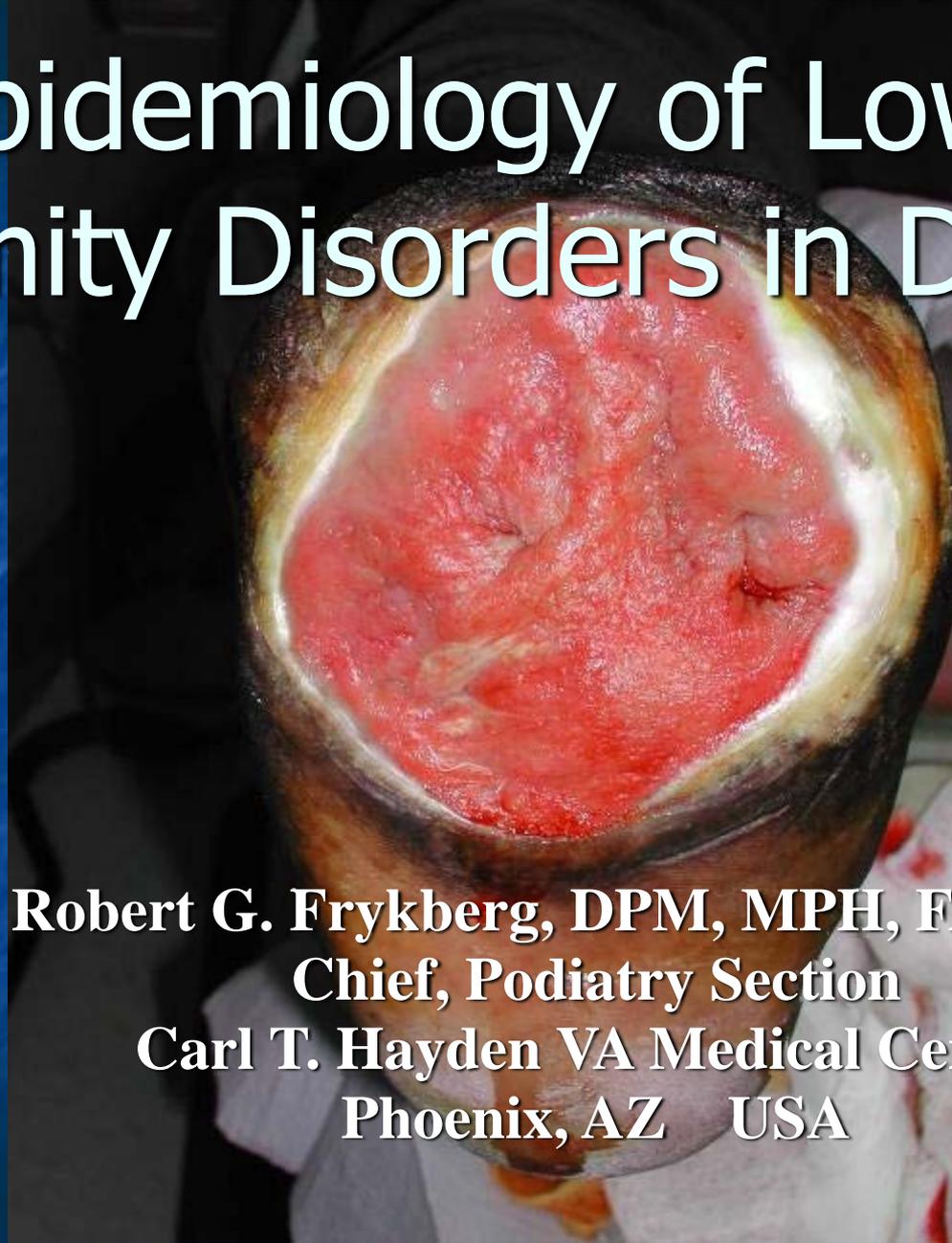
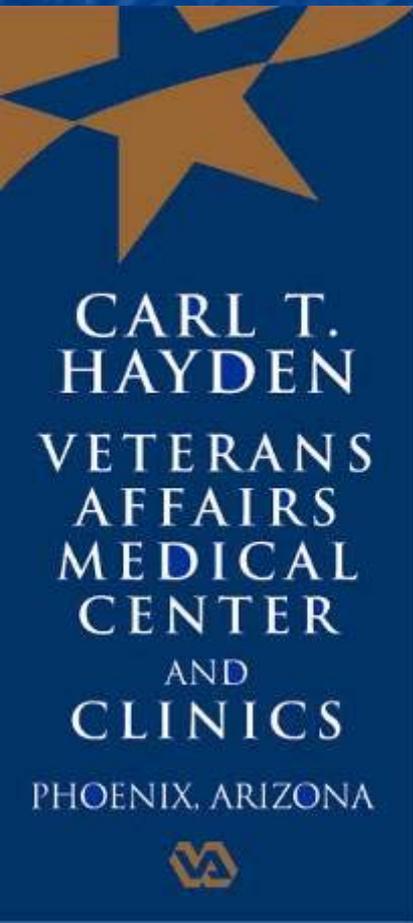


Epidemiology of Lower Extremity Disorders in Diabetes



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Diabetes in the USA

- ❖ Prevalence of Diabetes (United States 2007)
 - ❖ 23.6 million people (7.8% of the population)
 - ❖ Diagnosed 17.9 million Undiagnosed 5.7 million
- ❖ Incidence: 1.6 million new cases
- ❖ Total costs \$174 Billion
 - ❖ Direct medical costs: \$116 billion
 - ❖ Indirect costs: \$58 billion
 - ❖ disability, work loss, premature mortality
- ❖ 7th leading cause of death in U.S. (2006)



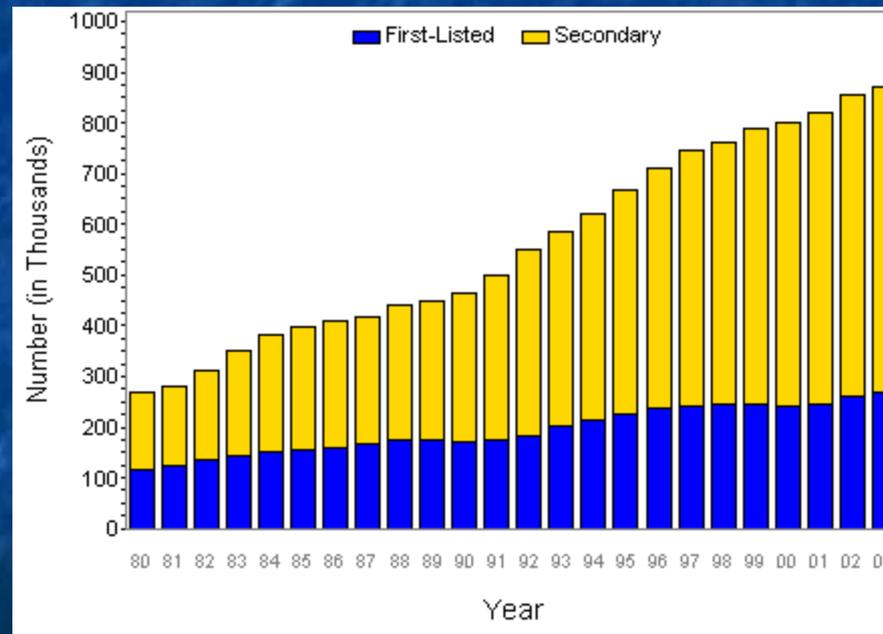
Significance of diabetes

- Major Lower Extremity Complications
 - Peripheral Neuropathy
 - Ulceration
 - Infection
 - Peripheral Arterial Disease
 - Lower extremity amputation
 - Charcot foot (Osteoarthropathy)



Hospitalizations for Lower Extremity Conditions

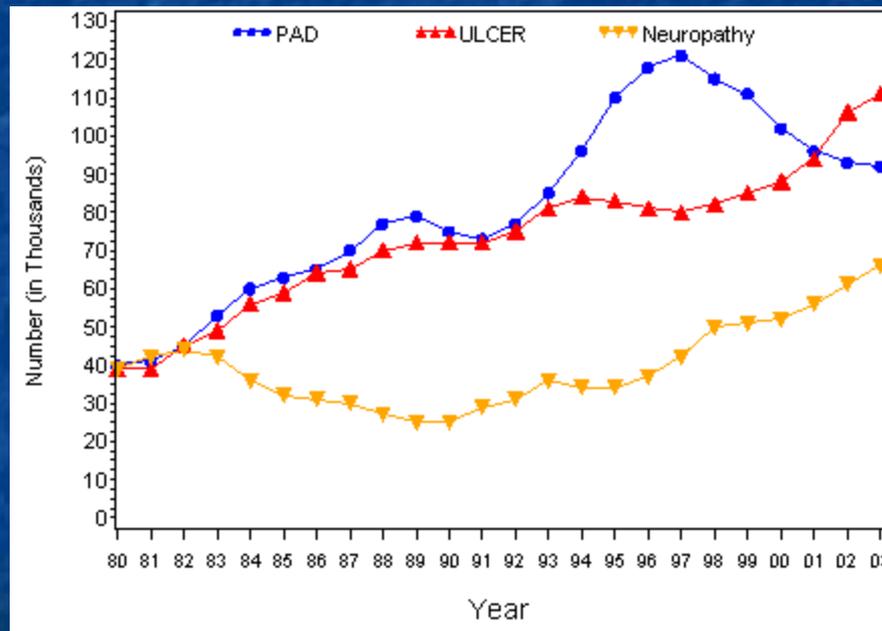
Number (in Thousands) of Hospital Discharges with a Lower Extremity Condition (LED) as First-Listed or Secondary Diagnosis and Diabetes as Any Listed Diagnosis, United States, 1980-2003



