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Trends in Collection of Microbiological Cultures Across Veterans Affairs Community Living Centers in the United States Over 8 Years

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ABSTRACT WORDS 297

OBJECTIVES: To describe and evaluate changes in the collection of microbiological cultures across Veterans Affairs (VA) Community Living Centers (CLCs) nationally.

DESIGN: Descriptive study.

SETTING: 146 VA CLCs.

PARTICIPANTS: We identified both positive and negative microbiological cultures collected during VA CLC admissions from January 2010 through December 2017.

MEASURES: We measured the average annual percent change (AAPC) in the rate of cultures collected per 1,000 bed days and per admission, overall and stratified by culture type (i.e. urine, blood, skin and soft tissue, respiratory). AAPCs were also calculated for the proportion and rate of positive cultures collected, overall and stratified by culture type and organism (i.e. *Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Enterococcus species [spp.], Pseudomonas aeruginosa, Klebsiella spp., Enterobacter spp., Morganella morganii, Citrobacter spp., Serratia marcescens, Streptococcus pneumoniae*). Joinpoint regression software was used to assess trends and estimate AAPCs and 95% confidence intervals (CI).

RESULTS: Over 8-years, 355,329 cultures were collected. The rate of cultures collected per 1,000 bed days of care decreased significantly by 6.0% per year (95% CI, -8.7 – -3.2%). The proportion of positive cultures decreased by 0.9% (95% CI, -1.4 – -0.4%). The most common culture types were urine (48.4%), followed by blood (27.7%). The rate of cultures collected per 1,000 bed days of care decreased per year by 6.3% for urine, 5.0% for blood, 4.4% for skin and soft tissue, and 4.9% for respiratory. In 2010, *Staphylococcus aureus* was the most common organism identified and in all subsequent years *Escherichia coli* was the most common.

CONCLUSION AND IMPLICATIONS: We identified a significant reduction in the number of cultures collected over time among VA CLCs. Our findings may be explained by decreases in the collection of unnecessary cultures in VA CLCs nationally due to increased antibiotic stewardship efforts targeting unnecessary culturing and antibiotic treatment.

BACKGROUND WORDS 2,345 REFERENCES 31 TABLES 5

Diagnostic uncertainty contributes to antibiotic overuse in long-term care facilities (LTCFs).[1] The presentation of common infections, such as urinary tract infections, lower respiratory tract infections, and skin and soft tissue infections may be atypical among older patients.[1, 2] The signs and symptoms of infection in older adults may include acute confusion or subtle changes in physical state or functioning without classic signs of infection, such as fever and chills, which may jeopardize accurate diagnosis.[1, 2] Cognitive impairment often limits the ability of residents to articulate their symptoms, which may further complicate clinical assessments.[3-6] These issues may prompt LTCF clinicians to respond to any change in status with collection of microbiological cultures, particularly urine cultures. If cultures result in positive growth due to colonization and/or contamination versus true infection this can lead to inappropriate and unnecessary antibiotic therapy.[1]

Despite the impact clinical microbiological cultures may ultimately have on antibiotic use, there have been no long-term studies describing the trends in the collection of cultures among LTCFs in the United States at the national level. Quantifying these trends may inform future targets for diagnostic stewardship intervention among LTCFs.[7, 8] Diagnostic stewardship has the same goal as antibiotic stewardship to improve antibiotic use, but intervenes at the level of the diagnostic test, to improve the way in which tests are ordered, preformed, and reported.[8] Additionally, over the past decade, the importance of antibiotic stewardship and infection control have been increasingly recognized, and may have led to reductions in the collection of cultures.[9, 10] Thus, the objective of this study was to describe national trends in the rates of microbiological cultures collected at VA LTCFs (referred to as Community Living Centers or CLCs in the VA Healthcare System) nationally from 2010 to 2017.

METHODS

We conducted a longitudinal study to describe annual trends in the collection of microbiological cultures among VA CLCs nationally. The study was approved by the Institutional Review Board (IRB) and the Research and Development (R&D) Committee of the Providence Veterans Affairs Medical Center prior to initiation. National VA clinical and administrative data, including data hospital and long-term care admissions, outpatient visits, medication administrations and dispensings, and laboratory results, were used in this study. All microbiology results among LTCF admissions entered in the electronic medical record were included in the study. From this data, we included all cultures collected during a stay at a VA CLC facility between January 1, 2010 and December 31, 2017. Cultures from 146 VA CLCs and from all culture types were included. We included all cultures, even in the case of multiple cultures from the same patient, on the same day, of the same culture type. VA bed days were captured from Veterans Health Administration Support Services Center.

