

How to Treat Diabetic Foot Infection



PODIATRY

UNIVERSITY OF MICHIGAN
HEALTH SYSTEM

Brian M. Schmidt, DPM



**UNIVERSITY OF
MICHIGAN HEALTH**
MICHIGAN MEDICINE

Associate Professor
Department of Internal Medicine
Division of Metabolism, Endocrinology & Diabetes – Podiatry
University of Michigan Medical School

Disclosures



National Institute of
Diabetes and Digestive
and Kidney Diseases

I am supported by multiple extramural grants:

1. NIDDK Diabetic Foot Consortium¹
 - Co-Investigator
 - *Study Chair* of the Biorepository Program ClinicalTrials.gov Identifier: NCT05092620
 - Co-PI of the Biomarker Analysis Unit of the Master Protocol
 - **U01 DK119083**
2. NIDDK K-awardee (“*The Role of the Microbiome in Diabetic Foot Ulcers*”)
 - Proudly representing Podiatry
 - **K23 DK131261**

OVERVIEW

- Scope and Magnitude of Diabetic Foot Ulcers and Infection
- Learn Classification Systems
 - Case Examples
- Antibiotic Approaches and Stewardship
 - Culture
 - Antibiotics of Choice
 - Referral
- Clinical Outcomes and Setting Expectations
- Conclusions

3

OUTLINE

- **Scope and Magnitude of Diabetic Foot Ulcers and Infection**
- Learn Classification Systems
 - Case Examples
- Antibiotic Approaches and Stewardship
 - Culture
 - Antibiotics of Choice
 - Referral
- Clinical Outcomes and Setting Expectations
- Conclusions

4

Diabetic Foot Magnitude

- Up to **25% will develop a diabetic foot ulcer (DFU)** in their lifetime^{1,2}
 - Overall prevalence of DFU is 1.3% - 12%
 - Annual incidence of approximately 2% - 5%
- Even when adherent to current standard of care, including:
 - DM control
 - Dressing changes
 - Offloading / Pressure reduction
 - Regular high-quality wound debridement
- **Less than half of DFU heal ...**
 - **25% - 50% of DFU develop infection³**

1. 2017 Jun 15;376(24):2367-2375. doi: 10.1056/NEJMra1615439.
 2. Diabetes research and clinical practice. 2020 Apr 1;162:108113
 3. *Diabetes care*. 2006;29(6):1288-1293

SOCIAL DETERMINANTS OF HEALTH

World Health Organization (2010)	Socioeconomic and Political Context <ul style="list-style-type: none"> ▪ Governance ▪ Macroeconomic policies ▪ Social policies (labor housing, land) ▪ Public policies (Education, health, social protection) ▪ Culture and societal values 	Socioeconomic Position <ul style="list-style-type: none"> ▪ Social class ▪ Gender ▪ Ethnicity (racism) ▪ Education ▪ Occupation ▪ Income 	Social Cohesion and Social Capital	Material Circumstances <ul style="list-style-type: none"> ▪ Housing and neighborhood quality ▪ Consumption potential (means to buy healthy food, warm clothes) ▪ Physical work environment 	Health Care <ul style="list-style-type: none"> ▪ Access 	
Healthy People 2020	Economic Stability <ul style="list-style-type: none"> ▪ Employment ▪ Food insecurity ▪ Housing instability ▪ Poverty 	Education <ul style="list-style-type: none"> ▪ Early childhood education and development ▪ Enrollment in higher education ▪ High school graduation ▪ Language and literacy 	Social and Community Context <ul style="list-style-type: none"> ▪ Civic participation ▪ Discrimination ▪ Incarceration ▪ Social cohesion 	Neighborhood and Built Environment <ul style="list-style-type: none"> ▪ Access to foods that support healthy eating patterns ▪ Crime and violence ▪ Environmental conditions ▪ Quality of housing 	Health and Health Care <ul style="list-style-type: none"> ▪ Access to health care ▪ Access to primary care ▪ Health literacy 	
County Health Rankings Model (2014)	Economic Factors <ul style="list-style-type: none"> ▪ Education ▪ Employment ▪ Income 		Social Factors <ul style="list-style-type: none"> ▪ Family and social support ▪ Community safety 	Physical Environment <ul style="list-style-type: none"> ▪ Air and water quality ▪ Housing and transit 		
Kaiser Family Foundation (2018)	Economic Stability <ul style="list-style-type: none"> ▪ Employment ▪ Income ▪ Expenses ▪ Debt ▪ Medical bills ▪ Support 	Education <ul style="list-style-type: none"> ▪ Literacy ▪ Language ▪ Early childhood education ▪ Vocational training ▪ Higher education 	Community and Social Context <ul style="list-style-type: none"> ▪ Social integration ▪ Support systems ▪ Community engagement ▪ Discrimination ▪ Stress 	Neighborhood and Physical Environment <ul style="list-style-type: none"> ▪ Housing ▪ Transportation ▪ Safety ▪ Parks, playgrounds ▪ Walkability ▪ Zip codes/geography 	Health and System <ul style="list-style-type: none"> ▪ Health coverage ▪ Provider availability ▪ Provider linguistic and cultural competency ▪ Quality of care 	Food Environment <ul style="list-style-type: none"> ▪ Hunger ▪ Access to healthy options