873,000

Hospitalizations for Lower Extremity Conditions

Number (in Thousands) of Hospital Discharges with Peripheral Arterial Disease (PAD), Ulcer/Inflammation/Infection (ULCER), or Neuropathy as First-Listed Diagnosis and Diabetes as Any-Listed Diagnosis, United States, 1980-2003



111,000 Ulcer

92,000 PAD

66,000 Neuropathy

CDC: National Diabetes Surveillance System 2007

Diabetic Foot Ulcers

- 15% Lifetime risk - multifactorial etiology
- neuropathic, ischemic, neuroischemic pathophysiology
- precursor to amputation ~ 80-85% of cases



Diabetic Foot Ulcer Incidence*



■ Moss 1992	2.5%
■ Smith 1994	5.6%
■ Young 1994	4.9%
■ Abbott 2002	2.2%
■ Holzer 1998	2.5%
■ Ramsey 1999	~ 2%
■ Moss 1999	~ 2%
■ Lavery 2003	6.8%

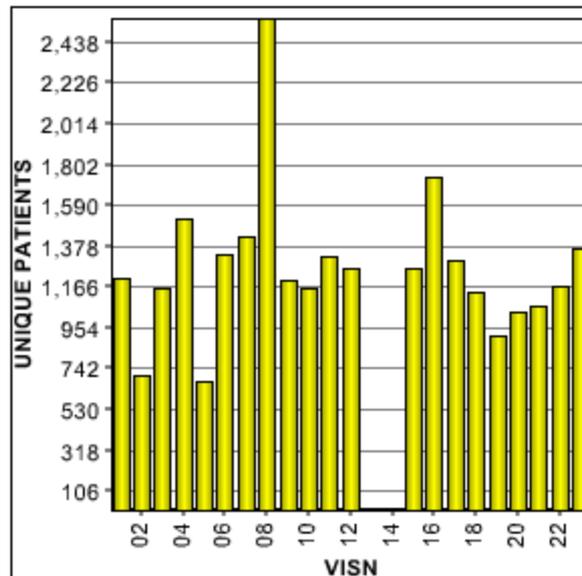
* estimated cumulative incidence/yr. Methodologies vary by study.

VA DM Ulcer Prevalence 2006 (unadjusted)

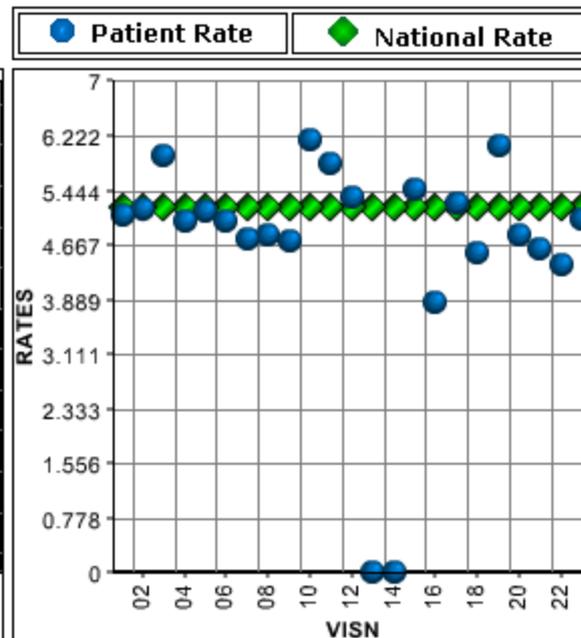
Charts on Ulcer Prevalence

Fiscal Year = **06**, VISN = **ALL**, Age Group = **ALL**, Rate = **Unadjusted**, Ulcer Type = **All Ulcer Types**,
Cohort = **Has Diabetes**

Number of Unique Patients by VISN



Ulcer Rate



This page requires the use of the Macromedia Flash Player. Download the [Macromedia Flash Player](#).

Risk Factors for Diabetic Foot Ulceration

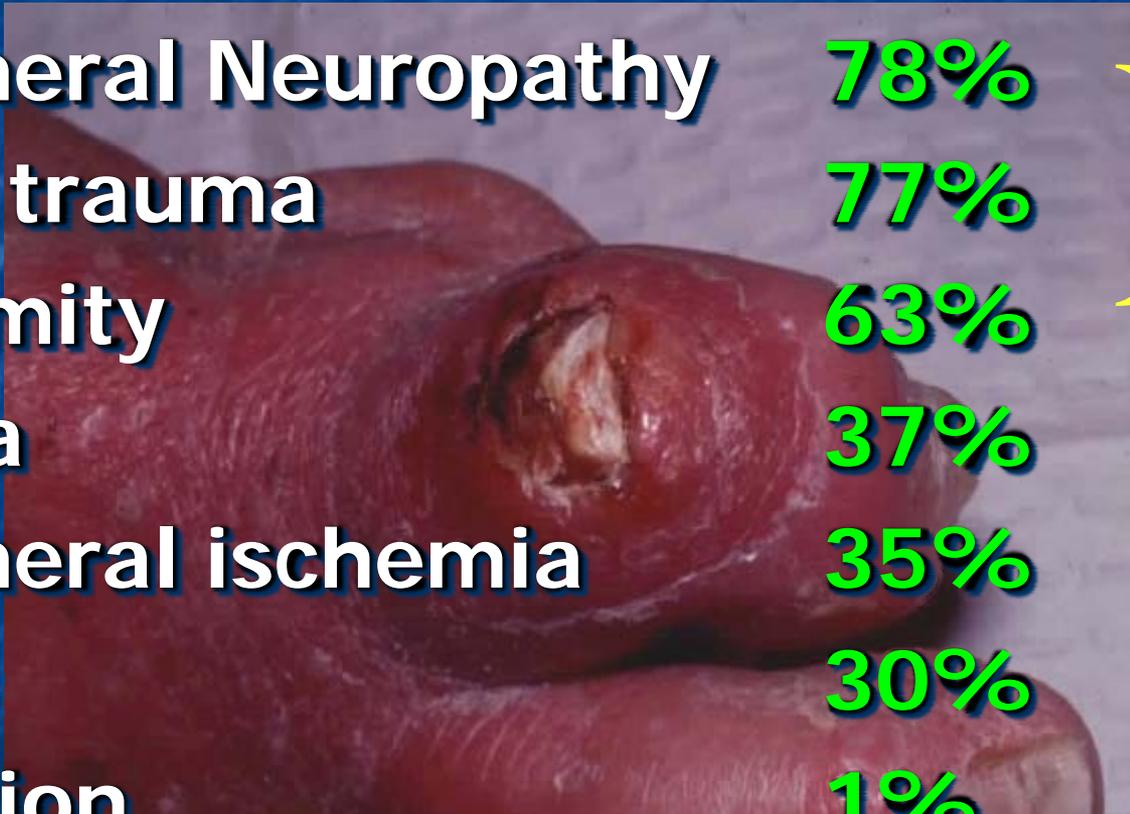
Intrinsic Factors

- **Neuropathy**
 - Sensorimotor
 - Autonomic
- **Vascular Disease**
 - Macrovascular
 - Microvascular
- **Immunopathy**
 - Susceptibility to Infection
- **Structural Deformity**
- **Limited Joint Mobility**
- **Nephropathy**
- **Age**
- **Duration of Diabetes**
- **Previous Ulceration**

Extrinsic Factors

- **Minor Trauma (mechanical)**
 - High Plantar Pressure
 - Shoe Pressure
 - High Impact
- **Callus**
- **Thermal Injury**
 - Hot Soaks, Frostbite
- **Chemical Burns**
- **Bathroom Surgery**
- **Occupational Hazards**
- **Living Alone**
- **Cigarette Smoking**
- **Poor Knowledge of Diabetes**
- **Psychological Factors**

Component Causes of Foot Ulcers



■ Peripheral Neuropathy	78%	} 63%
■ Minor trauma	77%	
■ Deformity	63%	
■ Edema	37%	
■ Peripheral ischemia	35%	
■ Callus	30%	
■ Infection	1%	

From: Reiber et al: Diabetes Care 22:157-162, 1999

North-West Diabetes Foot Care Study: Incidence and risk factors for ulceration

Abbott et al: Diab Med 2002

- Community based cohort n= 9710 (2 yr follow-up)
- 2.2% average ulcer incidence

■ <u>Risk factors</u> for <u>foot ulcer</u> :	<u>RR</u>
Baseline ulcer present	5.32
Past ulcer history	3.05
Abnormal NDS ($\geq 6/10$)	2.32
LOPS to monofilament	1.80
Reduced pulses	1.80

Incidence, Outcomes, and Costs of Diabetic Foot Ulcers

Ramsey et al: Diabetes Care 1999

- 3 yr cumulative incidence DFU 5.8%
- 15% developed osteomyelitis
- 15.6% required amputation
- 3 yr survival 72% vs 87% in non ulcer pts
- attributable 2 yr cost of ulcer - \$27,987
- relative cost of care 5.4 x greater



