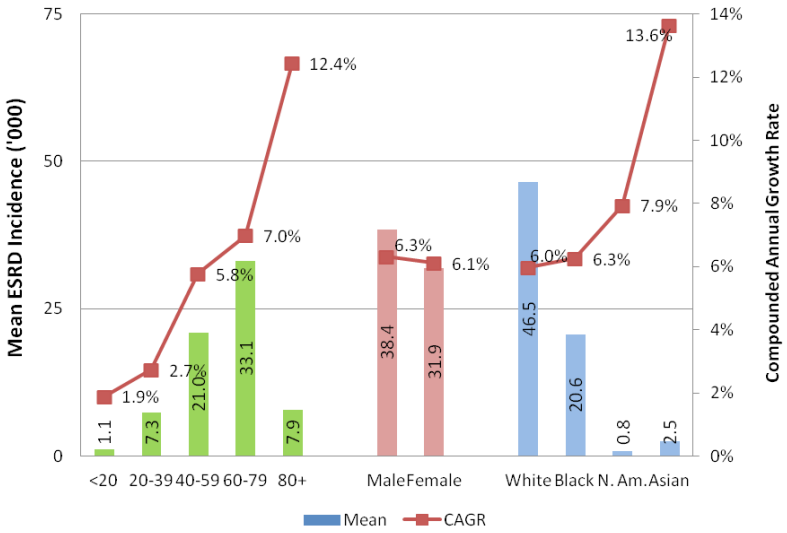

Figure 3: ESRD Incidence and Growth Rate (1980-2011). The green bars here represent the age groups, the red bars represent the gender groups and the blue bars represent the race groups. This graph is describing the CAGR, i.e. the Compounded Annual Growth Rate, versus the Mean ESRD incidence, i.e. the average incidence from 1980-2011 in units of 1000 cases.

kidney disease. After 2002, the rates per year stabilized, possibly due to an improvement in healthcare during recent years.

Gender

In 1980, males and females had PMP incidences of 87.5 and 65.7 cases, respectively (**Figure 2**). The gender incidence gap in the incidence increased slightly over time, yielding growth rates of 6.31% and 6.11%, respectively (**Figure 3**).

Race

ESRD incidence for whites and African Americans increased steadily (**Figure 4**), but the latter group had a slightly higher growth rate. Although whites had the highest ESRD incidence, African Americans had the highest per capita rates. Asians had a high growth rate of 13.63% (**Figure 3**). Native Americans' PMP incidences varied; they had an overall growth rate of 7.94%.

Underlying Factors

The four disease factors by which USRDS categorized the data have collectively contributed to 81% of all ESRD cases. Anand et al. [23] also showed that these factors comprised about 44% to 80% of diseases requiring renal replacement therapy.

Age

Figure 5 shows that glomerulonephritis was the causal factor in 77% of all under-20 year-olds' cases.

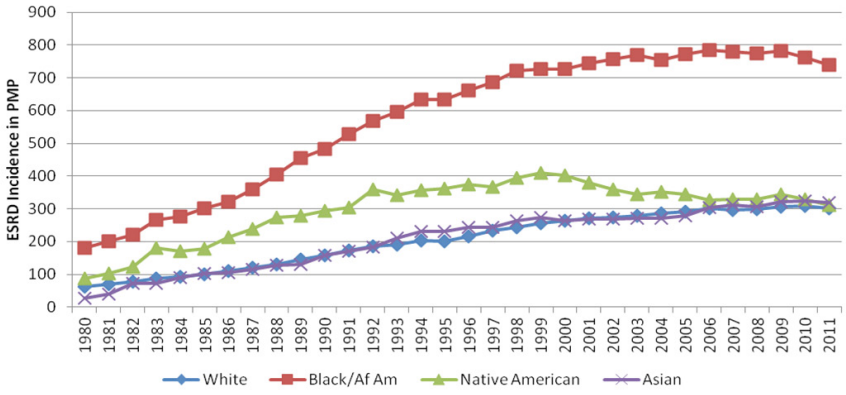

Figure 4: ESRD incidence by Race in PMP. The blue line in this graph represent the white population ESRD incidence, the red trend describes the African-American incidence, the green line represents the Native American incidence and the purple line is the Asian population incidence.

