The Epidemic of Diabetes Mellitus in the ESRD Population

United States Renal Data System
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Structure of the USRDS

Larry Agodoa, MD
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NIH, NIDDK, DKUHD
United States Renal Data System

Cardiovascular SSC

Economic SSC

Nutrition SSC

Rehabilitation/Quality of Life SSC

United States Renal Data System Coordinating Center
United States Renal Data System

- **New USRDS**
  - Coordinating Center-Director Allan Collins, Deputy Director Bertram Kasiske
  - Cardiovascular SSC-Director Charles Herzog, Deputy Director Blanche Chavers
  - Economic SSC-Director Lawrence Hunsicker, Deputy Director John Brooks
  - Rehabilitation/Quality of Life SSC-Director Nancy Kutner, Deputy Director Donna Brogan
  - Nutrition/Malnutrition SSC-TBA

- **2001 Annual Data Report**
  - online at: [WWW.USRDS.ORG](http://WWW.USRDS.ORG)
The Epidemic of Diabetes Mellitus in the ESRD Population

- Trends in Diabetes in the General Population
  - Allan Collins, MD, FACP
- Incidence, Prevalence, and Development of Diabetes in the ESRD Population
  - Blanche Chavers, MD
- Complications of Diabetes in ESRD
  - Charles Herzog, MD
- Diabetes in the Renal Transplant Patient Population
  - Bertram Kasiske, MD
The Epidemic of Diabetes Mellitus in the ESRD Population

- USRDS team contributing to this presentation
  - Dave Gilbertson, PhD
  - Shuling Li, MS
  - Michael Palzer, BS
  - Jon Snyder, MS
  - Eric Frazier, BS
  - Cheryl Arko
  - Shu-Cheng Chen, MS
  - Jennie Ma, PhD
  - Lingu Du, MS
  - Susan Everson, PhD
  - Edward Constantini, MS
  - Delaney Berrini, BA
  - Anne Murray, MD
  - Marshall McBean, MD
The Epidemic of Diabetes Mellitus in the ESRD Population

Allan J. Collins, MD FACP
Director
USRDS Coordinating Center
Trends in DM and CKD the General Medicare Population

- Prevalent population: Entry period
  - Prevalence of diabetes in the Medicare Fee For Service population
  - Prevalence of Chronic Kidney Disease in the Medicare Fee For Service population
  - Comorbidities in the DM and CKD population
  - ASHD, CHF, CVA/TIA, and major amputation/PVD

- Incidence of new DM, CKD, and ESRD:
  - Predicted in a one-year follow-up
Study population: 5% Medicare sample; Inclusion criteria

- Continuously enrolled in Medicare Part A and Part B during any two consecutive calendar years from 1996-1999
- Excluded patients: enrolled in HMO or diagnosed with End-Stage Renal Disease any time during study period
- Resided in 50 states
- Population cohorts: all patients surviving two years
  - 1996-1997 (N=1,286,780)
  - 1997-1998 (N=1,265,831)
  - 1998-1999 (N=1,252,189)
Identification of Diabetics and Chronic Kidney Disease (CKD) in the 5% sample

- Each patient survived the full two-year entry period in order to survey the Medicare claims*:
  - One or more claims from Part A services (inpatient hospitalization, or skilled nursing facility, or home health agency), or
  - Two or more claims from Part A (outpatient), or Part B physician/supplier services

- CKD inclusion

## Prevalence of Diabetes in the Medicare Population: Age 65+

<table>
<thead>
<tr>
<th>Sample size</th>
<th>1992-1993*</th>
<th>1,286,780</th>
<th>1,265,831</th>
<th>1,252,189</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Age group (year)</th>
<th>Prevalence of diabetes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>67-74</td>
<td>13.4</td>
</tr>
<tr>
<td>75 +</td>
<td>13.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Male</td>
<td>13.9</td>
<td>17.0</td>
<td>17.8</td>
<td>18.7</td>
</tr>
<tr>
<td>Female</td>
<td>13.4</td>
<td>15.8</td>
<td>16.5</td>
<td>17.2</td>
</tr>
</tbody>
</table>

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</thead>
<tbody>
<tr>
<td>White</td>
<td>12.8</td>
<td>15.3</td>
<td>16.0</td>
<td>16.7</td>
</tr>
<tr>
<td>African American</td>
<td>21.5</td>
<td>25.9</td>
<td>26.8</td>
<td>28.0</td>
</tr>
<tr>
<td>Overall</td>
<td>13.6</td>
<td>16.3</td>
<td>17.0</td>
<td>17.8</td>
</tr>
</tbody>
</table>