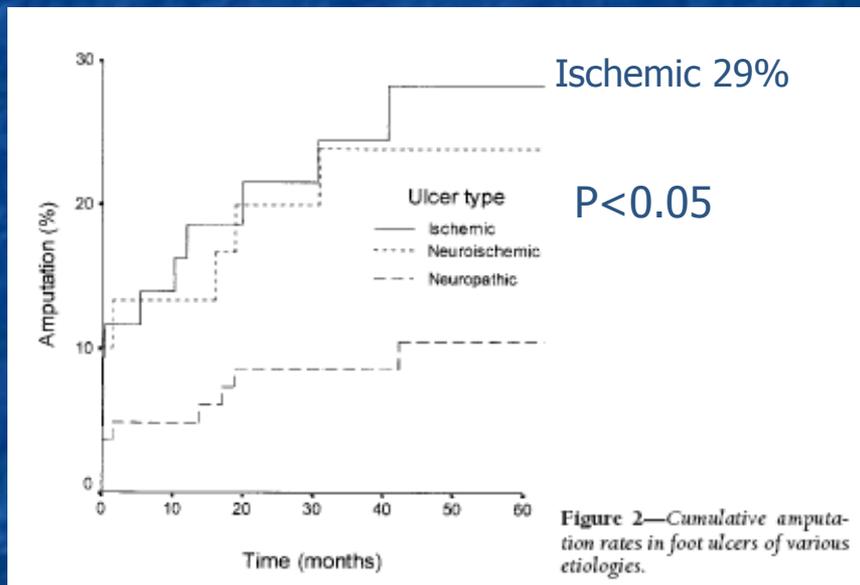
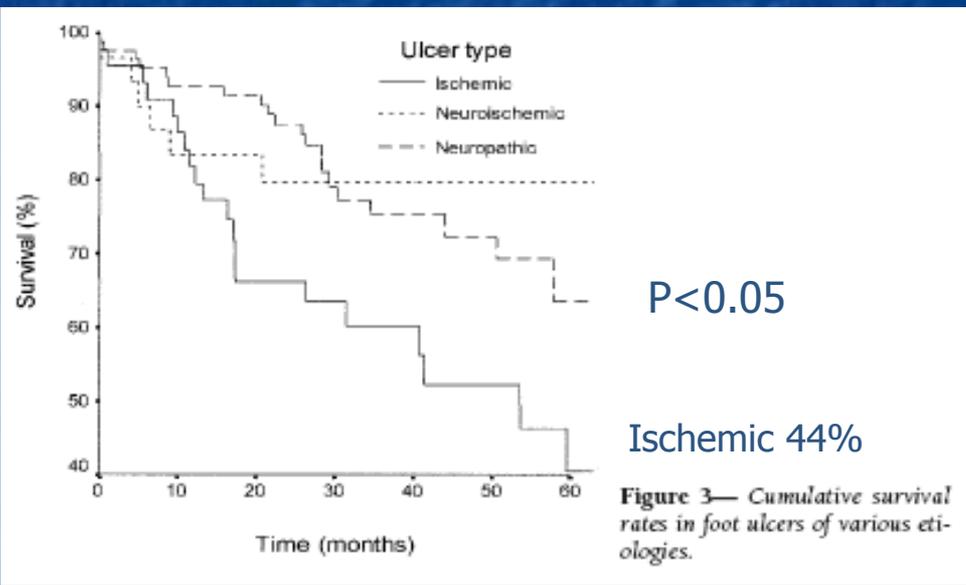
Increased Mortality associated with Diabetic Foot Ulcer

- Boyko 1996
 - Two-fold increased risk of death in persons with ulcers after adjustment for age, duration, and smoking.
- Moulik 2003
 - Five year mortality rate 44%
(highest in ischemic ulcers)
- Young 2008
 - Five year mortality 26.8%
(highest in neuroischemic ulcers 36%)



Amputation and Mortality in New-Onset Diabetic Foot Ulcers Stratified by Etiology

Moulik P, Mtonga R, Gill G: Diabetes Care 26:491-494, 2003

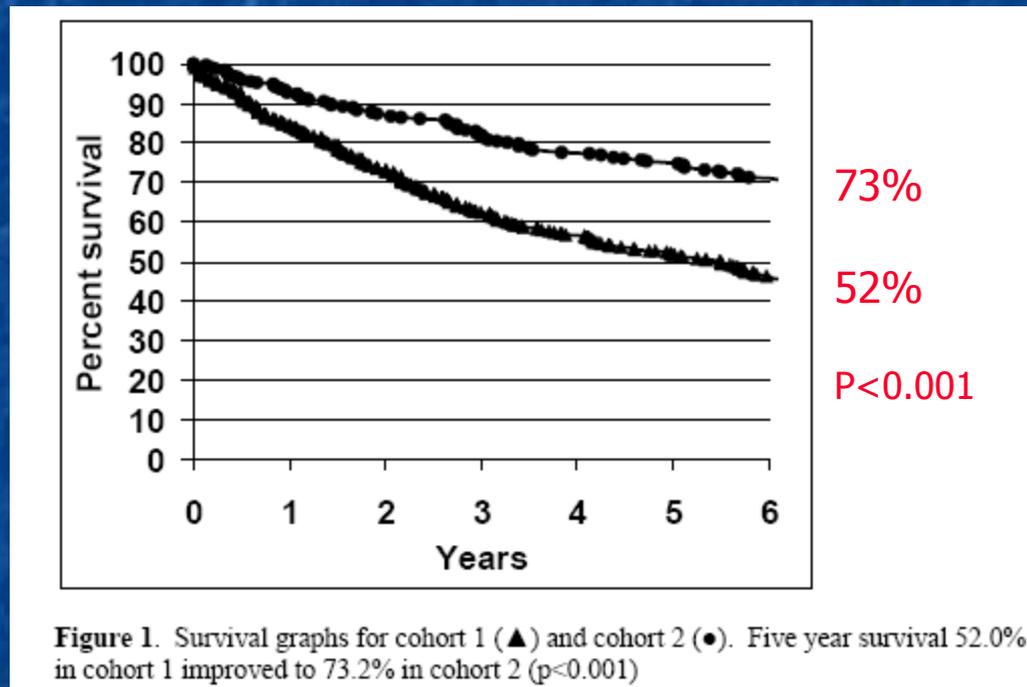


Survival

Amputations

Improved Survival of Diabetic Foot Ulcer patients 1995-2008, possible impact of aggressive cardiovascular risk management

Matthew Young et al: Diabetes Care 2008



Foot Ulcers are major risk factors for subsequent amputations

**80 to 85% of Diabetic
LEA's are preceded
by Ulceration**

Pecoraro 1990
Apelquist 1995



AMPUTATIONS



Diabetes Related Amputations

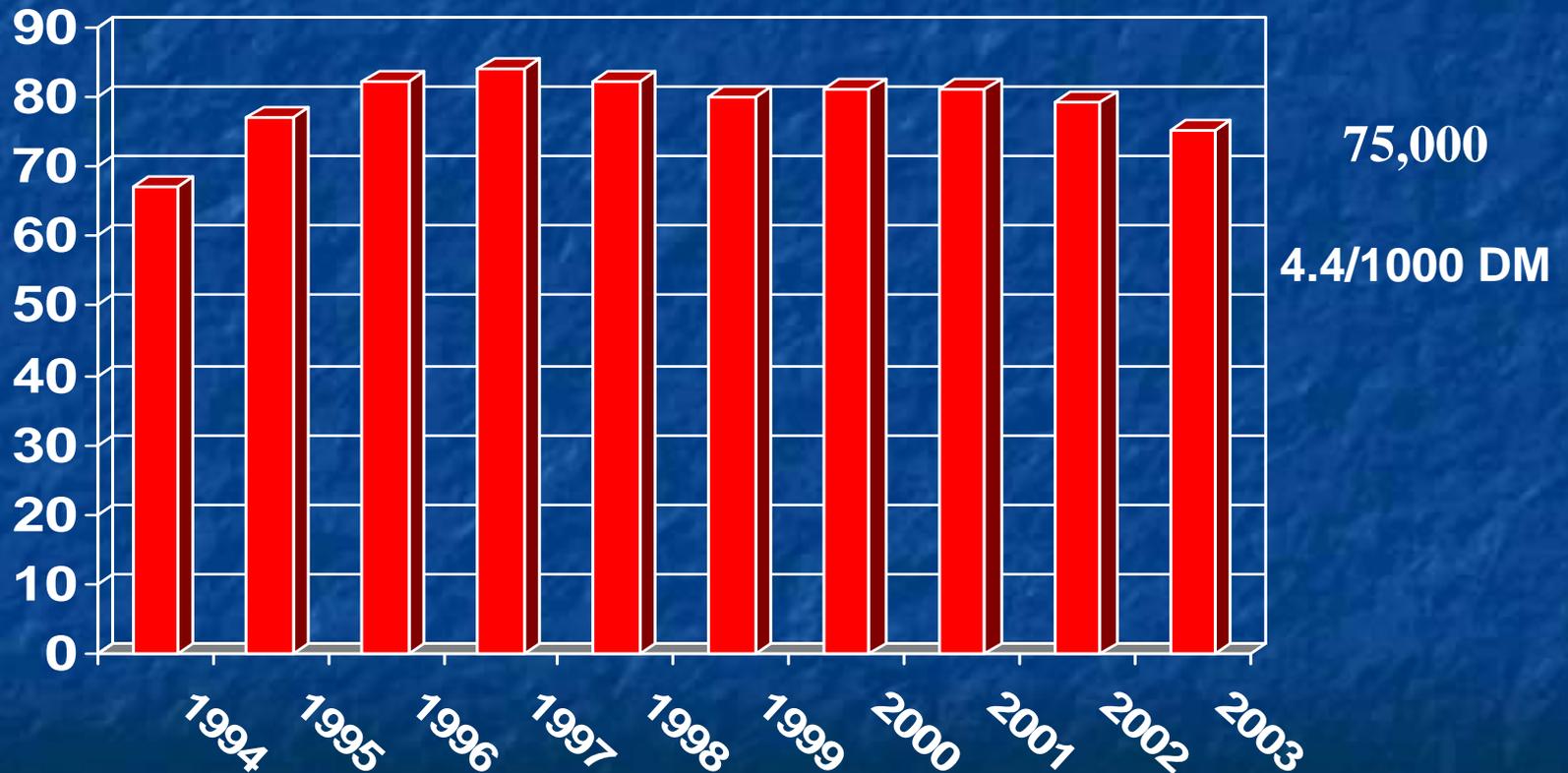
- More than 60% of non-traumatic LEA's in U.S. (only 7% of population)
- Rates elevated in:
 - men, elderly, minorities, renal insufficiency
- Negatively impacts survival
 - Increased mortality with more proximal levels
- Average cost LEA ~ \$24,000 –
\$40,000

