

**Joint Meeting of the Diabetes Mellitus Interagency Coordinating Committee and the
Urology Interagency Coordinating Committee (UICC)**

**Treatment of Diabetes and Urinary Tract Infection:
Evidence and Research Methods from Studies in Nursing Homes and Skilled Nursing
Facilities**

Friday, July 13, 2018
9:00 a.m. - 12:00 p.m.
6707 Democracy Blvd. Room 7050, Bethesda, MD

Meeting Minutes

Dr. Tamara Bavendam, the Women’s Urology Program Director within KUH, opened the meeting and meeting participants introduced themselves, also noting their agency affiliations. Dr. Judy Fradkin, Division Director for the Division of Diabetes, Endocrinology, and Metabolic Diseases at NIDDK, commented that this is a complex and understudied area of research. Elderly patients with diabetes and incontinence are overrepresented in nursing homes and more investment is needed to explore treatment in this area. Dr. Fradkin also commented that the idea for this meeting came from a paper titled “A National Implementation Project to Prevent Catheter-Associated Urinary Tract Infection in Nursing Home Residents.” The outcome of this study showed that in a large-scale national implementation project involving community-based nursing homes, combined technical and socioadaptive catheter-associated UTI prevention interventions successfully reduced the incidence of catheter associated UTIs.

Part I: CAUTI Prevention and Treatment

Setting the Stage: o Catheter-associated Urinary Tract Infections (CAUTI)

Dr. Bavendam began her talk by discussing how diabetes is associated with bladder problems and UTIs, and how diabetes can impact benign urology conditions such as the UTI. In turn, UTI symptoms can worsen the symptoms of diabetes. Dr. Bavendam presented the following national data on UTIs, demonstrating the high instance of overuse of catheters:

- 40% of all nosocomial infections are UTI’s
- UTIs are associated with a 2.8 fold increased risk of death
- 66%-86% of UTI’s follow instrumentation of the urinary tract
 - Catheter-associated Urinary Tract Infections or “CAUTIs”
 - Occurs at a rate of 3%–10% per day of catheterization and the incidence approaches 100% within the 30 hospital days.
 - In critically ill patients, it can lead to bacteremia, which is one of the leading causes of mortality and morbidity among hospitalized patients.

In addition to the overuse of catheters, many patients with indwelling catheters report symptoms of pain, discomfort, and a restriction in daily living activities. Decreased activity also increases risk of pressure sore and venous thromboembolism. Prevention strategies include not inserting unnecessary urinary catheters, and if needed, removing catheters as soon as possible, using good hygiene practices such as handwashing, dependent drainage, and securing catheter to body as well as the junction between the catheter and drainage device.

Agency for Healthcare Research and Quality (AHRQ) Research and Implementation Programs: Healthcare Associated Infections and Combating Antibiotic Resistant Bacteria

Dr. Dale Burwen, MD, MPH, AHRQ, noted that his agency is involved in activities to prevent healthcare-associated infections (HAI) and combat antibiotic-resistant bacteria (CARB). The AHRQ also supports the translation of research into tools and promotes implementation of HAI prevention and CARB. Dr. Burwen noted several grant funding opportunities, mostly program announcements, of research to implementation efforts for HAI prevention and CARB. Although this discussion is focused on nursing home patients, the AHRQ's research interests encompass multiple settings: acute care, ambulatory care, and long-term care.

As an example of translation of research into tools, Dr. Burwen cited the Nursing Home Antimicrobial Stewardship Guide, which was developed from four AHRQ-funded research projects. The Guide includes two developed toolkits on communication and clinical decision-making about potential infections and two developed toolkits on antibiograms. Dr. Burwen noted that the Guide was developed through a contractor and is available online at: <https://www.ahrq.gov/nhguide/index.html>.

Another AHRQ initiative titled "Comprehensive Unit-based Safety Program (CUSP)", was developed at Johns Hopkins University with AHRQ grant funding. This Program combines improvement in safety culture, teamwork, communication, and engagement, to promote consistent use of evidence-based practices. The National Project Team, part of the CUSP initiative, involved 30 state or regional lead organizations such as state nursing home associations, corporations or state provides associations. The CUSP Project Team included faculty coaches, a long-term care facility team, and residents and families. Dr. Burwen noted that the Project used both clinical and behavioral interventions. The result of this intervention project was a 54% decrease in catheter associated urinary tract infections (CAUTI). Information about the Toolkit Development is included on the AHRQ website at <https://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/tools/cauti-ltc/about-toolkit.html>.