Socioeconomic Perspective

- The prevalence of diabetes increases with age
- The prevalence of diabetes decreases with
 - increasing education and
 - increasing household income level
- The prevalence of diabetes was higher among Black, non-Hispanics (16.7%) compared to white, non-Hispanic adults (11.8%)
- The prevalence of diabetes is similar by gender

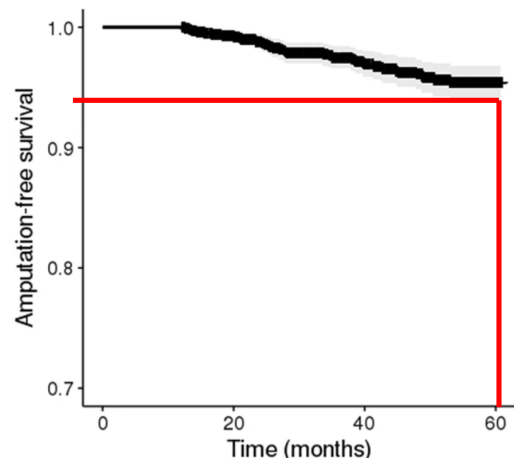
Michigan Behavioral Risk Factor Surveillance System, 2022

7

Socioeconomic Perspective

- Equality (& equity) in health care according to the need has been an important goal for health care policy
- Socioeconomic position (SEP) is strongly associated with DFU outcomes

- Predictors of Amputation in people with DFUs
 - **Low SEP (HR 5.13; $p = 0.018$),**
 - Male sex (hazard ratio [HR], 2.41; $p < 0.01$),
 - Circulatory complications (HR 2.14; $p = 0.020$)
 - Ophthalmopathy (HR, 1.89; $p = 0.028$)

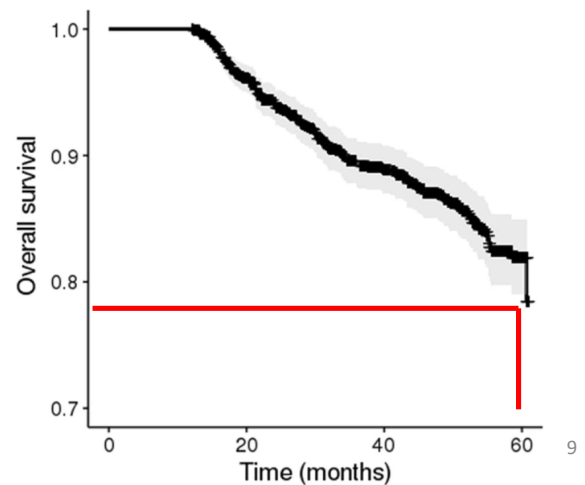


Socioeconomic Perspective

• Equality (& equity) in health care according to the need has been an important goal for health care policy