Diabetes in America, 2nd Ed., 1995
CDC: Diabetes Surveillance, 2007
Pecoraro 1990
Aulivola 2004



Amputations

Non-Traumatic LEA in Patients with Diabetes



CDC: Diabetes Surveillance System 2007

Risk Factors for Amputation

- Neuropathy
- Ischemia
- Infection
- Ulceration
- Gangrene
- Prior amputation
- Trauma



Pecoraro : Diabetes Care.1990
Apelquist 1995
Larsson 1998
Adler et al: Diabetes Care, 1999

Early Predictors for Lower Extremity Amputation in a Diabetic Population: Results of a Case-Controlled Study

Smith et al: Lower Extremity Wounds 2002

- NHDS data 1997-1999 sampled for DM admissions
 - Cases: 2098 DM amputees
 - Controls: 2206 DM without LEA

Table 2. Multivariate (Adjusted) Risk for Amputation for Comorbid Conditions of Cases and Controls

	Adjusted OR (95% CI)	p-value
Male	1.00 (1.76-2.26)	.0001
Diabetic retinopathy	1.65 (1.21-2.27)	.0017
Diabetic nephropathy	1.70 (1.36-2.13)	.0001
Coronary artery disease	0.66 (0.56-0.79)	.0001
Hypertension	0.78 (0.69-0.89)	.0002
Transient ischemic attacks	0.09 (0.03-0.24)	.0001
MI	0.17 (0.12-0.25)	.0001

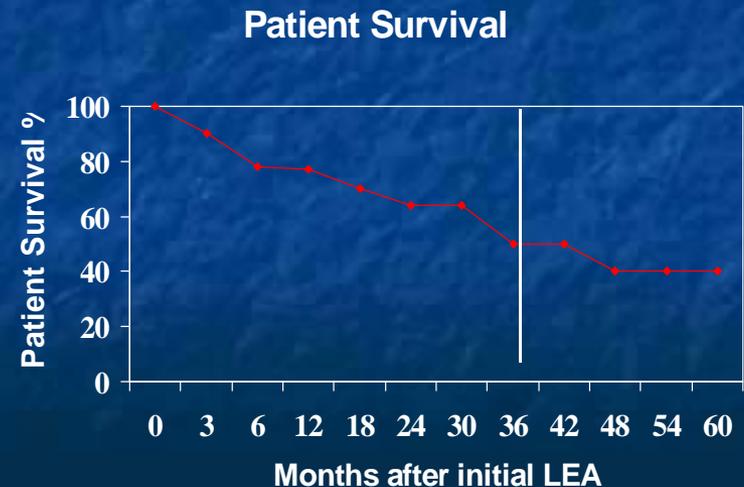
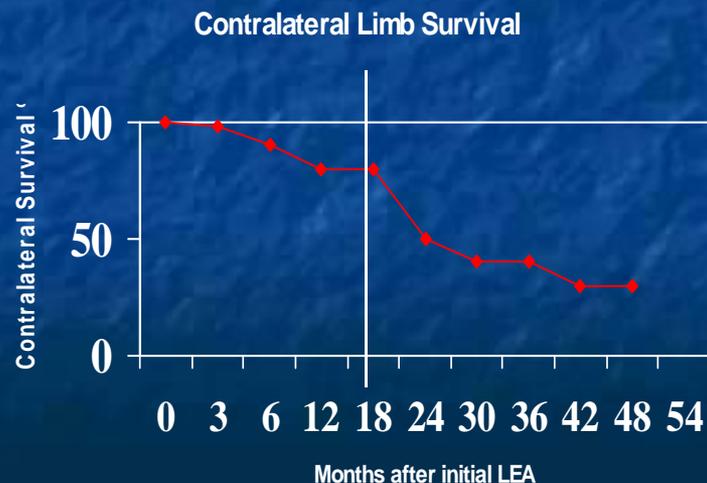
OR= odds ratio, CI = confidence interval, MI =myocardial infarction.

Did not evaluate for PAD

Contralateral Limb and Patient Survival

Bodily and Burgess: Am J Surg 1983

- 50% of patients undergoing initial major LEA require contralateral amp within 24 mos.
- 50% die within 36 mos after initial major LEA



Mortality following LEA in DM

- Perioperative mortality (≤ 30 days) averaged 5.8% 1989-92
- Generally, survival is poor in pts with DM after LEA
 - **1 yr mortality 11-41%**
 - **5 yr mortality 39-68%**
- Cardiac and renal complications often the cause of death
- Generally, higher levels of LEA have higher mortality rates
- 48 - 50% incidence contralateral amp in two years



Reiber et al 1995
Larsson et al 1998

Major Lower Extremity Amputation: Outcome of a Modern Series

Aulivola et al: Arch Surg 2004; 139:395-399

- Retrospective database/record review 1990-2001
- 959 consecutive major LEA in 788 patients (80.6% DM)
 - 704 BKA (73.4%) 255 AKA (26.6%)
- Mean age 66.7 yrs Men 57.2%
- Actuarial overall survival
 - 1 yr 69.7%
 - 5 yr 34.7%
- BKA 1 yr- 74.5% 5 yr- 37.8%
- AKA 1 yr- 50.6% 5 yr- 22.5%

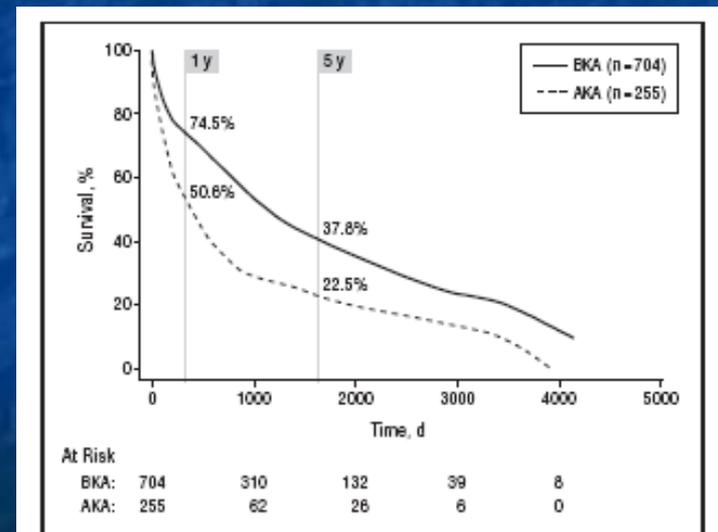
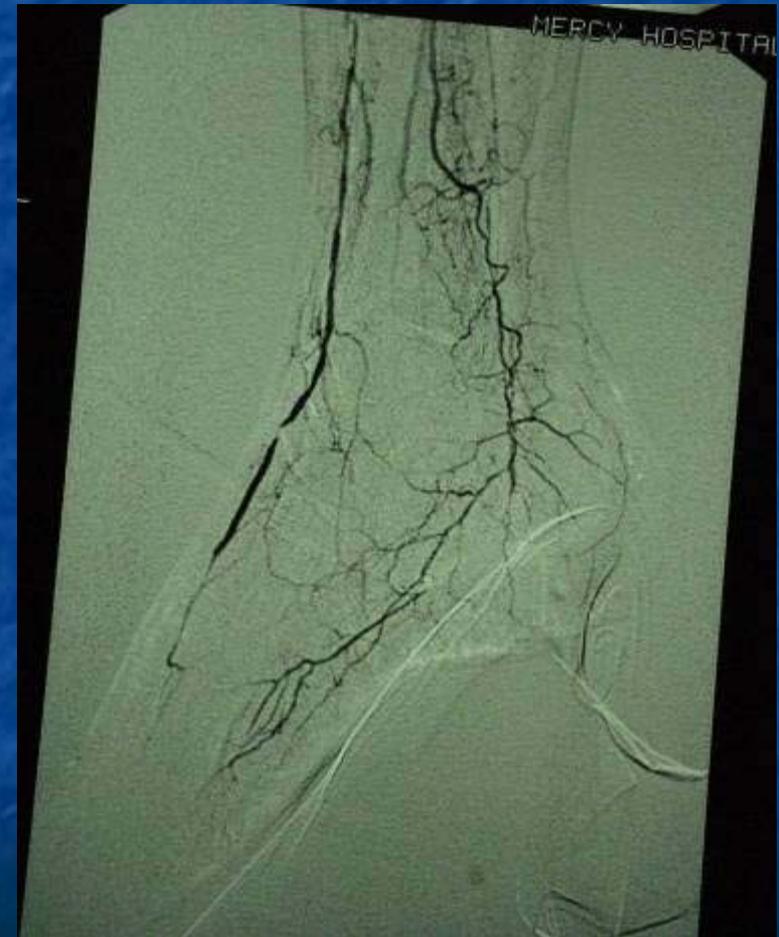


Figure 1. Actuarial survival in below-knee amputation (BKA) patients vs above-knee amputation (AKA) patients ($P < .001$).