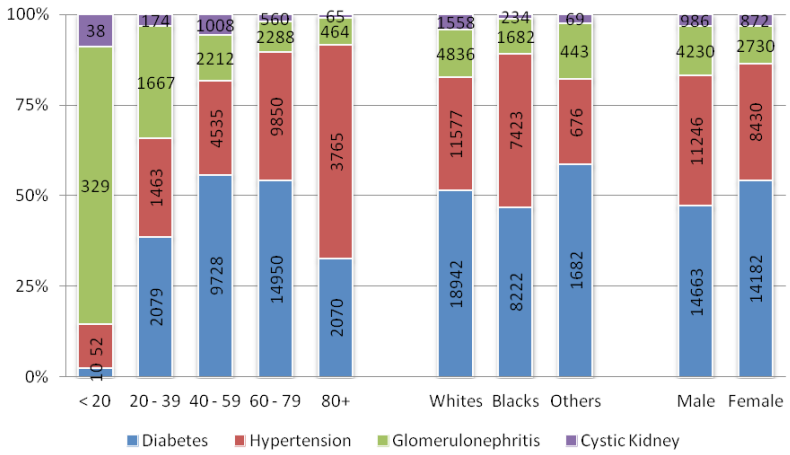

Figure 5: Percentage distribution of factors within each disease category. This graph represents the total incidence for the 32 year period for each factor group within each disease.

Diabetes alone contributed to about 50% of the ESRD cases among the 20–79-year-olds. Among the 80+ year-olds, hypertension was the most prevalent factor. These four diseases contributed to about 70% of ESRD cases among all age groups.

Gender

Figure 5 illustrates that the percent disease incidence for both genders are similar. Diabetes contributed to about 50% of cases among males and females. The four disease factors comprised about 80% of all cases for males and females.

Race

Figure 5 also shows that diabetes is the most dominant disease factor, with a contribution of about 50% for both whites and African-Americans. Hypertension had slightly lower values associated with these two groups.

Statistical Analysis and Person Characteristics

ANOVA

In order to determine if the differences in the mean ESRD incidence were only observational or if they were statistically different, an analysis of variance (ANOVA) was performed **(Table 1**) on the 1980–2011 data. Using the data values from the 32-year study period of ESRD incidence, the ANOVA was conducted on each factor (age, gender, etc.) separately. The time data for the study period and rates of incidence were not considered for the ANOVA. The absolute ESRD incidences for each year of the 32-year study period were the input data for these analyses. Thus, for instance, there were 32 ESRD values each for males and females; an ANOVA on gender would therefore compare the incidence using the dataset of 32 incidence values for each category. In the case of age, there were 32 ESRD incidence values across time for each of the five age groups. Similarly, four sets of 32 values were subjected to ANOVA in the case of race; the same is true of disease factor. As an example, the result of the ANOVA on gender is depicted in **Table 1**. After ANOVA was conducted on each of the four factors, the results were compiled into **Table 2**. The null hypothesis was that the mean ESRD incidence would be the same among the groups within each parameter, while the alternate hypothesis was that they would be significantly different among the groups within each parameter.

Performing ANOVA on the 32 values each for the five age categories (degrees of freedom = 5-1) gave an F_{stat} of 68.05, which is more than the F_{crit} of 2.43; this means the p-value will be much less than 0.05 (95% confidence interval). Thus, the null hypothesis can be rejected, meaning that the mean ESRD incidence values among

ANOVA

Source of Variation	*SS*	*df*	*MS*	*F*	*P-value*	F_{crit}
Between Groups	6.78E+08	1	6.78E+08	2.413714	0.125367	3.995887
Within Groups	1.74E+10	62	2.81E+08			
Total	1.81E+10	63				

Table 1: Gender ANOVA Result

	df	F_{stat}	F_{crit}	*p-value*	Reject Null?	Remarks
Age	4	68.05	2.43	3.80E-33	Yes	Mean ESRD values are significantly different at 5% significance.
Race	3	103.07	2.68	1.57E-33	Yes	
Disease	3	51.55	2.68	1.06E-21	Yes	
Gender	1	2.41	4.00	0.125	No	Not different

Table 2: ANOVA Summary for 4 study factors

the five age groups are significantly different from each other. This was also the case with race and disease.