• Socioeconomic position (SEP) is strongly associated with DFU development

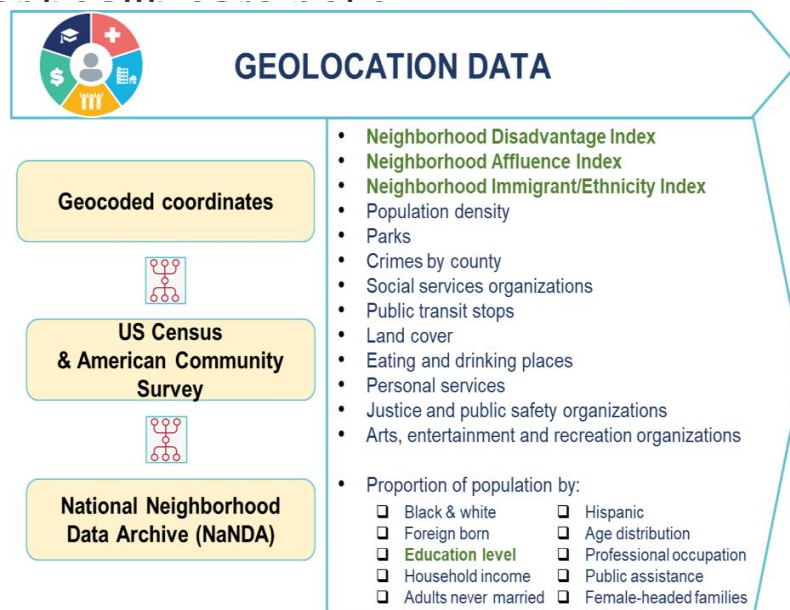
- Predictors of Mortality in people with DFUs
 - **Low SEP (HR, 2.65; $p < 0.01$),**
 - Ophthalmopathy (HR, 1.74; $p < 0.01$),
 - Circulatory complications (HR, 1.71; $p < 0.01$)
 - Advanced age (HR 1.06; $p < 0.01$)



BMC Public Health. 2021;21:1395.

Socioeconomic Perspective

• Equality (& equity) in health care according to the need has been an important goal for health care policy



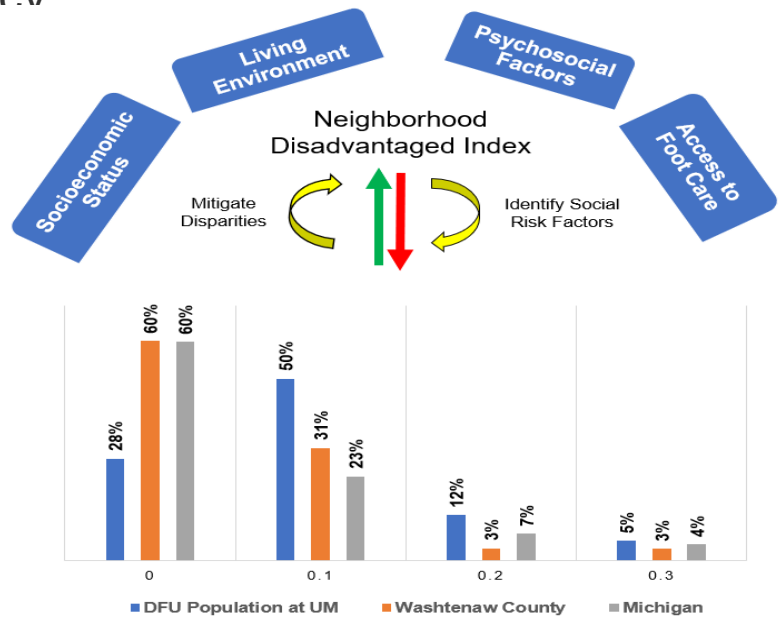
Courtesy of UM Precision Health

Socioeconomic Perspective

• Equality (& equity) in health care according to the need has been an important goal for health care policy

• When we critically examined the DFU patient population at UM, they are found, on average, to have increased neighborhood disadvantaged status:

- **MM DF population** 0.11
- Washtenaw County 0.06
- State of Michigan 0.07



Data generated from UM Precision Health Tools (UM IRB: HUM00217319)

11

Socioeconomic Perspective



• Direct costs of care for diabetes (in general) was **\$415 billion** in 2021¹

- Incremental payer burden of DFU range:
 - \$11,710 **Medicare** cost differential / DFU
 - \$16,883 **Private Insurance** cost differential / DFU
- Account for indirect costs:
 - “Costs of missed work due to disability among the subset of patients”
- One-third of all diabetes care attributable to care for lower extremity complications?
 - Only estimate do not stratify costs for foot ulcer and/or amputation.
 - These are lumped in with “cardiovascular diseases”

> \$100,000,000,000

1. International Diabetes Federation (IDF) Diabetes Atlas, December 2021
 2. J Foot Ankle Res. 2020; 13: 16.

12

OUTLINE

- Scope and Magnitude of Diabetic Foot Ulcers and Infection
- **Learn Classification Systems**
 - **Case Examples**
- Antibiotic Approaches and Stewardship
 - Culture
 - Antibiotics of Choice
 - Referral
- Clinical Outcomes and Setting Expectations
- Conclusions

13

Diabetic Foot Ulcer Infection

Facts:

- **>85%** of diabetic foot infections are preceded by DFU
 - The prevalence of these infections have been reported to range between **25-60%**
- Patients who develop an infection have a **155-fold increased risk of amputation** compared to those who do not develop infection
- Studies evaluating the development of infection are much less common, so treatment is key!