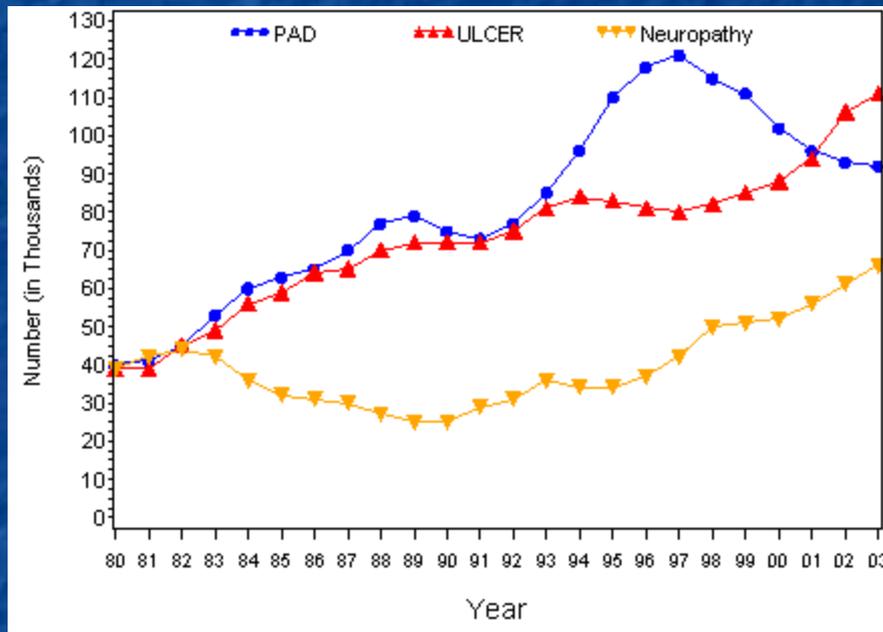
Peripheral Arterial Disease

- Atherosclerotic occlusive disease of the lower extremities
 - Largely asymptomatic
- Risk factor for amputation
- Marker of cardiovascular and cerebrovascular disease
 - Increased mortality
- Microvascular dysfunction also prevalent in diabetes, but it is not occlusive



Hospitalizations for Lower Extremity Conditions

CDC: Diabetes Surveillance System 2007



111,000 Ulcer

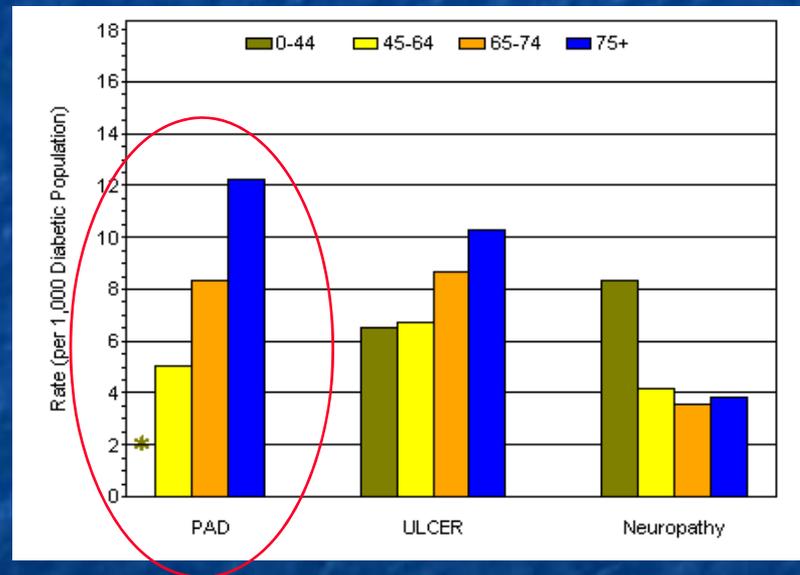
92,000 PAD

66,000 Neuropathy

PARTNERS: 29% with PAD (16% of these PAD & CVD)
Primary Care survey patients >70; DM>50 yrs
Hirsch et al: JAMA 2001

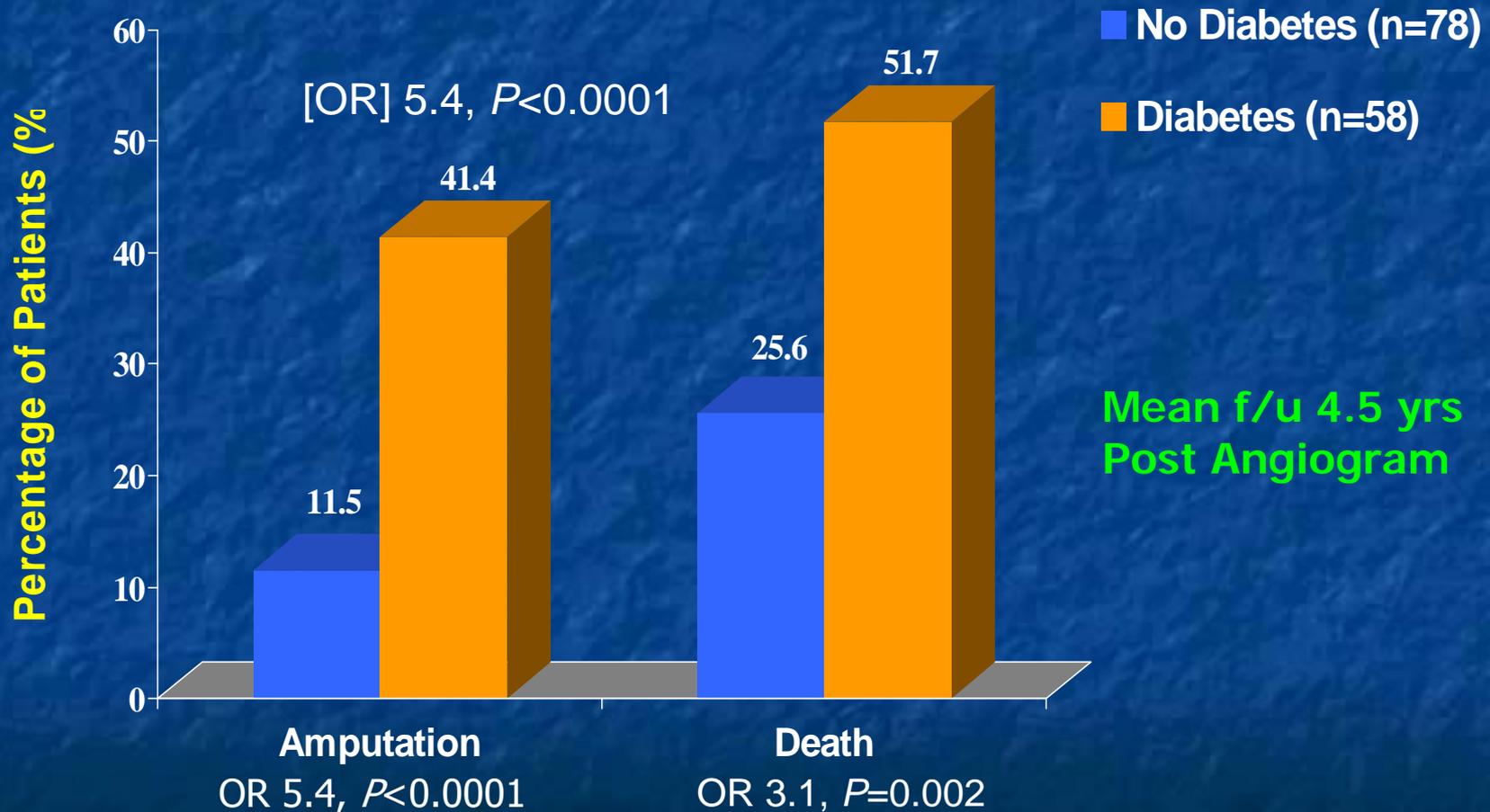
Hospitalizations for Lower Extremity Conditions

Hospital Discharge Rates for **Peripheral Arterial Disease (PAD)**, **Ulcer/Inflammation/Infection (ULCER)**, or **Neuropathy** as First-Listed Diagnosis per 1,000 Diabetic Population, by **Age**, United States, **2003**