However, in the case of gender (i.e., ANOVA on 32 values each for males and females) the p-value is 0.125 (> 0.05), meaning that the mean ESRD incidence between males and females is not statistically different. Therefore, in the case of gender, an additional analysis was conducted for the male-female difference in ESRD incidence over the 32-year study period (**Figure 6**). The trend line for these data had an R^2 of 0.9679 and a correlation of 0.984. This strong R value and increasing trend indicate that, despite not being significant, there is a difference in ESRD incidence over time due to gender.

Top Ten Person Characteristics

All of the top incidence groups, compiled from the individual groups of a specific age, gender, race and disease characteristics, featured 50+ year-old Whites (**Figure 7**). Six groups included diabetics, while four consisted of hypertensive patients.

This process was repeated for PMP analysis (**Figure 7 right panel**). Nine categories included African-Americans; six categories included diabetes and four comprised hypertension, and all included 60+ year-olds. The top two categories were 80+ and 70–79 year-old African-American men who had hypertension and diabetes, respectively.

Discussion

Data analysis showed that the population grew at a much lower rate of 0.99% than ESRD incidence (6.23%). One reason for this difference could be the increasing awareness about and consequent diagnosis of ESRD cases. While young ESRD patients' mortality rate was 30 times that of non-afflicted children, their survival rate increased over time [12]. The high ESRD incidence among the 40+ year-olds could be due to lifestyle factors such as stress and lack of exercise. The results from this work show that the incidence gap between males and females has increased recently, even though a clear relationship could not be drawn due to a lack of record-level data. Analysis suggested that females are at a lower ESRD risk than are males. Native Americans experienced the lowest growth rate, probably due to lack of awareness about ESRD; additional research is required in this area. Asians had higher rates than whites possibly due to increased awareness or access to healthcare [24]. African-Americans had three times the PMP incidence of whites, likely because of increased hypertension risk. Consistent with literature, diabetes is a major cause of ESRD. Glomerulonephritis was significantly prevalent in the under-20 year-olds. Further research into the impact of diabetes and hypertension on ESRD would help provide ways to address the growing ESRD burden.

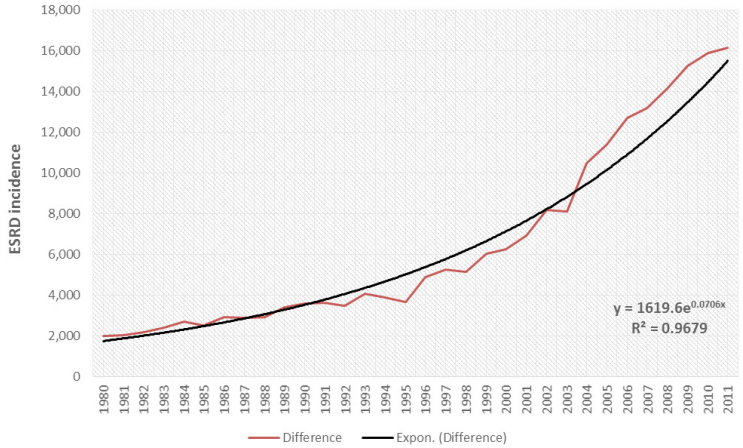

Figure 6: Difference in Male and Female ESRD incidence over time. In this figure, the "difference" trend is the difference between the male and female incidence across the time period, and the "expon. Difference" line describes the exponential regression line for the difference line.