14

Clinical Manifestation of Infection	PEDIS Grade	IDSA Infection Severity
No symptoms or signs of infection	1	Uninfected
Infection present, as defined by the presence of at least 2 of the following items: Local swelling or induration Erythema Local tenderness or pain Local warmth Purulent discharge (thick, opaque to white or sanguineous secretion)		
Local infection involving only the skin and the subcutaneous tissue (without involvement of deeper tissues and without systemic signs as described below). If erythema, must be >0.5 cm to ≤2 cm around the ulcer. Exclude other causes of an inflammatory response of the skin (eg, trauma, gout, acute Charcot neuro-osteopathy, fracture, thrombosis, venous stasis).	2	Mild
Local infection (as described above) with erythema > 2 cm, or involving structures deeper than skin and subcutaneous tissues (eg, abscess, osteomyelitis, septic arthritis, fasciitis), and No systemic inflammatory response signs (as described below)	3	Moderate
Local infection (as described above) with the signs of SIRS, as manifested by ≥2 of the following: Temperature >38°C or <36°C Heart rate >90 beats/min Respiratory rate >20 breaths/min or PaCO ₂ <32 mm Hg White blood cell count >12 000 or <4000 cells/μL or ≥10% immature (band) forms	4	Severe ^a

Lipsky BA, Berendt AR, Cornia PB, Pile JC, Peters EJ, Armstrong DG, Deery HG, Embil JM, Joseph WS, Karchmer AW, Pinzur MS. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clinical infectious diseases. 2012 Jun 15;54(12):e132-73. 15

CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild**
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance:

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate
- D.) 3 – Severe



CLASSIFICATION PRACTICE

Classify wound based on clinical appearance

- A.) 0 – No infection
- B.) 1 – Mild
- C.) 2 – Moderate**
- D.) 3 – Severe**

➤ If osteomyelitis, outcomes are worse



OUTLINE

- Scope and Magnitude of Diabetic Foot Ulcers and Infection
- Learn Classification Systems
 - Case Examples
- **Antibiotic Approaches and Stewardship**
 - **Culture**
 - **Antibiotics of Choice**
 - **Referral**
- Clinical Outcomes and Setting Expectations
- Conclusions

APPROPRIATE CULTURE

- **Tissue culture is essential to best identify causative organisms in DFI**
 - Obtain **post-debridement soft tissue cultures** rather than superficial swabs for evaluation of infected diabetic foot ulcers.
 - If wound swab is the only available method of obtaining a culture, perform it **post-debridement of soft tissue cultures**
 - If osteomyelitis is suspected, obtain bone culture to guide antibiotic therapy rather than soft tissue culture if clinically feasible; **do not obtain superficial swabs**.
 - When obtaining bone specimens, send the specimen for **both histopathology and culture**, as either can make the diagnosis of osteomyelitis.