For each calendar year, we calculated the number of cultures collected, including positive and negative cultures, as well as the rate of cultures collected per admission and per 1,000 bed days of care. We described the number of cultures collected per admission per year, which accounts for turnover but does not account for occupancy, and the number of cultures collected per bed days of care per year, which accounts for occupancy but does not account for turnover.[11, 12] Positive cultures were those in which any organism was recovered from the culture by the microbiological laboratory that tested the specimen and negative cultures were those in which no organisms were identified.

Cultures were categorized by culture type and organism. Culture types were grouped into broad categories (urine, blood, skin and soft tissue, or respiratory) based on the body site where the specimen was collected (e.g. an expectorated sputum or endotracheal aspirate were grouped into respiratory and a skin swab or skin lesion aspirate were grouped into skin and soft tissue). “Other” was used to group cultures that did not fit into these broad categories. Positive cultures were grouped into the following organism categories: *Escherichia coli, Proteus mirabilis, Staphylococcus aureus, Enterococcus species (spp.), Pseudomonas aeruginosa, Klebsiella spp., Enterobacter spp., Morganella morganii, Citrobacter spp., Serratia marcescens, Streptococcus pneumoniae*, and other (positive for any another organism). Culture types and bacterial organisms were selected *a priori* due to their clinical importance and prevalence in the CLC setting.[13, 14] Polymicrobial cultures were counted as a single positive culture, however each organism identified was counted and categorized separately into organism types.

Average annual percent changes (AAPC) were calculated for the rate of cultures collected per admission and per 1,000 bed days over the study period, overall and stratified by culture type and organism.[15, 16] AAPCs were also calculated for proportion of positive cultures collected and the rate of positive cultures collected. The AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment. The Joinpoint Regression Program version 4.6.0.0 (National Cancer Institute, Bethesda, MD, USA) was used to calculate AAPCs and 95% confidence intervals (CI). Significance was set at $p<0.05$.

RESULTS

Between 2010 and 2017, 355,329 cultures were collected from residents admitted to 146 VA CLCs. Positive microbial growth was reported in 42.0% of cultures (n=149,069). The number of cultures collected per admission was 1.6 in 2010 and 0.9 in 2017 and decreased significantly by 8.3% per year (95% CI, -9.6 – -6.9%, **Table 1**). Similarly, the number of cultures collected per 1,000 bed days of care decreased significantly by 6.0% per year (95% CI, -8.7 – -3.2%, **Table 2**).

Trends in Cultures Collected by Culture Type

The most common culture type collected (both positive and negative) during the study period was urine (48.4%, n=172,081), followed by blood (27.7%, n= 98,422), other (11.8%, n= 42,093), skin and soft tissue (8.5%, n= 30,292), and then respiratory (3.5%, n= 12,441). The annual rates and trends in cultures collected by culture type are presented in **Table 1** (rates per admission) and **Table 2** (rates per 1,000 bed days)**.** The rate of cultures collected per 1,000 bed days of care decreased by 6.3% per year for urine (95% CI, -8.2 – -4.4), 5.0% per year for blood (95% CI, -5.8 – -4.3), 4.4% per year for skin and soft tissue (95% CI, -6.6 – -2.3), and 4.9% per year for respiratory (95% CI, -6.9 – -2.7%, **Table 2**).

Trends in Positive Cultures Collected

The rates of positive cultures collected (per admission and per 1,000 bed days) decreased over the study period, as did the proportion of positive cultures (AAPC = -0.9%, 95% CI, -1.4 – -0.4%). The annual distribution and trends in rates (per 1,000 bed days of care) of positive cultures are presented in **Table 3**. Similar results were observed in rates per admission but are not presented in the Tables.

The proportion of positive cultures collected remained stable for urine cultures at about 53% (AAPC = 0.2%, 95% CI, -0.1 – 0.5%) and skin and soft tissue cultures at about 62% (AAPC = 0.1%, 95% CI, -1.0 – 1.2%). The proportion of positive cultures decreased over the study period for blood cultures from about 14% to 12% (AAPC = -1.7%, 95% CI, -2.9 – -0.6%) and respiratory cultures from about 54% to 43% (AAPC = -2.8%, 95% CI, -4.0 – -1.7%).

