

Antibiotic Stewardship- Implications for ESRD Facilities

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Atlantic Quality Innovation Network (AQIN)

- The federally funded Medicare Quality Innovation Network – Quality Improvement Organization (QIN-QIO) for New York State, the District of Columbia, and South Carolina.
- Led by IPRO.
- Partners include
 - Delmarva Foundation in the District of Columbia and
 - The Carolinas Center for Medical Excellence in South Carolina.
- One of 14 QIN-QIOs operating across the U.S.

Atlantic Quality Innovation Network (AQIN)

- Works toward better care, healthier people and communities, and smarter spending
- Catalyzes change through a data-driven approach to improving healthcare quality.
- Collaborates with providers, practitioners and stakeholders at the community level to share knowledge, spread best practices and improve care coordination.
- Promotes a patient-centered model of care, in which healthcare services are tailored to meet the needs of patients.

Antibiotic Stewardship- What It Is.

Antibiotic Stewardship is defined as, “coordinated interventions designed to improve and measure the appropriate use of antibiotic agents by promoting selection of the optimal drug regimen including dosing, duration of therapy and route of administration”. IDSA and SHEA

“Antimicrobial stewardship is a coordinated program that promotes the appropriate use of antimicrobials (including antibiotics), improves patient outcomes, reduces microbial resistance, and decreases the spread of infections caused by multidrug-resistant organisms”. APIC

Antibiotic Stewardship- What It Is.

“The goals of antimicrobial stewardship programs include attenuating or reversing antimicrobial resistance, preventing antimicrobial related toxicity, and reducing the costs of inappropriate use and health care associated infections.” ASHP

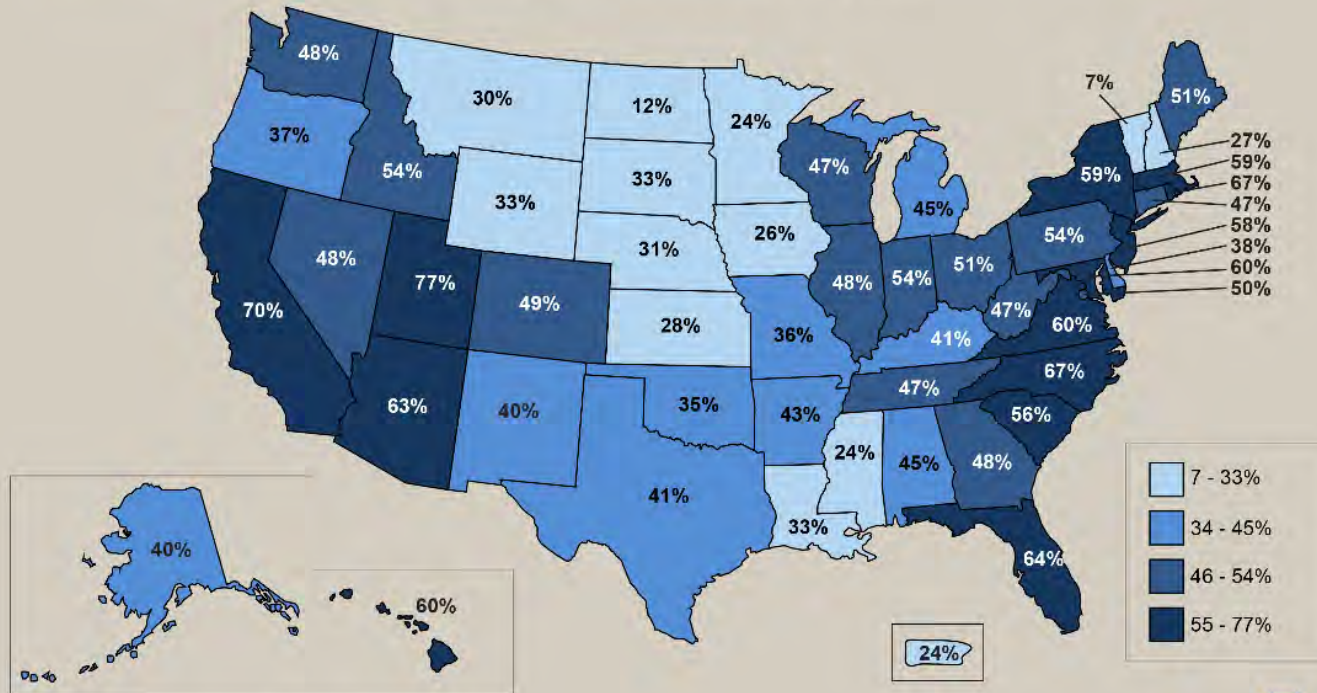
“Antibiotic stewardship programs are multi-faceted approaches to optimize antibiotic prescribing, encompassing components such as policy, guidelines, surveillance, education, epidemiology of current resistance, and process measurement. Successful antibiotic stewardship programs monitor and direct antimicrobial use, providing a standard, evidence-based approach to judicious antibiotic use in a healthcare facility”. AMA