* Hebert et al, American Journal of Medical Quality 1999, 14:270-277
Participated Medicare Current Beneficiary Survey (MCBS) Access to Care 1992-1993
Prevalence of Diabetes, Overall

CDC BRFSS Report 2000* and 5% Medicare population

* BRFSS - Behavioral Risk Factor Surveillance System
Mokdad et al, JAMA 2001, 286:1195-1200
Prevalence of diabetes, by race

CDC BRFSS Report 2000* and 5% Medicare population

* BRFSS - Behavioral Risk Factor Surveillance System
Mokdad et al, JAMA 2001, 286:1195-1200
Prevalence of diabetes per 100 patients
5% Medicare sample

USRDS ASN 2001
Prevalence of diabetes and CKD
5% Medicare sample

<table>
<thead>
<tr>
<th>Year</th>
<th>DM, CKD</th>
<th>DM, no CKD</th>
<th>No DM, CKD</th>
<th>No DM, no CKD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1996-1997</td>
<td></td>
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<td>1998-1999</td>
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</tr>
</tbody>
</table>
Cardiovascular Comorbidities, 5% Medicare sample, by Diabetes and CKD status, 1996-1997
New CKD and Diabetes*: 1997-1998 Cohort
5% Medicare patients not diagnosed with CKD or DM in the 2 years entry period: 1 year follow-up

<table>
<thead>
<tr>
<th>Status in the entry period</th>
<th>New CKD</th>
<th>Follow-up period</th>
<th>New DM</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM/Non-CKD</td>
<td>5.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NDM/Non-CKD</td>
<td>2.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CKD/NDM</td>
<td></td>
<td>4.77</td>
<td></td>
</tr>
<tr>
<td>Non-CKD/NDM</td>
<td></td>
<td></td>
<td>2.86</td>
</tr>
</tbody>
</table>

*unadjusted

USRDS ASN 2001
**Incidence rate of ESRD**: 1997-1998 Cohort

5% Medicare patients, one year follow-up

<table>
<thead>
<tr>
<th>Status in the entry period</th>
<th>ESRD / 100 patients years</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM/CKD</td>
<td>4.13</td>
</tr>
<tr>
<td>DM/Non-CKD</td>
<td>0.14</td>
</tr>
<tr>
<td>NDM/CKD</td>
<td>1.44</td>
</tr>
<tr>
<td>NDM/Non-CKD</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*Unadjusted
Conclusions: Diabetes in the general population

- The prevalence in DM in the Medicare population has increased 31% in the last 6 years.
- Blacks and Hispanics have the highest prevalence of diabetes at approximately 25%.
- The highest prevalence of DM is in the industrial NE and the southeastern part of the US.
- Approximately 4% of the Medicare population carries a diagnosis of CKD (Est. N=1.1 million).
- Co-morbidity is highest in those patients with DM and CKD.
- Approximately 5% of non-DM patients develop DM in a year.
Trends in ESRD Incidence Rates for Diabetes

Blanche Chavers, MD
Co-investigator
USRDS Coordinating Center

Deputy Director,
Cardiovascular Special Studies Center
United States Renal Data System
Incident rates for diabetic ESRD, all patients
adjusted for age, gender, ethnicity & race
Incident rates: diabetes, all per million population, by HSA, smoothed & adjusted for age, gender, & race (2001 ADR, fig 1.8)
Incident rates, by primary diagnosis & race
dialysis patients, adjusted for age & gender (2001 ADR, fig 1.14)
Incident rates for diabetic ESRD, adjusted for race & gender

Pediatrics (0-19)

Adults (20+)

USRDS ASN 2001
Diabetes at initiation, by race/ethnicity
1999, all patients (2001 ADR, fig 2.18)
Incident rates for diabetic ESRD, by ethnicity, all dialysis patients, adjusted for age & gender
Incident rates for diabetic ESRD, HD
by race, adjusted for age & gender

0
100
200
300
400
500
600


per million population

White
Black
Native American
Asian
First- & second-year death rates, by primary diagnosis: hemodialysis
incident patients, adjusted for age, gender, & race (2001 ADR, fig 8.11)
First- & second-year death rates, by primary diagnosis: peritoneal dialysis incident patients, adjusted for age, gender, & race (2001 ADR, fig 8.12)
Likelihood of NDM patients developing DM on dialysis