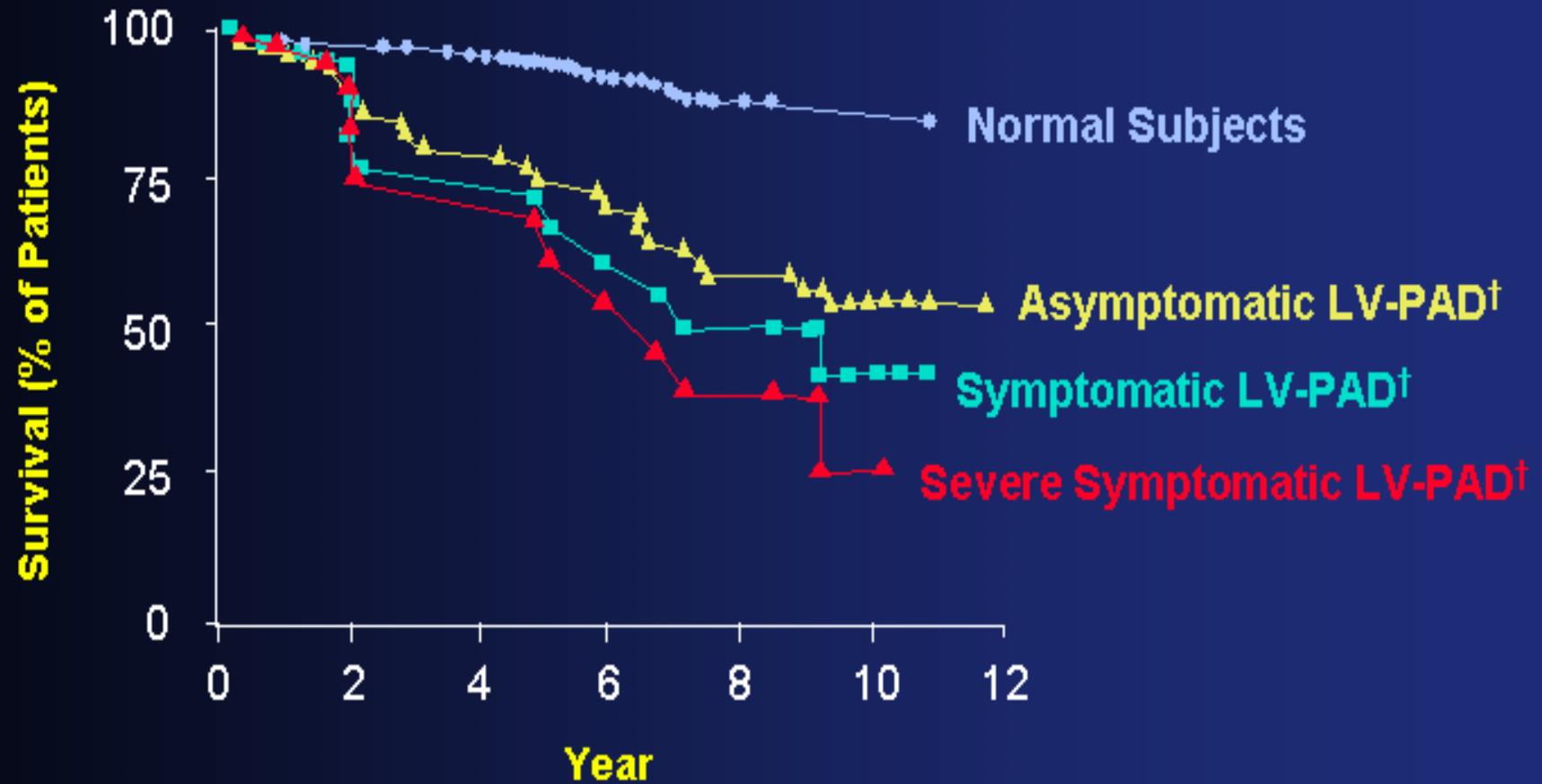


CDC: National Diabetes Surveillance System 2007

Diabetic Patients with PAD are at Increased Risk for Poor Outcomes



Peripheral Arterial Disease (PAD) Mortality*

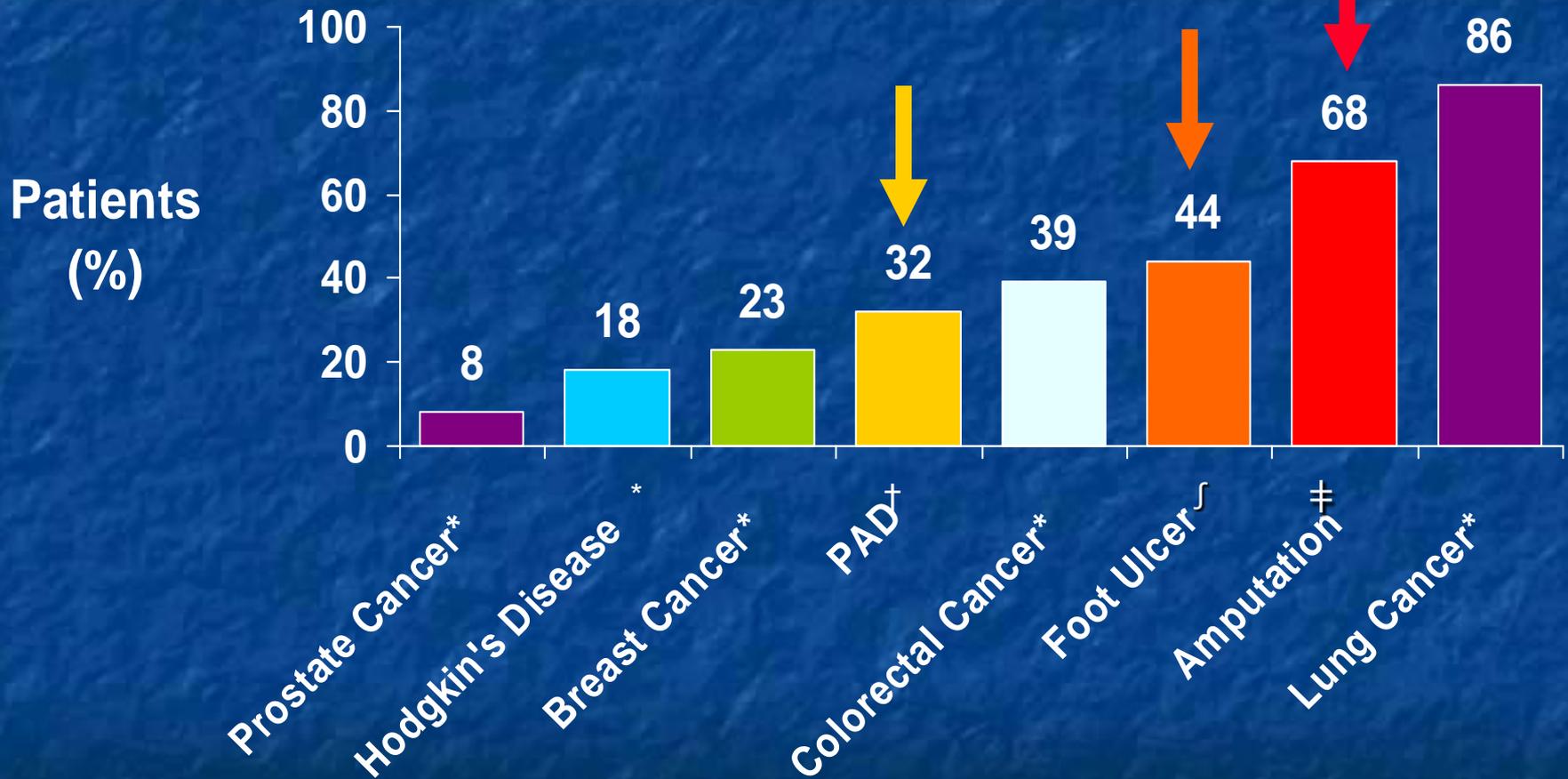


*Kaplan-Meier survival curves based on mortality from all causes.

†Large-vessel PAD.

Crigui MH et al. *N Engl J Med*. 1999;326:381-386

Relative 5-Year Mortality Rates



*American Cancer Society. *Cancer Facts and Figures*, 2000.

†Criqui MH et al. *N Engl J Med*. 1992;326:381-6.