CDC CORE ELEMENTS OF ANTIBIOTIC STEWARDSHIP

Hospital (2014)	Long Term Care (2015)	Outpatient (2016)
Leadership Commitment	Leadership Support	Commitment
Accountability	Accountability	Action
Drug Expertise	Drug Expertise	Tracking and Reporting
Action	Actions to Improve Use	Education and Expertise
Tracking- Monitoring Antibiotic Prescribing and Resistance Patterns	Tracking-Monitoring Antibiotic Prescribing, Resistance, Use	
Reporting-Regular reporting of information on antibiotic use and resistance to doctors, nurses and relevant staff	Reporting Information to Staff on Improving Antibiotic Use and Resistance	
Education	Education	

Percent of Hospitals with Antibiotic Stewardship Programs by State, 2015*

Nationally, 48.1% of all hospitals have stewardship programs (2,199 of 4,549); the national goal is 100% of hospitals by 2020.



*A hospital stewardship program is defined as a program following all 7 of CDC's Core Elements of Hospital Antibiotic Stewardship Programs.

Source: CDC's National Healthcare Safety Network (NHSN) Survey



Antibiotic Stewardship Program Guidelines- IDSA and SHEA

Summary - Recommendations

- **Preauthorization and or prospective audit and feedback**
- Development of facility specific clinical practice guidelines
- ASP interventions to improve antibiotic use and clinical outcomes that target patients with specific infectious diseases
- **ASP interventions designed to reduce the use of antibiotics associated with a high risk of CDI**
- Use of strategies to encourage providers to perform routine review of antibiotic regimens to improve prescribing
- Incorporation of clinical decision support (CDS) at the time of prescribing into ASP
- **Recommend the implementation of PK monitoring and adjustment programs for aminoglycosides and vancomycin**
- Advocate for the use of alternative dosing strategies vs. standard dosing for broad spectrum B-lactams to decrease cost
- **Recommend programs to increase both appropriate use of oral antibiotics for initial therapy and timely transition of patients from IV to PO**

Barlan T.F. et al. Implementing an antibiotic stewardship program: Guidelines by the infectious disease society of America and the Society for Healthcare Epidemiology of America. CID 2016; 62: e51-e77.

Antibiotic Stewardship Program Guidelines- IDSA and SHEA

Summary -Recommendations

- ASPs should promote allergy assessments and penicillin skin testing when appropriate
- **ASPs should implement guidelines and strategies to reduce antibiotic therapy to the shortest effective duration.**
- Suggest ASPs develop stratified antibiograms
- ASPs should recommend selective and cascade reporting of antibiotics over reporting of all antibiotics
- Suggest the use of rapid viral testing for respiratory pathogens
- Suggest rapid diagnostic testing in addition to conventional culture and routine reporting on blood specimens if combined with active ASP support and interpretation.
- Suggest the use of serial PCT measurements in adults in ICUs to decrease antibiotic use
- Suggest monitoring antibiotic use as Days of Therapy in preference to Defined Daily Dose
- **Measure antibiotic costs based on prescriptions or administration instead of purchasing data**

Joint Commission- New Antimicrobial Stewardship Standard

- **Medication Management Standard- MM.09.01.01** The organization has an antimicrobial stewardship program based on current scientific literature.
- **Effective January 1, 2017**
- **Standard for Hospitals, Critical Access Hospitals, and Nursing Care Centers**
- **CDC core elements are included in stewardship program**

The Joint Commission. R3 Supplemental Report January 2017

Joint Commission- New Antimicrobial Stewardship Standard- Sample Performance Element

The hospital's antimicrobial stewardship program uses organization-approved multidisciplinary protocols (for example, policies and procedures). *Note: Examples of protocols are as follows:*