- Type of study: Incident patients, 1995-1999 (n=139,241)
- Define NDM cohort:
  - Non-DM primary cause of renal disease on ME form
  - No secondary Dx of DM in the comorbidity part of the ME form
- Entry period: all patients survived one year past the ESRD first service date
- Variables: Age, gender, race and comorbidity as defined in the one-year entry period from Medicare claims
- Endpoint: DM in the 1, 2 and 3 year follow-up period
- Statistical method: Cox regression, likelihood of developing DM in the follow-up period
- Censoring at death, transplant, LTF and end of the study
Percent patients developing DM in NDM incident dialysis patients: cohorts 1995-1999* 

NDM in one-year entry: % developed DM in the follow-up period

*Adjusted for age, gender, race and comorbidity in the one-year entry
Conclusions

- Incident rates for ESRD due to diabetes showed a persistent increase in the number of U.S. adult dialysis patients from 1991 to 1999.
- Incident rates for ESRD due to diabetes increased in adults across all racial groups from 1991 to 1999.
Hispanics have the highest incident rates of ESRD secondary to diabetes.

Between 1991 and 1998, new onset of diabetes developed in about 2% of children and 18% of adults who survive an entire year.

Non-diabetics who survive an entire year have a 12% adjusted likelihood of developing diabetes in the second year.
Complications of Diabetes in ESRD
Charles A. Herzog, MD

Director,
Cardiovascular Special Studies Center
United States Renal Data System
Study design

- Retrospective
- Data source: USRDS database (including Part A (institutional) and Part B (physician/provider) claims data
- Incident dialysis patients (Medicare-eligible), 1995-1999
- All patients in study survived one year after dialysis initiation
- Follow-up time begins one year after dialysis initiation
Study design (cont.)

- Comorbid conditions at time of dialysis initiation determined from Medical Evidence Form 2728
- Event rates estimated by Cox regression
- Survival of subgroups estimated by life table method and Cox regression
- Endpoints: AMI, cardiac arrest, PVD, CVA/TIA, coronary revascularization, cardiac death, all-cause death
Study design
Patient groups by diabetic status

- Group 1: Diabetic ESRD (1 year cause of ESRD=DM)
- Group 2: Non-diabetic ESRD (1 year cause of ESRD ≠ DM); DM as comorbid condition at dialysis initiation
- Group 3: Non-diabetic ESRD (1 year cause of ESRD ≠ DM); no DM at dialysis initiation; “new” diagnosis of DM in the first year after dialysis initiation
- Group 4: No DM in first year after dialysis initiation
Gender

- Male: 47.2%
- Female: 52.9%
Patient group (DM)

Group 1 N = 124,000
Group 2 N = 18,100
Group 3 N = 29,529
Group 4 N = 109,712
Comorbid conditions at beginning of study

Comorbid conditions

Group 1 (Primary DM)
Group 2 (Med.evid DM)
Group 3 (Claim DM)
Group 4 (Non-DM)

ASHD  CHF  Card. oth.  CVA/TIA  PVD  COPD  Cancer
Event rates for AMI
Adjusted for age, race, gender, and comorbidity

Follow-up (years)
rate per 1,000 patient years
group 1 (Primary DM)
group 2 (Med.evid DM)
group 3 (Claim DM)
group 4 (Non-DM)
Event rates for coronary revascularization
Adjusted for age, race, gender, and comorbidity

Follow-up (years)
rate per 1,000 patient years
group 1 (Primary DM)
group 2 (Med.evid DM)
group 3 (Claim DM)
group 4 (Non-DM)
Event rates for CVA/TIA
Adjusted for age, race, gender, and comorbidity

Follow-up (years)
rate per 1,000 patient years

- group 1 (Primary DM)
- group 2 (Med.evid DM)
- group 3 (Claim DM)
- group 4 (Non-DM)
Event rates for PVD
Adjusted for age, race, gender, and comorbidity

Follow-up (years)
rate per 1,000 patient years

- group 1 (Primary DM)
- group 2 (Med.evid DM)
- group 3 (Claim DM)
- group 4 (Non-DM)
Adjusted event-free survival for PVD

- Group 1 (Primary DM)
- Group 2 (Med. Evid. DM)
- Group 3 (Claims DM)
- Group 4 (Non-DM)
Adjusted event-free survival for cardiac arrest

Graph showing event-free survival over months for different groups:
- Group 1 (Primary DM)
- Group 2 (Med. Evid. DM)
- Group 3 (Claims DM)
- Group 4 (Non-DM)
Adjusted event-free survival for cardiac death
Adjusted event-free survival for all-cause death

- Group 1 (Primary DM)
- Group 2 (Med. Evid. DM)
- Group 3 (Claims DM)
- Group 4 (Non-DM)
Survival after cardiac events:
Coronary revascularization
AMI
All-cause survival after coronary revascularization: Diabetic