‡Larsen, Apelqvist et al: 1998 §Moulik et al: 2003

Belch et al: *Arch Int Med* 2003; 163:884-892

Epidemiology of diabetic foot problems and predictive factors for limb loss

Aziz Nather^{a,*}, Chionh Siok Bee^b, Chan Yiong Huak^c, Jocelyn L.L. Chew^a, Clarabelle B. Lin^a, Shuhui Neo^a, Eileen Y. Sim^a

^a*Department of Orthopaedic Surgery, National University Hospital, Singapore*

^b*Division of Endocrinology, Department of Medicine, National University Hospital, Singapore*

^c*Biostatistics Unit, Yong Loo Lin School of Medicine, National University of Singapore, Singapore*

Received 8 August 2006; received in revised form 28 March 2007; accepted 23 April 2007

- Prospective study of 202 diabetic patients admitted with Diabetic Foot Problems
 - Gangrene 31.7% Infection 28.7% Charcot osteoarthropathy 2%
- Surgery required in 74.8%
 - Major Amputation 27.2% (BKA 20.3% AKA 6.9%)
- PVD was the strongest adjusted predictor for LEA
OR 8.4 (3.9-18.3) p<0.001

The Association Between Baseline Characteristics and the Outcome of Foot Lesions in a UK Population with Diabetes

Ince P, Kendrick D, Game F, Jeffcoate W: Diabetic Med 24, 977-981, 2007

- Retrospective single cohort of 449 ulcer pts – Nottingham, UK
- Baseline characteristics recorded S(AD) SAD classification
Size (Area, Depth) Sepsis Arteriopathy Denervation

Results: (maximum f/u 1 year)

- Mean age e 63.7%
 - **42.7%** h
 - **68.3%** he
 - 4 variable
 - Increased
 - **Incre**
 - Ulcer s
 - Durati
- amination only)**
s most common 60.5%
an time to heal:
0.24-0.67)
(0.37-0.67)
0.49-0.96)
0.48-0.92)



Diabetic Foot Infections



Quantifying the Risk of Infection in Persons with Diabetes

- Retrospective cohort study (n=513,749/ group)
- 46% of all persons with DM had infection
- RR for all Infectious Diseases 1.21 (1.20-1.22)
- RR for Cellulitis 1.81 (1.76-1.86)
- RR for Osteomyelitis 4.39 (3.80-5.06)
- RR for Post-op Infection 2.02 (1.80-2.27)
- RR for Death from Infection 1.84 (1.73-1.95)

Major Risk Factors for Diabetic Foot Infection

- Peripheral neuropathy
- Peripheral arterial disease
- Poor glycemic control
- Abnormal Host Response
 - Neutrophil dysfunction
 - Impaired chemotaxis
 - Impaired phagocytosis
 - Impaired bacterial killing



Bagdade 1973
Nolan 1978
McMahon 1995
Lipsky 2004

Risk Factors for Foot Infections in Individuals with Diabetes

Lavery LA, Armstrong DG, et al: Diabetes Care 29:1288, 2006

1666 consecutive diabetic patients - 2 year follow-up

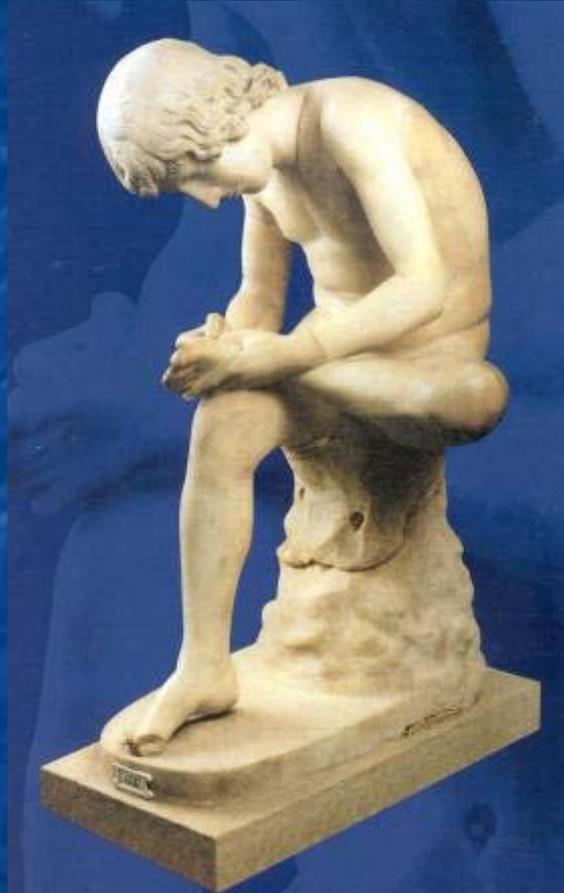
- 151 (9.1%) developed 199 foot infections
- All but one associated with wound or penetrating injury
- 19.9% had culture proven osteomyelitis
- Amputation risk in infected patients OR: 154.5 (P<0.001)
- Significant independent risk factors for Infection:
 - Probe to Bone OR: 6.7
 - Wounds >30 days OR: 4.7
 - Recurrent Wounds OR: 2.4
 - Traumatic Wounds OR: 2.4
 - PVD OR: 1.9



SUMMARY

- Diabetic foot complications are leading causes for diabetes – related hospitalizations
- Neuropathy, PAD, ulceration, and infection are major risk factors for amputation
- Both Ulceration *and* Amputation adversely affect survival
- Knowledge of risk factors for complications provides an opportunity for early intervention and prevention

THANK YOU!



CARL T.
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Predictors, consequences and costs of diabetes-related lower extremity amputation complicating type 2 diabetes: The Fremantle Diabetes Study

W. A. Davis · P. E. Norman · D. G. Bruce ·
T. M. E. Davis

Received: 2 March 2006 / Accepted: 31 July 2006 / Published online: 26 September 2006
© Springer-Verlag 2006

Abstract

Aims/hypothesis The aims of this study were to assess the incidence, predictors, consequences, and inpatient cost of lower extremity amputation (LEA) in a community-based cohort of type 2 diabetic patients.

Methods Between 1993 and 1996, 1,294 patients with type 2 diabetes were recruited to the longitudinal, observational Fremantle Diabetes Study. LEAs and mortality from cardiac causes were monitored until 30 June 2005. Inpatient costs (in A\$ in year 2000), derived using a case-mix approach, were available for the period from 1 July 1993 to 30 June 2000.

Results During follow-up 44 patients without LEA at baseline had a first-ever diabetes-related LEA, an incidence of 3.8 per 1,000 patient-years. Independent predictors of first-ever LEA included foot ulceration (hazard ratio [95% CI]: 5.56 [1.24–25.01]), an ankle brachial index ≤ 0.90 (2.21 [1.11–4.42]), HbA_{1c} (increase of 1%: 1.30 [1.10–1.54]) and neuropathy (2.65 [1.30–5.44]). The risk of cardiac death was significantly increased in patients with LEA at baseline, although this was not an independent risk factor. The median (interquartile range) inpatient cost per

LEA admission was A\$12,485 (A\$6,037–A\$24,415), with a median length of stay of 24 (10–43) days.

Conclusions/interpretation First-ever LEAs in type 2 patients were associated with poor glycaemic control, foot ulceration and evidence of microvascular and macrovascular disease. Patients with LEA were at increased risk of cardiac death. LEAs contribute disproportionately to diabetes-related inpatient costs.

Keywords Cohort study · Cost · Epidemiology · Lower extremity amputation · Type 2 diabetes

Abbreviations

ABI	ankle brachial index
ACR	urinary albumin:creatinine ratio
CVD	cerebrovascular disease
DRG	diagnostic related group
FDS	Fremantle Diabetes Study
HR	hazard ratio
ICD	International Classification of Diseases
IQR	interquartile range
LEA	lower extremity amputation

Reduction in Diabetic Amputations Over 11 Years in a Defined UK Population

Krishnan et al: *Diabetes Care* 31:99-101, 2008

- Prospectively assessed amputation rates in well defined diabetic population- Ipswich 1995-2005 after introduction of **Multidisciplinary Foot Team**
- Major amputations fell 62% as expressed per 100,000 general population (7.4 to 2.8)
- **Diabetic Population (rates per 10,000 DM)***
 - Total LEAS fell 70% (53.2 to 16.0)
 - Major LEAS fell 82% (36.4 to 6.7)

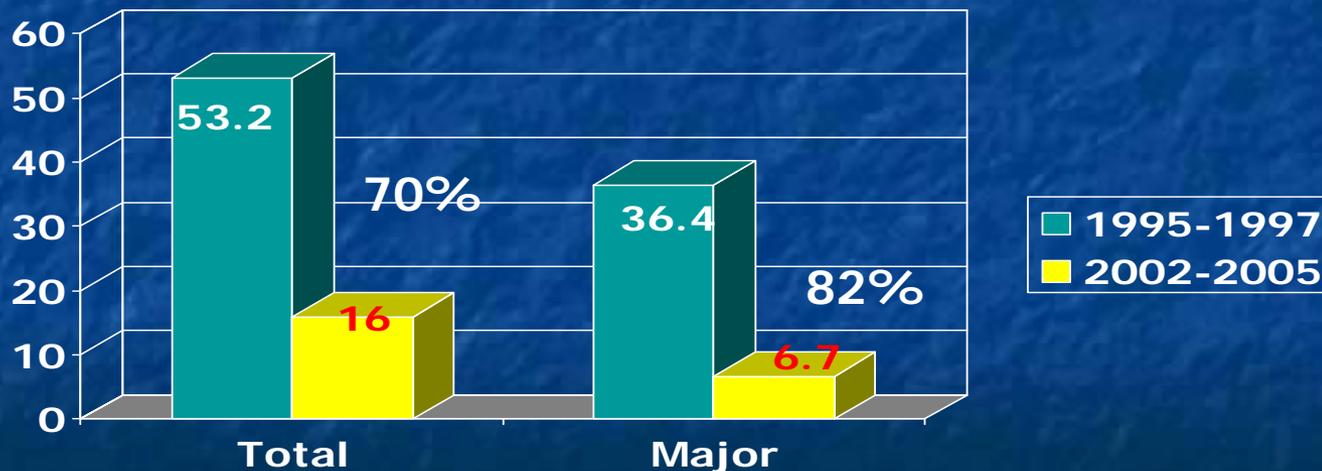
* Crude rates not age adjusted although no change in mean age (70.7 yrs)