Dr. Burwen noted that another AHRQ effort focuses on patient safety and improving antibiotic use within CUSP. The goal is to improve antibiotic use and promote antibiotic stewardship. This current effort uses a long-term, acute, and ambulatory care cohort. For the long-term cohort, the participation goal is 250-500 long-term care (LTC) facilities

and implementation begins in December 2018. The acute care cohort is currently ongoing with more than 400 hospitals participating. The ambulatory care cohort will begin in December 2019. More information about this program is available at <https://www.ahrq.gov/professionals/quality-patient-safety/hais/tools/antibiotic-stewardship/index.html>.

CAUTI Prevention Research in Older Adults: From Bench to Bedside

Dr. Lona Mody, MD, MSc, from the University of Michigan, began her presentations by discussing the burden of catheter associated urinary tract infections (CAUTI) in older adults and research results from local and national study. Dr. Mody displayed statistics that emphasized the burden of infections in nursing facilities:

- Human toll: 2 million infections annually
- Economic toll: 4 billion in costs annually
- Societal toll: safety concerns
- Urinary tract infection most common
- 1.4 million patients in nursing facilities
 - 70,000-100,000 with urinary catheter
- Infection prevention programs understaffed

Dr. Mody outlined three studies completed by her team. The first, a targeted infection prevention study, was a cluster-randomized trial that included 12 nursing homes located in SE Michigan. The study included residents with indwelling urinary catheters and/or feeding tubes and follow up was completed for this population over the course of 3 years. Nursing homes were stratified by ownership (for profit vs. not-for-profit), then assigned to intervention status using computer-generated randomization by the statistician. Six nursing homes were randomized to the intervention group and six to the control group. Both the groups were generally well matched with respect to number of residents eligible, number enrolled, and number with more than 1 follow-up visit as well as total number of follow-up visits. Dr. Mody noted that the most common reason for non-enrollment was refusal of consent or inability to reach the next-of-kin.

The study found no significant differences between intervention group nursing homes and control group nursing homes with respect to number of beds, ownership status, CMS star rating. In this targeted study, the intervention used: 1) gowns and gloves, 2) microbial disease resistant organism (MDRO) and infection surveillance, and 3) education (interactive in-services, hand hygiene, and dissemination tools). Dr. Mody noted that the strategy was to coach frontline clinicians in using simple strategies consistently. At intervention sites, staff used gowns and gloves consistently for high risk patients and during high risk activities. Health care workers were given a quick reference guide on how to define UTIs, pneumonias, and skin/soft tissue infections. These efforts were complimented by an educational program that was fun and interactive. Study outcomes included overall MDRO prevalence, incident rate of new MDROs, and clinically defined infections. Dr. Mody noted that the data analyses accounted for cluster design and used mixed effects multi-level modelling, adjusting for

age, gender, race, and length of stay within a facility prior to enrolment. The result was an overall reduction in MDRO prevalence and new incidents in terms of reducing resistant organisms and key infections. Furthermore, the research team showed that this pre-packaged intervention would cost about 15,000 to the nursing homes; however, administrators can save up to \$40,000 dollars per nursing home to the payors by preventing hospitalization. The study resulted in a paper titled “A Targeted Infection Prevention Intervention in Nursing Home Residents with Indwelling Devices” and a summary is available at <https://www.ncbi.nlm.nih.gov/pubmed/25775048>.

The second study in Dr. Mody’s talk focused on 12-month cohorts in a large scale randomized controlled trial (RCT) and included both a technical and socio-adaptive intervention. The technical component emphasized catheter removal, aseptic insertion, use of basic infection prevention practices, regular assessments to detect complications and data feedback, training for catheter care and maintenance as well as incontinence care planning and hydration. This technical bundle was coupled with a socio-adaptive component that focused on emphasizing teams (forming nursing home infection prevention project team with a project lead at each site), using good communication skills between team members, assessing what was working, scheduling regular meetings to discuss data, and strategies to sustain efforts. Also included in the intervention were educational events and materials. Educational events included: webinars, training module webinars, content webinars, coaching calls, learning sessions, and site visits. Materials included videos, power point presentations with notes, easy to use tools, train-the-trainer materials, facility Implementation Guide and a long-term care toolkit. Dr. Mody noted that implementation partners included the government and private sectors.