- STENT
- PTCA
- CAB(IMG-)
- CAB(IMG+)

P < .0001
All-cause survival after AMI: Diabetic
Conclusions

- Diabetic dialysis patients are a high risk group for cardiovascular complications.
- Diabetic status (irrespective of the primary cause of ESRD) is an important determinant of cardiovascular morbidity and mortality.
- Diabetic dialysis patients have high mortality after cardiac events.
Diabetes in the Renal Transplant Population

Bertram Kasiske MD, Jon Snyder MS

Coordinating Center
United States Renal Data System
Population
drug information only available past 1996

First UNOS transplants 1996-1998
34,575

Non-DM, Medicare Primary Payer, No Group Health Coverage, Alive for at least 1-year post-transplant
10,228

With Drug Information at Time of Transplant
8,818

30%
86%

Population drug information only available past 1996
Transplants Per Year

- 1996: 3,077
- 1997: 3,199
- 1998: 2,766

USRDS ASN 2001
Development of DM First Year Post-Transplant

- 1996: 14.1%
- 1997: 15.2%
- 1998: 16.9%
Modeling the Development of DM in the First Year Post-Transplant

- **Recipient Characteristics**
  - Age, race, and gender
  - Primary cause of disease
  - Education level
  - Employment ability
  - Hispanic ethnicity
  - Recipient obesity

- **Transplant Characteristics**
  - Transplant year
  - Preemptive transplantation
  - HLA mismatches
  - Cold ischemia time
  - PRA
  - Maintenance immunosuppression therapy at time of transplant

- **Donor Characteristics**
  - Age, race, and gender
  - Donor type
Significant Predictors of Developing DM
Odds of developing DM within the first year post-transplant

Odds Ratio

- 0.5
- 1.8
- 1.5
- 0.7
- 0.9
- 1.5
- 1.7
- 1.9
- 1.2
- 2.2
- 3.1
- 1.6
- 0.9
- 1.0
- 1.5
- 2.0
- 2.5
- 3.0
- 3.5
- 4.0

Age: 0-17, 45-59, 60+
Race: Black, Other Race, Hispanic
Education: College+
Employment: Able to Work
Body Mass: Obese
Donor: Male
Immunosuppression: Tacrolimus
Ref: 18-44
Ref: White
Calcineurin Inhibitor Use

1996-1998 Combined

8.7% Cyclosporin

66.5% Neoral

17.9% Tacrolimus

0% 20% 40% 60% 80% 100%


Cyclosporin

Neoral

Tacrolimus

USRDS ASN 2001
Odds Ratios: Immunosuppression Treatment, Univariate Results
Odds of developing DM within the first year post-transplant
Odds Ratios: Tacrolimus Use
Odds of developing DM within the first year post-transplant

Tacrolimus was the only therapy found to have an effect in and of itself. Other therapies had significant interactions with one another. Probabilities based on drug combinations are presented in the slides that follow.

Note: Developed from the full model including relevant drug interactions.
## 10 Most Common Immunosuppressive Therapy Combinations regardless of steroid use

- Neoral + antimetabolite (N=5,081)
- Tacrolimus + antimetabolite (N=1,218)
- Neoral (N=617)
- antimetabolite (N=539)
- Cyclosporin + antimetabolite (N=533)
- No calcineurin inhibitor or antimetabolite (N=257)
- Tacrolimus (N=251)
- Cyclosporin (N=141)
- Neoral + Tacrolimus + antimetabolite (N=83)
- Cyclosporin + Neoral + antimetabolite (N=55)

- These 10 account for 93.2% of all patients
1-5 Highest Probabilities of Developing DM
Probability of developing DM within the first year post-transplant

Note: Adjusted for all relevant covariates and drug interactions.
Conclusions

- Non-diabetic transplant patients appear to develop diabetes at a rate of 15% per year.
- Older transplant patients appear to have a 2-3 times greater likelihood of developing diabetes than patients aged 18-44.
- Compared to the white population, minority transplant patients have a 50-80% greater likelihood of developing diabetes in the post-transplant period.
Conclusions (cont.)

- Higher levels of education and greater ability to work appear to be associated with a lower risk of developing diabetes in the post-transplant period.
- After adjusting for other factors, including obesity and immunosuppressive drug combinations, Tacrolimus is associated with a 70% greater likelihood of developing diabetes in the first year after a transplant.
Conclusions: Epidemic of Diabetes

- The epidemic of diabetes appears to be present not only in the general population, but also in the dialysis and transplant populations.
- Given the growing burden of diabetes, increased surveillance and treatment of all populations is needed to reduce the associated morbidity and mortality.