- Antibiotic Formulary Restrictions
- Assessment of Appropriateness of Antibiotics for Community-Acquired Pneumonia
- Assessment of Appropriateness of Antibiotics for Skin and Soft Tissue infections
- Assessment of Appropriateness of Antibiotics for Urinary Tract Infections
- Care of the Patient with *Clostridium difficile*
- Guidelines for Antimicrobial Use in Adults
- Guidelines for Antimicrobial Use in Pediatrics
- Plan for Parenteral to Oral Antibiotic Conversion
- Preauthorization Requirements for Specific Antimicrobials
- Use of Prophylactic Antibiotics

Reference: The Joint Commission. R3 Supplemental Report January 2017

Quality Payment Program (MACRA/MIPS)

- **Quality measure- appropriate treatment of methicillin sensitive *staphylococcus aureus* (MSSA) bacteremia.**
- **Quality measure- adult sinusitis- appropriate choice of antibiotic**
- **Quality measure- avoidance of antibiotic treatment in adults with acute bronchitis**
- **Quality measure- prevention of central venous catheter related bloodstream infection**
- **Improvement activity- implementation of antibiotic stewardship program**

Available at <https://qpp.cms.gov/measures/performance>

Outcomes of Antibiotic Stewardship

- **Improve Patient Outcomes**
- **Avoid/Reduce Resistance**
- **Decrease Antibiotic Adverse Effects**



Commonly Used Oral Antibiotics

Antibiotic	ADE	Indication
Trimethoprim/Sulfamethoxazole (Bactrim or Septra)	Rash, Stevens-Johnson, Renal Failure, photosensitivity, Hematologic (neutropenia/anemia), Diarrhea	Urinary Tract Infection Uncomplicated Chronic Bronchitis
Nitrofurantoin (Macrobid)	GI Intolerance, Neuropathies, Pulmonary Reactions, Diarrhea, Optic Neuritis, Anemia, Hepatitis- BEERS LIST	Urinary Tract Infection Uncomplicated
Fosfomycin (Monurol)	Diarrhea, Headache, Angioedema, Vaginitis, Nausea, Optic Neuritis, Vaginitis, Cholestatic Jaundice, Anemia	Urinary Tract Infection Uncomplicated (women)
Quinolones (Ciprofloxacin (Cipro), Levofloxacin (Levoquin), Moxifloxacin (Avelox))	Hypersensitivity, Photosensitivity, GI symptoms, Dizziness, Confusion, Diarrhea, Tendinitis and Tendon Rupture, Stevens-Johnson, QT Prolongation, Leukopenia, Thrombocytopenia, Tremors, Hallucinations, Peripheral Neuropathy, Hepatitis	Urinary Tract Infection Uncomplicated, Pyelonephritis Uncomplicated Chronic Bronchitis Atypical Pneumonia Pneumonia Skin and Soft Tissue
Tetracycline-Doxycycline (Monodox)- Minocycline (Minocin)	Nausea, Diarrhea, Renal Toxicity, Stevens-Johnson, Anemia, Thrombocytopenia, Neutropenia, Intracranial Hypertension, Hepatotoxicity, Rash, Photosensitivity	Chronic Bronchitis Atypical Pneumonia Rhinosinusitis

Commonly Used Oral Antibiotics

Antibiotic	ADE	Indication
Cefdinir (Omnicef), Cefpodoxime Proxetil (Vantin), Cephalexin	Hypersensitivity, Rash, Diarrhea, Seizures, Stevens-Johnson, Vaginitis, Leukopenia, Anemia, Renal Dysfunction, Thrombocytopenia, Interstitial Nephritis	Pyelonephritis Uncomplicated Chronic Bronchitis Pneumonia (with macrolide)
Ampicillin, Amoxicillin, Augmentin	Hypersensitivity, Diarrhea, Vaginitis, Anemia, Increase in Liver Enzymes, Leukopenia, Thrombocytopenia, Glossitis, Rash, GI symptoms, interstitial nephritis	Chronic Bronchitis Rhinosinusitis Skin and Soft Tissue
Erythromycin, Clarithromycin (Biaxin), Azithromycin (Zithromax)	Stevens-Johnson, Hepatotoxicity, Drug Reaction with Eosinophilia and Systemic Symptoms, Diarrhea, QT Prolongation, Vomiting, Rash, Vaginitis	Chronic Bronchitis Atypical Pneumonia
Linezolid (Zyvox)	Anemia, Leukopenia, Pancytopenia, Thrombocytopenia, Lactic Acidosis, Nausea, Vomiting, Diarrhea, Serotonin Syndrome, Optic Neuropathy, Convulsions, Tooth/Tongue Discoloration	Pneumonia Skin and Skin Structure Diabetic Foot Infections