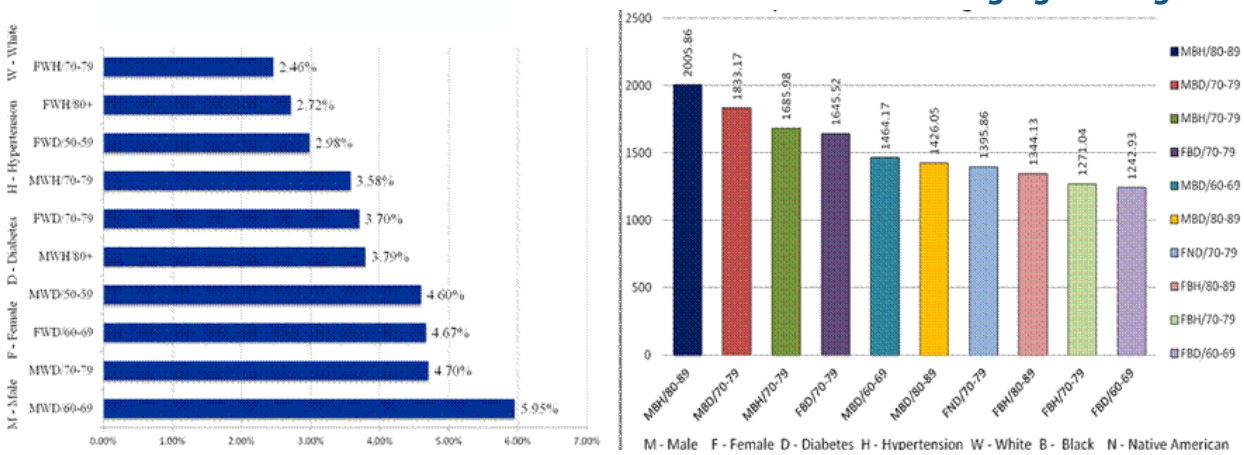

Figure 7: Top Ten Person Types in Absolute (%) and PMP ESRD Incidence. IIn this figure, which represents the top ten person incidence types, M represents male, F represents female, D represents diabetes, H represents hypertension, W represents white, B represents black, and N represents Native American.

In summary, hypotheses 1, 2, and 4 were shown to be true, while hypothesis 3 could not be disproved. The ESRD burden in the US continues to grow, with regression models predicting that the incidence will peak by the year 2050 [25]. Each subsequent age group showed higher risk; the 80+ year-olds experienced the highest growth rate. This demonstrates the need to attend to ESRD-afflicted senior citizens. Males were at a slightly higher risk than females, possibly due to lifestyle differences. In absolute terms, white Americans had the highest ESRD incidence, but African-Americans had higher incidence in PMP terms. Similar to other works, this research also showed that diabetes was the predominant factor.

This work illustrated that ESRD is an important public health concern for both medical researchers and patients. Trend analysis has shown that certain groups (i.e. older, male, African-American patients with diabetes) have a higher risk of suffering from ESRD. Researching why these groups are at a greater risk and developing a mathematical model are avenues for future research.

Materials and Methods

The USRDS data was frequently referred to in the literature. Although the database was extensive, only relevant information from the Annual Data Report Reference Table A [7] was selected. These data were available for the years 1980–2011. Microsoft Excel was used to analyze the data and create summary graphs and models. The original age data from the USRDS were grouped under 14 age categories. For more manageable analysis, the data were grouped into five intervals in 20-year increments. The data comprised four race categories, i.e. white, black, Native American, and Asian. With regard to medical conditions, the race categorical data were used in their original format (i.e., White, Black, and Other). Initially, the absolute number of incidences was evaluated. After noting that the population size within the various factors varied, the absolute values were converted to PMP, rates for normalized analysis. For the medical conditions analysis, the absolute values were converted to percentages in order to assess the influence of a particular condition within the study groups. For the analysis of the ten groups with the highest absolute and PMP incidences, the original nine age groups from USRDS, two genders, four race groups, and four disease factors were compiled to produce 288 combinations of individual-level characteristics. The percent of total absolute ESRD incidences for the combinations were computed and sorted in a descending order.

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