Dr. Mody noted that in 4 cohorts over 30 months, 568 community-based nursing homes were recruited and 404 met inclusion criteria for analysis. Final study results are listed below:

- Unadjusted catheter-associated UTI rates decreased from 6.78 to 2.63 infections per 1,000 catheter-days. With use of the regression model and adjustment for facility characteristics, the rates decreased from 6.42 to 3.33.
- Catheter use was 4.5% at baseline and 4.9% at the end of the project. Catheter utilization remained unchanged in adjusted analyses.
- The number of urine cultures ordered for all residents decreased from 3.49 per 1000 resident-days to 3.08 per 1000 resident-days. Similarly, after adjustment, the rates were shown to decrease from 3.52 to 3.09.

An abstract of this study is available at <https://www.ncbi.nlm.nih.gov/pubmed/28525923>.

Lastly, Dr. Mody discussed the latest study, funded my NIA, and completed by her team: A Longitudinal Assessment Of Multidrug-Resistant Organisms In Newly Admitted Nursing Facility Patients: Implications For An Evolving Population. Dr. Mody discussed the global concern about the spread of MDRO and MDRO transmission in healthcare

systems, which remains understudied. To reduce hospital stays, nursing facilities have increasingly assumed care of post-acute populations. The team conducted a prospective, longitudinal cohort study of newly admitted patients in six nursing facilities in southeast Michigan. The team used active microbial surveillance of multiple anatomic sites sampled at enrollment, days 14 and 30, and monthly thereafter for up to 6 months. The team enrolled 651 patients and collected 7,526 samples over 1,629 visits, with an average of 29 days of follow-up per participant. Nearly all participants were admitted for post-acute care (95%). More than half (56.8%) were colonized with MDROs at enrollment: methicillin-resistant *Staphylococcus aureus* (MRSA), 16.1%; vancomycin-resistant enterococci (VRE), 33.2%; and resistant gram-negative bacilli (R-GNB), 32.0%. Risk factors for colonization at enrollment included prolonged hospitalization (>14 days), functional disability, antibiotic use, or device use. The study surmised that short-stay nursing facility patients exhibit a high prevalence of MDROs near the time of admission, as well as at discharge, and may serve as a reservoir for spread in other healthcare settings. Future interventions to reduce MDROs should specifically target this population. An abstract of this study is available at <https://www.ncbi.nlm.nih.gov/pubmed/29635360>.

Discussion: Research Needs for Prevention and Treatment of UTI

- Dr. Narva noted that frontline care includes aides, nursing assistants and LPNs. Dr. Mody discussed the importance of creating simplistic educational tools for nurse's aides that are easily understood. Dr. Mody noted that the group did not focus too much on pharmacy interventions.
- Meeting attendees commented enthusiastically on the education materials developed for nursing home staff.
- One meeting attendee suggested creating supplemental funding for these efforts.
- A participant noted that there is a limit to how much researchers can maintain this environment and efforts to decrease in CAUTIs. Nursing homes administrators must implement policy to move change forward as hand hygiene is very problematic within nursing homes.
- Dr. Mody noted that 2 nursing home institutions implemented alcohol-based hand strategies following the study and that effort was coordinated with the local fire department.
- One participant queried Dr. Mody how she handled the team's nursing facility staff's continuing education efforts with such a high staff turnover in nursing homes. Dr. Mody noted that data was not collected on this topic. It was problematic creating in-service trainings for staff given high turnover rates. Staff permission to attend to these trainings was also limited.
- Dr. Abbott commented on the availability of datasets in nursing homes from CMS. Dr. Mody noted that this is a valuable resource, but it has been underused.
- Dr. Mody noted that in hindsight, it would have been helpful to collect urine samples; however, this was not the primary aim.

- Dr. Mody noted that feedback was not given back to the control group because no intervention was performed; however, feedback was given to the intervention group monthly.
- Dr. Mody noted that patient advocates/patient engagement professionals are helpful for advancing this research.