Antibiotic Classes and *Clostridium-Difficile**

Class	Association with C-Difficile Infection
Clindamycin, Ampicillin, Amoxicillin, Cephalosporins (second generation and higher), Fluoroquinolones	Very Common
Other Penicillins, Sulfonamides, Trimethoprim, Macrolides	Somewhat Common
Aminoglycosides, Bacitracin, Metronidazole, Teicoplanin, Rifampin, Chloramphenicol, Tetracyclines, Carbapenems, Daptomycin, Tigecycline	Uncommon

Longo D.L. NEJM 2015;372:1539-48

FDA Warning- Quinolone Drugs for Systemic Use- Update Due to Disabling Side Effects

- **Warning posted July 26, 2016**
- **FDA has determined that the quinolone antibiotics should be reserved for use in patients with no other treatment option for sinusitis, chronic bronchitis, uncomplicated urinary tract infection. Risk>Benefit**
- **Boxed warning for tendinitis, tendon rupture, worsening myasthenia gravis, peripheral neuropathy (may be irreversible), CNS effects**
- **Disabling and potentially permanent side effects of the tendons, muscles, joints, nerves and CNS that can occur together in the same patient.**

Resistance Update



How Antibiotic Resistance Happens

1.

Lots of germs.
A few are drug resistant.



2.

Antibiotics kill
bacteria causing the illness,
as well as good bacteria
protecting the body from
infection.



3.

The drug-resistant
bacteria are now allowed to
grow and take over.



4.

Some bacteria give
their drug-resistance to
other bacteria, causing
more problems.



CDC Antimicrobial Threat Report

Urgent Threat

HAZARD LEVEL

URGENT



These are high-consequence antibiotic-resistant threats because of significant risks identified across several criteria. These threats may not be currently widespread but have the potential to become so and require urgent public health attention to identify infections and to limit transmission.

Clostridium difficile (*C. difficile*), Carbapenem-resistant Enterobacteriaceae (CRE), Drug-resistant *Neisseria gonorrhoeae* (cephalosporin resistance)

CDC website accessed 5/5/17- https://www.cdc.gov/drugresistance/biggest_threats.html

CDC Antimicrobial Threat Report

Serious Threat

HAZARD LEVEL

SERIOUS



These are significant antibiotic-resistant threats. For varying reasons (e.g., low or declining domestic incidence or reasonable availability of therapeutic agents), they are not considered urgent, but these threats will worsen and may become urgent without ongoing public health monitoring and prevention activities.

Multidrug-resistant *Acinetobacter*, Drug-resistant *Campylobacter*, Fluconazole-resistant *Candida* (a fungus), Extended spectrum β -lactamase producing Enterobacteriaceae (ESBLs), Vancomycin-resistant *Enterococcus* (VRE), Multidrug-resistant *Pseudomonas aeruginosa*, Drug-resistant Non-typhoidal *Salmonella*, Drug-resistant *Salmonella* Typhi, Drug-resistant *Shigella*, Methicillin-resistant *Staphylococcus aureus* (MRSA), Drug-resistant *Streptococcus pneumoniae*, Drug-resistant tuberculosis (MDR and XDR)

New Threats

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *The Lancet* November 2015

- MCR-1 causes resistance to colistin, a last-resort drug for treating resistant infections- May 2016
- “Superbug gene MCR-1 found in a Connecticut toddler” - Sep 2016 -A new case of the superbug gene MCR-1, which makes *E. coli* resistant to most antibiotics, was found in a toddler living in Connecticut. This is the fourth time that physicians detect a superbug in the United States.

Emergence of *Candida Auris*

- *Candida auris*, an emerging multidrug-resistant (MDR) yeast, is causing invasive healthcare-associated infections with high mortality
- Resistance documented to 3 classes of antifungal agents.

Outpatient Stewardship Facts- CDC

- The most important modifiable risk factor for antibiotic resistance is inappropriate prescribing of antibiotics.
- Approximately 50% of outpatient antibiotic prescribing in humans might be inappropriate, including antibiotic selection, dosing, or duration, in addition to unnecessary antibiotic prescribing.
- At least 30% of outpatient antibiotic prescriptions in the United States are unnecessary.
- Antibiotic treatment is the most important risk factor for *Clostridium difficile* infection.