25

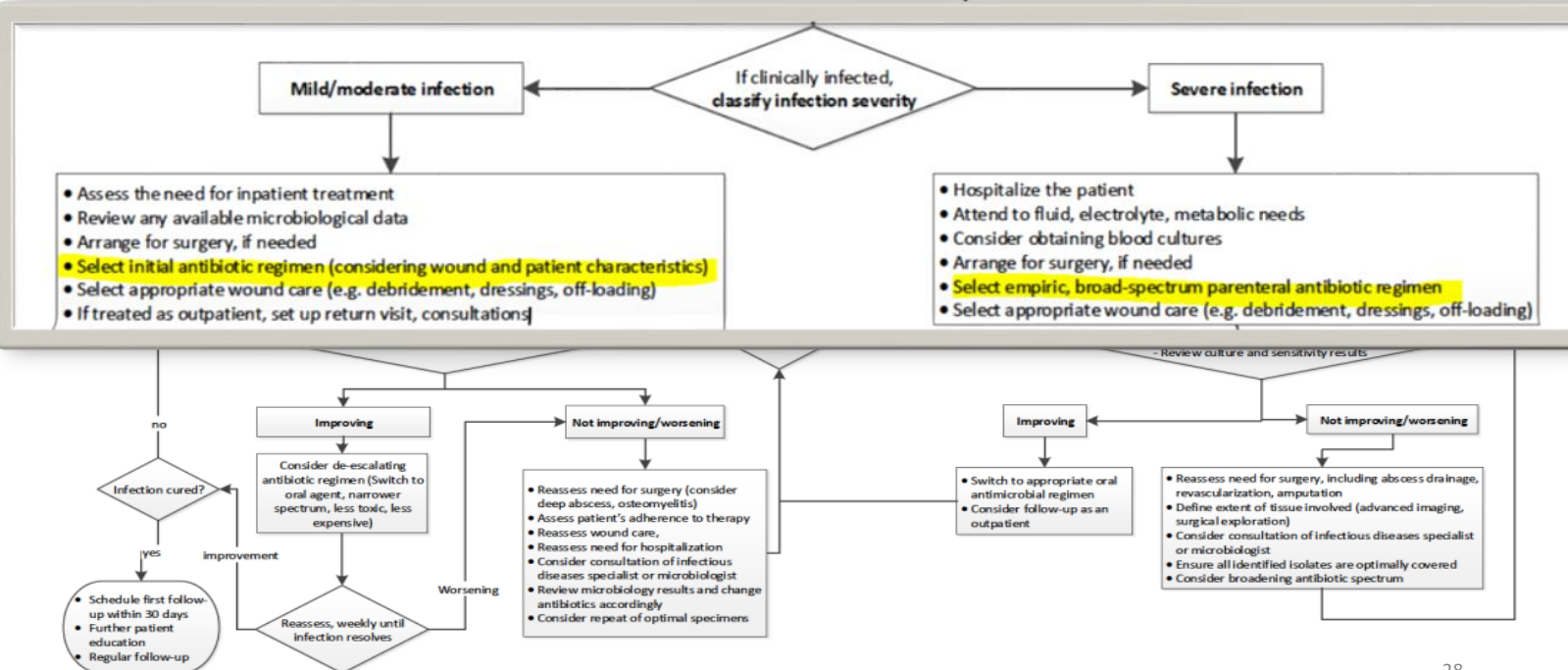
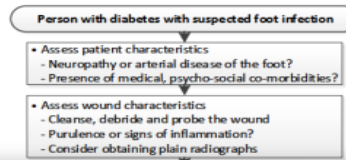
TO CULTURE

- Culturing
 - When ?
 - From where?



26

While you wait for cultures to finalize ...



Empiric Therapy:

1. Select empiric antibiotic regimen on basis of **severity of infection** and **likely etiologic agent(s)** (strong, **low**)
 - For mild to moderate infection, target *aerobic GPC* (weak, **low**)
 - For more severe infections, start broad spectrum (strong, **low**)
 - Empiric therapy for *Pseudomonas aeruginosa* is unnecessary except for this with risk factors (weak, **low**)
 - Consider coverage for MRSA when:
 - Prior history of MRSA;
 - High local prevalence;
 - Clinically severe infection

Lavery LA, Ryan EC, Ahn J, Crisologo PA, Oz OK, La Fontaine J, Wukich DK. The infected diabetic foot: re-evaluating the Infectious Diseases Society of America diabetic foot infection classification. *Clinical Infectious Diseases*. 2020 Apr 10;70(8):1573-9. 29

ANTIBIOTIC CHOICE

- IDSA Mild Infection
 - Preferred option for individual not suspected of having MRSA infection:
 - Cephalexin 500mg PO QID
 - Previous MRSA infection:
 - Add trimethoprim/sulfamethoxazole DS 1-tab PO BID-TID.
 - Consider higher dosing if patient is greater than 80 kg or has extensive disease.
 - Alternative for cephalosporin allergy:
 - Linezolid 600 mg PO BID

Infection present with 2 or more of:
Local swelling or induration
Erythema <2cm around ulcer
Local tenderness or pain
Local warmth
Purulent discharge
Local infection involving skin and subcutaneous tissue only without systemic signs.
Other causes of inflammatory response should be excluded (gout, trauma, Charcot arthropathy, fracture, thrombosis, venous stasis)