Reduction in Diabetic Amputations Over 11 Years in a Defined UK Population

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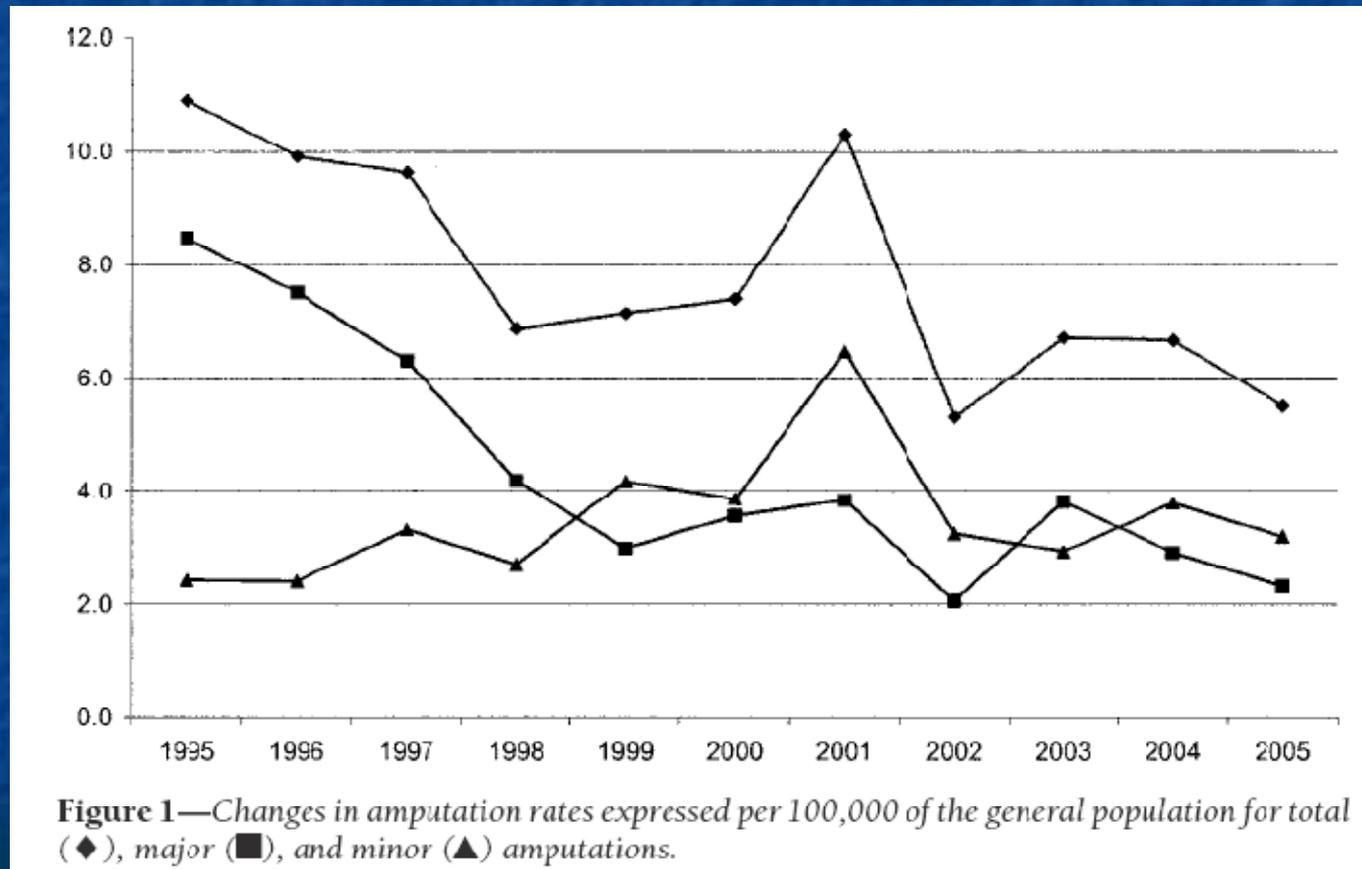
Rates per 10,000 DM persons



* Crude rates not age adjusted although no change in mean age (70.7 yrs)

Reduction in Diabetic Amputations Over 11 Years in a Defined UK Population

Krishnan et al: *Diabetes Care* 31:99-101, 2008

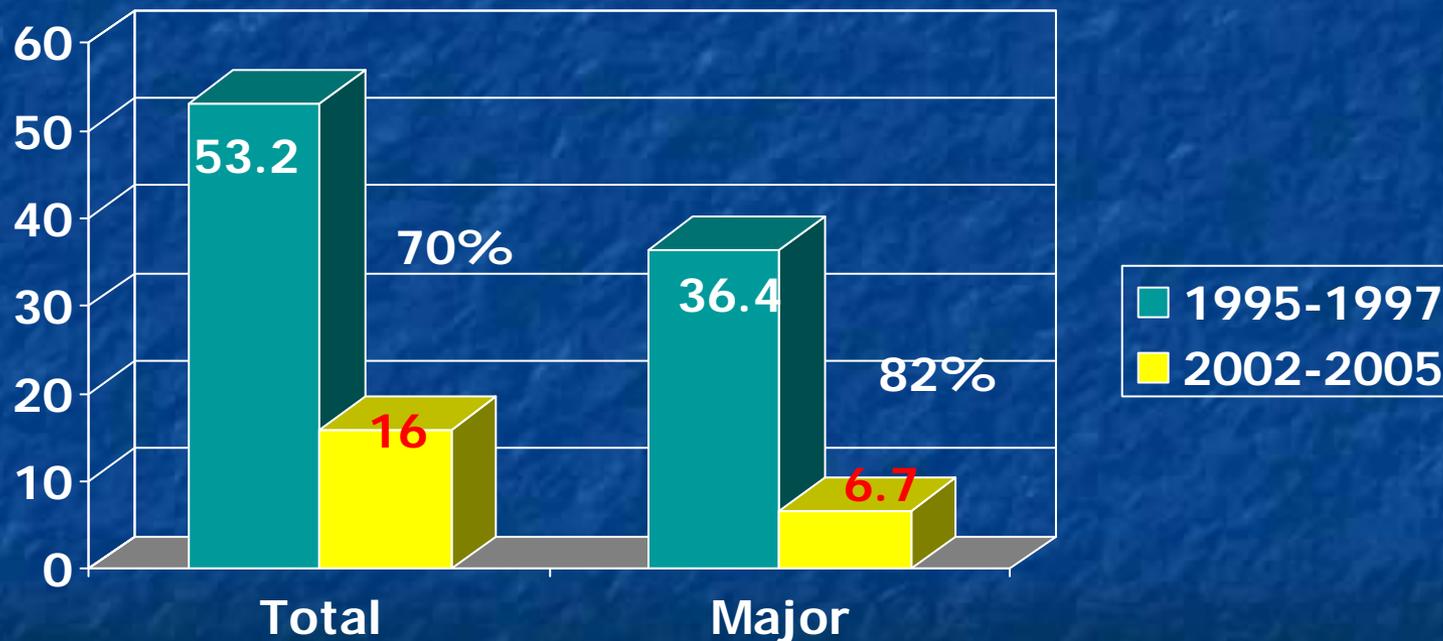


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Reduction in Diabetic Amputations Over 11 Years in a Defined UK Population

Krishnan et al: Diabetes Care 31:99-101, 2008

Rates per 10,000 DM persons



* Crude rates not age adjusted although no change in mean age (70.7 yrs)

Association Between Renal Failure and Foot Ulcer or Lower-Extremity Amputation in Patients with Diabetes

Margolis et al: *Diabetes Care* 31:1331-1336, 2008

- Retrospective cohort study N=90,617 DM pts enrolled 2002-2006 in Health Information Network, UK
 - All pts had baseline eGFR Median Observation 2.4 years
 - Mean age 62.9 yrs 53% Women
 - CKD (eGFR < 60 ml/min per 1.73 m²) in 23,350 (26%)
 - Group 1 (eGFR ≥ 60 ml/min per 1.73 m²)
 - Group 2 (eGFR ≥ 30 and < 60 ml/min per 1.73 m²)
 - Group 3 (eGFR < 30 ml/min per 1.73 m²)

Association Between Renal Failure and Foot Ulcer or Lower-Extremity Amputation in Patients with Diabetes

Margolis et al: *Diabetes Care* 31:1331-1336, 2008

	Adjusted HRs (95%CI)	
	DFU	LEA
Prior DFU	7.85 (7.16-8.62)	13.06 (10.55-16.18)
Prior LEA	8.00 (6.74-9.49)	31.03 (23.93-40.23)
HgA1c>9%	1.66 (1.50-1.83)	2.77 (2.10-3.64)
Hx PAD	3.80 (3.51-4.12)	12.00 (9.74-14.77)
LOPS	2.17 (1.88-2.51)	2.34 (1.62-3.38)
ESRD	6.12 (3.54-10.55)	15.66 (6.48-37.86)

All P<0.001

Association Between Renal Failure and Foot Ulcer or Lower-Extremity Amputation in Patients with Diabetes

Margolis et al: *Diabetes Care* 31:1331-1336, 2008

Results: DFU 2619 LEA 378

CDK risk:

Group 2:	HR 1.85 (1.71-2.01)	HR 2.08 (1.68-2.58)
Group 3:	HR 3.92 (3.23-4.75)	HR 7.71 (5.29-11.26)

p < 0.001