Published Literature on Antibiotic Stewardship in the Outpatient Setting including ESRD Dialysis Setting

Prevalence of Inappropriate Antibiotic Prescriptions US Ambulatory Care

- Study time frame- 2010-2011
- Of the 184,032 sampled visits for adults and children, 12.6% resulted in antibiotic prescriptions.
- Sinusitis was the single diagnosis with most antibiotic prescriptions (56/1000 population)
- Other common diagnoses in adults: skin, cutaneous and mucosal infections, urinary tract infections, bronchitis.
- In 2010-2011, 506 antibiotic prescriptions/1000 population were written, 353/1000 estimated to be appropriate.

Fleming K et al. JAMA. 2016; 315(17): 1864-1873

Effects of Knowledge, Attitudes, and Practices on Antibiotic Selection

- Interviews with 36 primary care providers (MD, NP, PA)
- Participants familiar with guideline recommendations for common infections but did not always comply.
- Reasons for non-adherence:
 - ❖ belief that non-recommended agents are more likely to cure infection
 - ❖ concern for patient satisfaction
 - ❖ fear of infectious complications
- Providers inconsistently defined broad and narrow spectrum

Sanchez et al. Emerging Infectious Disease 2014Vol 20; No 12.

Nudging Guideline Concordant Antibiotic Prescribing. A Randomized Trial.

- Trial in 5 outpatient primary care clinics
- Total of 941 adults with acute respiratory infection
- 449 patients treated by clinicians randomized to the posted commitment letter, 505 patients treated by clinicians randomized to standard therapy.
- 1 year time frame including flu season
- Baseline inappropriate prescribing rates 43.5% and 42.8%, rate increased to 52.7% in control group and decreased to 33.7% in intervention group.

Meeker et al JAMA 2014 174: 425-431

Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing in Primary Care

- **Study conducted in 47 primary care practices**
- **248 clinicians randomized to 0, 1, 2 or 3 interventions for 18 months.**
- **All clinicians received education on antibiotic prescribing guidelines.**
- **Three behavioral interventions: suggested alternative, accountable justification, peer comparison**
- **Mean antibiotic prescribing rates significantly decreased for all three interventions types**

Meeker et al. JAMA 2016 315: 562-570

Association Between Outpatient Antibiotic Prescribing and Community C-Difficile Infection

- 2011 active adult population and laboratory based surveillance – 9 US geographic locations to identify CA-CDI cases.
- Patients were >20 years of age with no positive test ≤ 8 weeks prior and no overnight stay in healthcare facility ≤ 12 weeks prior.
- Providers prescribed 5.2 million courses of antibiotics for 2010 for an average of 0.73 per person
- Reducing antibiotic prescribing rates by 10% were associated with 17% decrease in CA-CDI rates
- Greatest decreases in CA-CDI with reductions in penicillin and amoxicillin clavulanate prescriptions

Dantes et al. Open Forum Infectious Disease 2015 ; OFID: 1-7

Antimicrobial Use and Stewardship Programs Among Dialysis Centers

- ❑ 30-40% of chronic hemodialysis patients receive at least 1 dose of an antimicrobial in outpatient centers over a 1 year time frame.
- ❑ Up to 30% of antimicrobials prescribed are inappropriate per national guidelines
- ❑ Inappropriate use:
 - ❑ Failure to de-escalate
 - ❑ Criteria for infection not met (SSTI)
 - ❑ Indications and duration for surgical prophylaxis do not follow recommended guidelines

D'Agata, Seminars in Dialysis 2013; 26:457-464

Antimicrobial Use in Outpatient Hemodialysis Units

- ❑ Retrospective analysis of antimicrobial use in 2 outpatient hemodialysis units
- ❑ Rate of antimicrobial use was 32.9 doses/100 patient months and 7.6 antimicrobial starts/100 patient months- (NHSN reported 3.5 starts/100 patient months)
- ❑ Most common inappropriately prescribed antimicrobials were vancomycin and third and fourth generation cephalosporins.
- ❑ Mean patient age was 66.7 and the mean duration of hemodialysis was 2.8 years, 53% had AV fistulas

Snyder et al. *Infection Control and Hospital Epidemiology* 2013; 34: 349-357

How Can The Patient Participate As Part Of The Antibiotic Stewardship Team?