In closing, Dr. Mody noted that change in policy comes from hospitals who are affiliated with nursing homes. Hospitals should mandate policies at their affiliated nursing home sites to address this issue.

Part II: Diabetes Management in Nursing Homes and Skilled Nursing Facilities

Review: Research on Older Adults with Diabetes Receiving Long-Term Care

Dr. Christine Lee, MS, a Program Director with the Division of Diabetes, Endocrinology, and Metabolic Diseases at NIDDK, began her talk with some background information about diabetes in older adults. The prevalence of Type 2 Diabetes Mellitus (T2DM) is highest for adults over the age of 65 and has also increased the most over time due to older adults with diabetes living longer. Dr. Lee outlined the following statistics:

- The prevalence of diabetes is highest in adults ≥ 65 years old
- The prevalence of diabetes among older adults has increased from 20-30% from 2000-2010
- 33% of older adults in 2012 have diabetes Health care expenditures attributed to diabetes generally increase with age, such that the average annual expenditures are over \$13,000 for those over 65.

Dr. Lee noted that approximately 61% of all health care expenditures attributed to diabetes are for health resources used by people 65 years and older, much of which is covered by the Medicare program. Despite the healthcare and financial burden of diabetes for older adults, this demographic is not commonly included in studies. In a National Study of Long-Term Care Providers, the prevalence of patients who need daily living activity is about two times more common in nursing homes than in residential care. Roughly 60% of nursing home residents required help eating. Glycemic control particularly impacts this patient population; for example, if insulin is given and meals are not provided on time. In addition, almost 90% of residents in nursing homes suffer from bowel and bladder incontinence or need help to use the restroom. This may have implications on the use of catheters and catheter associated UTIs. Diabetes patients who employ long-term services and support have more hospitalizations and repeat hospitalizations, greater use of rehab services, and more hospital expenditures, than diabetes patients who do not have long-term services and support.

Dr. Lee discussed how researchers need to understand how factors like disability, can impact outcomes and agree that it's equally important to prevent hyper and hypoglycemia as they may have implications on risk for UTIs, dehydration, falls and ultimately hospitalization. Quality of life factors such as fracture and cognitive

dysfunction are also important to look at when trying to prevent any diabetes complications. There is a lot of variation in care that can contribute to these outcomes, even among long-term care settings like nursing homes and skilled nursing facilities which factor in the number of patients.

Dr. Lee closed her presentation with these future initiatives for the care of older adults in long-term care settings:

- Observational studies to understand the heterogeneity in patient, setting and care factors on glycemia, complications and health care utilization, and QOL
- Clinical trials to test interventions on this varied patient population in different settings to improve on outcomes and assist with standards of care for older adults receiving LTC.

Management of Type 2 Diabetes in Long-term Care and Skilled Nursing Facilities

Dr. Guillermo Umpierrez, Professor of Medicine in the Division of Endocrinology and Metabolism at Emory University School of Medicine, and Chief of Diabetes and Endocrinology at Grady Memorial Hospital, began his presentation with the following background information:

- Adults aged 65 years and older are the fastest growing segment of the U.S. population
 - Number is expected to double to 89 million between 2010 and 2050.
- Diabetes mellitus (DM) is prevalent in the elderly
 - 20% of adults aged 65-75 years
 - 40% of adults > 80 years
- Estimated prevalence of diabetes in LTC facilities
 - 15% to 32%
- Nursing home residents with DM have:
 - Higher rates of hospital complications, length of stay, and mortality.

Dr. Umpierrez discussed the management of diabetes in long-term care settings as recommended by the American Diabetes Association:

- Management of diabetes among older adults in LTC facilities is challenging due to heterogeneity in this population.
- Simplified treatment regimens are preferred, and the sole use of sliding scale insulin (SSI) should be avoided.
- The risk of hypoglycemia is the most important factor in determining glycemic goals due to the catastrophic consequences in this population.
- Simplified treatment regimens are preferred and better tolerated. E
- Sole use of SSI should be avoided.