ANTIBIOTIC CHOICE

Moderate Infection

Local infection with erythema >2 cm or involving deeper structures and no systemic inflammatory response

- IDSA Moderate Infection
 - Preferred option:
 - Piperacillin/tazobactam
 - Alternative option for patients with non-life-threatening penicillin allergy:
 - Cefepime
 - Alternative option for patients with life threatening penicillin allergy:
 - Aztreonam

Lipsky BA, Aragon-Sanchez J, Diggle M, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev. 2016;32 Suppl 1:45-74.
Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132-73

ANTIBIOTIC CHOICE

Severe Infection (including necrotizing fasciitis, or wet gangrene)

Local infection with signs of SIRS with ≥ 2 of:

- IDSA Severe Infection
 - Preferred option:
 - Piperacillin/tazobactam + vancomycin
 - Alternative option for patients with non-life-threatening penicillin allergy:
 - Cefepime + Vancomycin + Metronidazole
 - Alternative option for patients with life threatening penicillin allergy:
 - Aztreonam + Vancomycin + Metronidazole
 - If necrotizing fasciitis is suspected, add clindamycin 900 mg IV q 8 hours, for its anti-toxin activity.

- Temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$
- HR >90 bpm
- RR >20 breaths/min or PaCO₂ <32 mmHg
- WBC >12000 or <4000 or $>10\%$ band forms

Lipsky BA, Aragon-Sanchez J, Diggle M, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. Diabetes Metab Res Rev. 2016;32 Suppl 1:45-74.
Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. Clin Infect Dis. 2012;54(12):e132-73

ANTIBIOTIC CHOICE

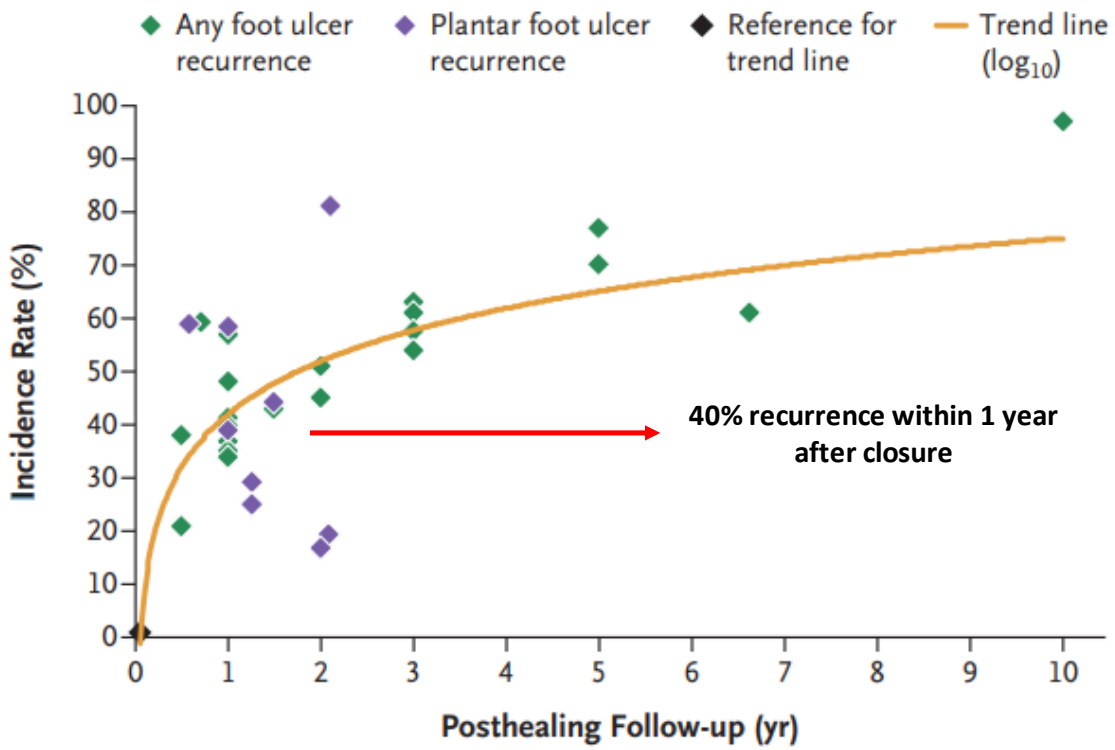
Diabetic Foot Infection Footnotes:

1. Tailor treatment to treat previously isolated pathogens in patients with recurrent diabetic foot infections
2. Modify antibiotic therapy when culture results and sensitivities are available
3. ID consult is recommended to help guide antibiotic treatment recommendations

Lipsky BA, Aragon-Sanchez J, Diggle M, et al. IWGDF guidance on the diagnosis and management of foot infections in persons with diabetes. *Diabetes Metab Res Rev.* 2016;32 Suppl 1:45-74.
Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis.* 2012;54(12):e132-73

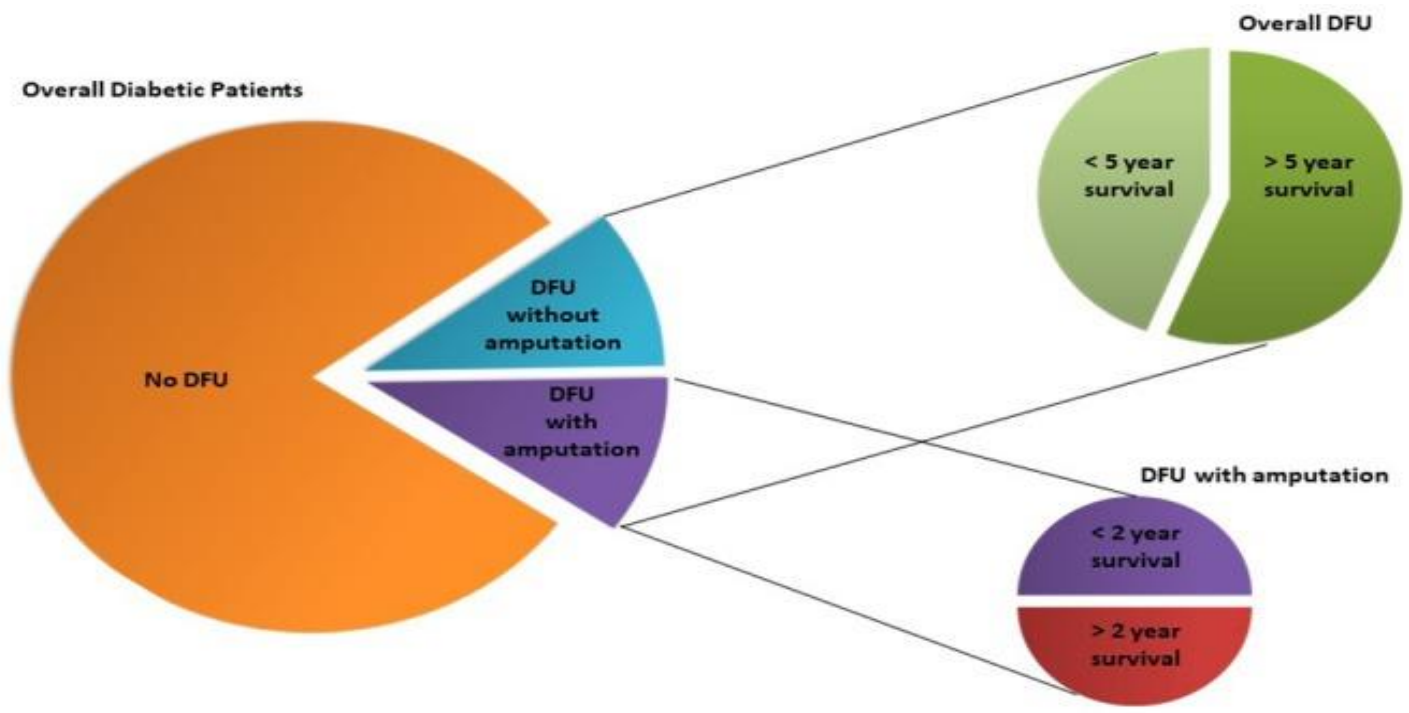
OUTLINE

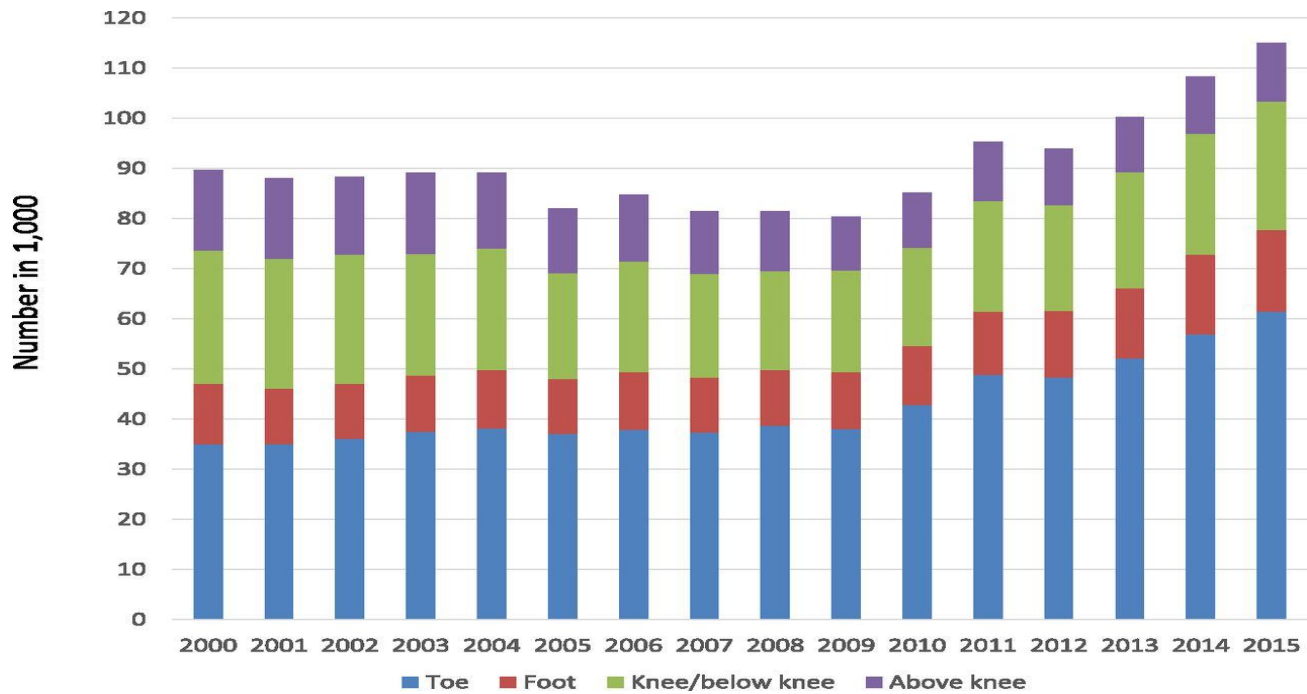
- Scope and Magnitude of Diabetic Foot Ulcers and Infection
- Learn Classification Systems
 - Case Examples
- Antibiotic Approaches and Stewardship
 - Culture
 - Antibiotics of Choice
 - Referral
- **Clinical Outcomes and Setting Expectations**
- Conclusions



2017 Jun 15;376(24):2367-2375. doi:10.1056/NEJMra1615439.

OUTCOMES