Questions to Ask your Healthcare Provider Before Asking for an Antibiotic

1. **Could my symptoms be caused by something other than bacteria (example a virus or something that is not an infection)?**
2. **What signs and symptoms should I look for that could mean I might need an antibiotic?**
3. **Can I be monitored to see if my symptoms improve with other remedies, without using antibiotics?**

CDC Get Smart Accessed May 2017

Questions to Ask your Healthcare Provider When you are Prescribed an Antibiotic

1. What infection is the antibiotic treating and how do I know I have that infection?
2. What side effects might occur from this antibiotic?
3. Could any of my medications interact with this antibiotic?
4. How will I be monitored to know whether my illness is responding to the antibiotic?

CDC Get Smart Accessed May 2017

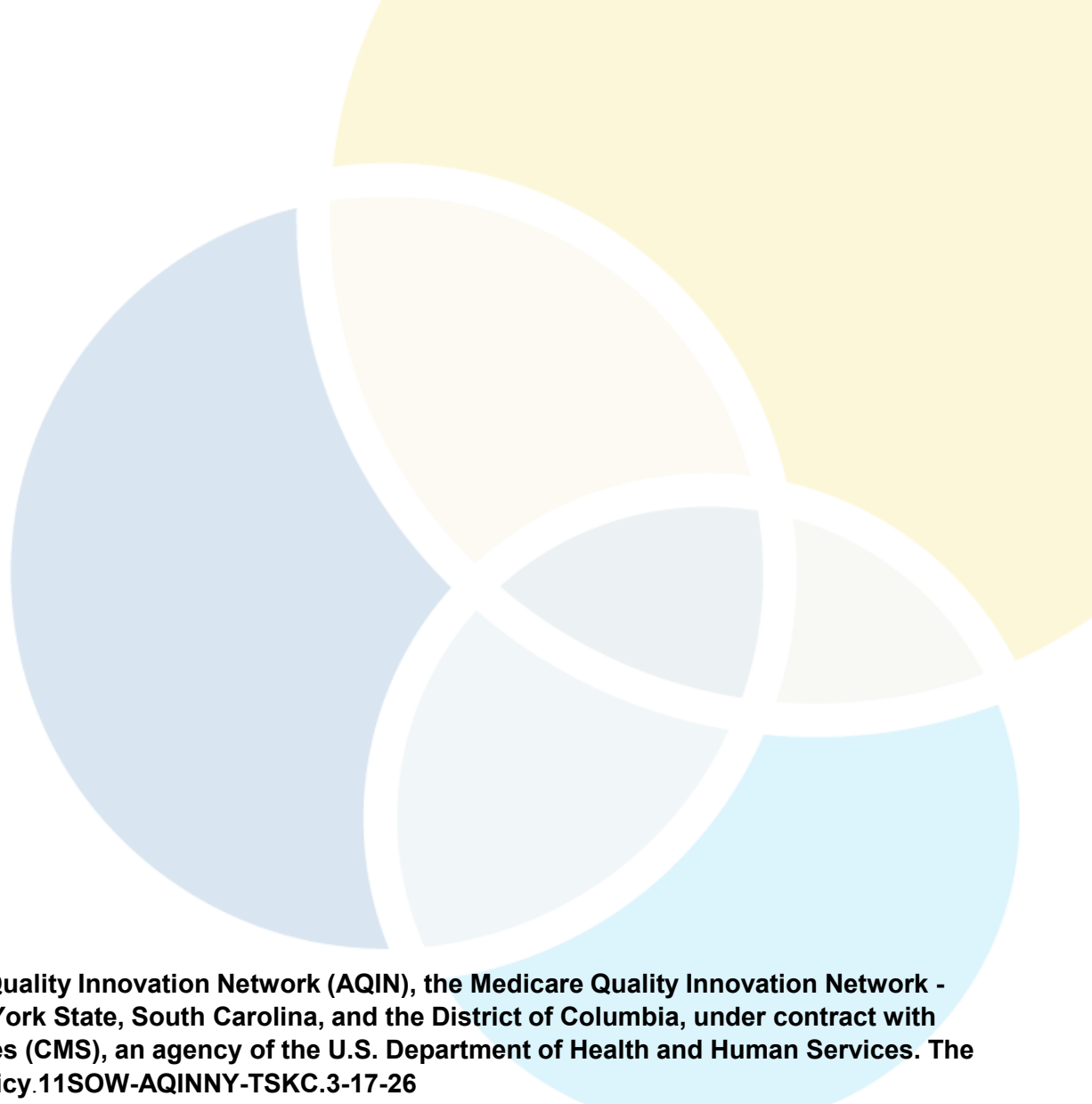
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