Strategies to replace SSI in long-term care include:

- Review average daily insulin requirement over prior 5-7 days
- Give 50-75% of average total daily insulin requirement as basal insulin

- Stop SSI
- Use non-insulin agents or fixed-dose mealtime insulin to Rx post-prandial hyperglycemia

Dr. Umpierrez noted that, nationally, glucose lowering medication prescribing has shifted towards insulin. Insulin accounts for under 68% of new drug prescriptions in long-term care. While older adults have the highest risk of insulin-related hypoglycemia, this area remains very understudied. According to CDC databases from 2007-2011, nationally, there were 97,648 insulin-related hypoglycemia and insulin errors reported.

Dr. Umpierrez discussed the study “A randomized controlled trial comparing treatment with oral agents and basal insulin in elderly patients with type 2 diabetes in long-term care facilities,” which was conducted through his group. Managing hyperglycemia and diabetes is challenging in geriatric patients admitted to long-term care (LTC) facilities. This randomized control trial enrolled patients with type 2 diabetes (T2D) with blood glucose (BG) >180 mg/dL or glycated hemoglobin >7.5% to receive low-dose basal insulin or oral antidiabetic drug (OAD) therapy as per primary care provider discretion for 26 weeks. Both groups received supplemental rapid-acting insulin before meals. The primary endpoint was difference in glycemic control as measured by fasting and mean daily glucose concentration between groups. Dr. Umpierrez noted that a total of 150 DM patients were enrolled and randomized to basal insulin and OAD therapy. There were no differences in the mean fasting BG between insulin and OAD groups, but patients treated with insulin had greater mean daily BG compared to those treated with OADs. There were no differences in the rate of hypoglycemia between insulin and OAD groups. In addition, there were no differences in the number of hospital complications, emergency room visits, and mortality between treatment groups. The results of this randomized study indicate that elderly patients with T2D in LTC facilities exhibited similar glycemic control, hypoglycemic events and complications when treated with either basal insulin or with oral antidiabetic drugs. An abstract of this study is available at <https://www.ncbi.nlm.nih.gov/pubmed/26336609>.

Dr. Umpierrez also discussed his latest study resulting in a paper titled: “A Randomized Controlled Study Comparing a DPP4 Inhibitor (Linagliptin) and Basal Insulin (Glargine) in Patients With Type 2 Diabetes in Long-term Care and Skilled Nursing Facilities: Linagliptin-LTC Trial.” The objective of this study was to implement treatment regimens safely and easily needed for the management of patients with type 2 diabetes mellitus (T2DM) in long-term care (LTC) and skilled nursing facilities. This 6-month open-label randomized controlled trial compared the efficacy and safety of a DPP4 inhibitor (linagliptin) and basal insulin (glargine) in LTC residents with T2DM. The study was conducted with three LTC institutions affiliated with a community safety-net hospital, US Department of Veterans Affairs and Emory Healthcare System in Atlanta, Georgia.

Dr. Umpierrez noted that a total of 140 residents with T2DM were treated with oral antidiabetic agents or low-dose insulin, with fasting or premeal blood glucose (BG). The

interventions used in the study included linagliptin or glargine. Both groups received supplemental rapid-acting insulin before meals.

Dr. Umpierrez stated that treatment with linagliptin resulted in no significant differences in mean daily BG compared to glargine. Linagliptin treatment resulted in fewer mild hypoglycemic events, but there were no differences in BG compared to glargine. There were no significant differences between-group differences in HbA1c, length of stay, complications, emergency department visits, or hospitalizations. The study concluded that treatment with linagliptin resulted in noninferior glycemic control and in significantly lower risk of hypoglycemia compared to insulin glargine in long-term care and skilled nursing facility residents with type 2 diabetes. An abstract of this study is available at

[https://www.ncbi.nlm.nih.gov/pubmed/?term=A+Randomized+Controlled+Study+Comparing+a+DPP4+Inhibitor+\(Linagliptin\)+and+Basal+Insulin+\(Glargine\)+in+Patients+With+Type+2+Diabetes+in+Long-term+Care+and+Skilled+Nursing+Facilities%3A+Linagliptin-LTC+Trial](https://www.ncbi.nlm.nih.gov/pubmed/?term=A+Randomized+Controlled+Study+Comparing+a+DPP4+Inhibitor+(Linagliptin)+and+Basal+Insulin+(Glargine)+in+Patients+With+Type+2+Diabetes+in+Long-term+Care+and+Skilled+Nursing+Facilities%3A+Linagliptin-LTC+Trial).