Number (in 1,000s) of NLEAs among adults with diagnosed diabetes by level of amputation. Blue, toe; red, foot; green, above foot/below knee/knee; purple, above knee.

OUTLINE

- Scope and Magnitude of Diabetic Foot Ulcers and Infection
- Learn Classification Systems
 - Case Examples
- Antibiotic Approaches and Stewardship
 - Culture
 - Antibiotics of Choice
 - Referral
- Clinical Outcomes and Setting Expectations
- **Conclusions**

CONCLUSIONS

1. DFU is a growing problem
2. DFU infection occurs
3. Do your part...
4. Call for help, sooner rather than later



39

Acknowledgements

Diabetic Foot Consortium

Rodica Pop-Busui, MD PhD
Crystal Holmes, DPM CWSP
Katherine Gallagher MD
Kayvan Najarian, PhD
Cathy Martin MS, APRN, CDE
Aaron Burant, BS
Nicole Baker, BS
Aimee Katona, BS
Kourtney Noll, BHA

Conference Organizers

Lynn Ang, MD
Rodica Pop-Busui, MD, PhD
Allison Picinotti
Erin Reau
Hailey Seymour

Podiatric Medicine and Surgery

Crystal Holmes, DPM CWSP
Michael Munson, DPM
Gary Rothenberg, DPM CWSP CDE
Sari Priesand, DPM
Garneisha Torrence, DPM MHMS
Alton Johnson, DPM CWSP
Brennen O'Dell, DPM
Kanika Kochhar, DPM