Discussion: Research Needs for Management of Diabetes in Long-term Care Facilities

- Dr. Fradkin queried the use of a sliding scale insulin that is not approved by the FDA. Dr. Umpierrez noted that most physicians support correction dose and a physician champion was available at each site for consultation.
- Dr. Umpierrez noted it was not feasible to collect good information on caloric intake at nursing homes.
- Dr. Umpierrez also discussed CKD patients and insulin dosing variability complications and noted that future studies will include patients on higher insulin doses. The goal is to reduce unnecessary medication.
- A meeting attendee commented on the need for a precision medicine approach to patients, based on caloric intake.
- Dr. Abbott commented that over treatment is common and there is a need to re-evaluate insulin doses and medications in kidney patients on dialysis. There is similar information in an upcoming paper from the UDA on veterans and hospitalizations.
- One meeting attendee suggested gathering confounding variables such as a nurse providing treatment versus a doctor.

Part III: Challenges and Strategies for Research in Nursing Homes and Skilled Nursing Facilities

Conducting Research in Long-term Care Facilities – NIA Perspective

Dr. Salive began his talk by noting a recently developed publication from NIA titled: “Aging Well In The 21st Century”, available at <https://www.nia.nih.gov/about/aging-well-21st-century-strategic-directions-research-aging>. Dr. Salive noted the mission of NIA includes understanding the dynamics of the aging process, improving the health,

wellbeing, and independence of adults as they age, and supporting the research enterprise. To support this mission, NIA developed several efforts:

- Grants for Early Medical/Surgical Specialists' Transition to Aging Research (GEMSTAR): GEMSTAR, an R03 initiative that requires a professional development plan, is a “pre-K” award program for junior faculty physicians to launch a research career bridging their specialty and aging.
- Pragmatic Trial of Video Education in Nursing Homes (PROVEN): PROVEN, is a pragmatic trial in nursing homes. This study will test whether watching a video about advance care planning for nursing home residents makes a difference in hospitalizations, presence of advance directives, and hospice care compared with residents who follow the usual advance care planning procedures. This video is an adjunct to counseling.
- NIA resources for nursing home studies:
 - Health and Retirement Study (hrsonline.isr.umich.edu),
 - National Health And Aging Trends Study (www.nhatsdata.org),
 - Pragmatic trials for dementia care in long-term services and support (LTSS) settings. This program announcement focuses on pragmatic trials for dementia care in LTSS settings designed to address practical comparative questions faced by Alzheimer’s Disease (AD) and AD-related dementia patients, clinicians and caregivers and intended to improve quality of care, quality of life, and improve cost-effectiveness and reduce disparities. Dr. Salive noted that this pilot research will test the feasibility of implementing and integrating LTSS interventions (R61 phase) that, if successful, can transition to an R33 phase for implementation of large pragmatic trials, using administrative review as basis to advance. This funding opportunity is available at <https://grants.nih.gov/grants/guide/pa-files/PAR-18-585.html>.

Discussion

- Dr. Lee noted that informed consent is problematic among dementia patients, particularly for large RCTs.
- Dr. Salive noted that the issue of care can be risky with known standard of care side effects. Preferred intervention is “minimal risk”; however, there is no concrete definition for this term.
- Dr. Salive noted transition of care research is desperately needed in this area. In addition, there were many administrative burdens such as packaging materials and tools for patients.
- Dr. Mody suggested more research that measures outcomes at the facility level to reduce identifiable data. Also, patient level colonization within a contaminated environment should be studied.
- Dr. Lee queried if there are any partnerships with nursing homes that would provide de-identified data? Dr. Salive noted that a study on flu shots was conducted in this manner.

- Dr. Salive also noted the need to build infrastructure within nursing homes for these pragmatic trials. In addition, nursing home staff turnover is a large challenge.
- ARHQ has a new R18 about making health care more efficient in long-term care and focuses on transitions between home and residential care facilities. Hypoglycemia would be a topic for this FOA.
- Dr. Lee also noted the R34 and R18 mechanisms to test intervention strategies outside nursing homes.

Meeting Adjourned