Trends in Cultures Collected by Species of Organism

In 2010, *S. aureus* was the most common organism identified. In subsequent years, *E. coli* was the most common organism identified. The annual distribution and trends in rates (per 1,000 bed days of care) of positive cultures by species of organism are presented in **Table 4**. Similar results were observed in rates per admission but are not presented in the Tables. The rate of positive cultures decreased for most organisms (i.e. *S. aureus, Enterococcus spp., E. coli, P. mirabilis*. *P. aeruginosa, Enterobacter spp., Citrobacter spp., M. morganii*, and *Serratia marcescens*) except *S. pneumoniae and Klebsiella spp.* which remained stable. The trends in rates (per 1,000 bed days of care) of positive cultures by species of organism and culture type are presented in **Table 5**. The rate of positive cultures growing *S. aureus* decreased for all culture types (urine, blood, skin and soft tissue, or respiratory).

DISCUSSION

We identified a significant reduction in the rate of microbiological cultures collected over an 8 year period, which may be related to increased infection control and antibiotic stewardship throughout the VA healthcare system.[17-19] Increased antibiotic stewardship efforts may lead to reduced culture collection rates through reduction of inappropriate or unnecessary microbiological cultures.

The overall rate of cultures collected over time was largely driven by a reduction in urine cultures, which may be related to an increased awareness of overdiagnosis and testing for UTIs over the study period.[4, 20] The appropriate diagnosis and treatment of UTIs has become one of the most important antibiotic stewardship targets among LTCFs, due to the high prevalence of asymptomatic bacteriuria among residents.[9] Previous smaller studies have demonstrated that UTI-focused antibiotic stewardship interventions are associated with reductions in the collection of urine cultures.[4, 20, 21] For example, a single center study in a VA CLC demonstrated a reduction in urine culture collection rate (from 3.7 to 1.5 per 1,000 resident days) after implementation of a pathway to limit urine testing without urinary symptoms.[20] Our research shows this trend on a national scale and suggests that the trend towards reduced urine testing has been occurring across the entire VA CLC system.

In addition to a reduction in urine cultures, we also observed significant reductions in blood, skin and soft tissue, and respiratory cultures collected from VA CLC residents, which suggests diagnostic stewardship may extend beyond urine testing. Similar to urine cultures, limiting over collection of skin and soft tissue cultures is an important stewardship target in LTCFs.[22] Wounds and pressure ulcers, which are common in older adults, are colonized by bacteria.[22] As such, collection of microbiological samples from skin or wounds in the absence of signs or symptoms of infection could lead to inappropriate antibiotic use.[3, 13] For respiratory and blood cultures, the role of diagnostic stewardship on culture reduction rates we observed in VA CLCs may be more related to efforts to reduce contamination rather than efforts to reduce unnecessary cultures. The role of respiratory cultures in LTCFs are generally limited, as residents are often not be able to produce expectorated sputum and even when respiratory cultures are available they are often contaminated. [23] Similarly, the role of blood cultures in LTCFs is limited, as they generally have a low yield in LTCF residents and most residents with suspected bacteremia are transferred to acute-care facilities.[23] Nonetheless, reduction of blood culture contamination is an important tenant of diagnostic stewardship and overall quality improvement in many healthcare settings.[24-26] Interestingly, when stratified by culture type, we did find the proportion of positive cultures collected remained stable for urine cultures and skin and soft tissue cultures, but the proportion of positive cultures decreased for blood cultures and respiratory cultures.

An important finding from this research is the overall reduction in the rate of positive cultures collected for particularly virulent organisms, such as *S. aureus, Enterococcus spp., E. coli,* and *P. aeruginosa,* among the VA CLC population. While we did not assess antibiotic resistance, previous work has demonstrated that the burden of infections due to methicillin-resistant *S aureus* has significantly declined in the VA since 2007 when a prevention initiative was implemented among all VA medical centers.[17, 18, 27, 28] This initiative may have also led to reductions in other non-*S. aureus* infections as well, through expanded infection control programs and resources.[29] However, similar trends have been observed nationally outside the VA, which may suggest shifts in strain epidemiology and may also contribute to our findings.[30] Further work in this area will need to occur to identify why the trends we observed occurred.

There are limitations inherent in our work. Our study included all cultures that were collected and did not assess the clinical significance of the cultures. Any culture in which any organism or any bacteria were recovered were defined as positive and as such, we cannot distinguish what proportion of positive cultures represent true infection versus colonization and/or contamination. Additionally, in our assessment of culture by organism there may be an overestimation of bacteria in which multiple positive cultures are obtained from the same patient with the same results. Moreover, the indications for the cultures are unknown. For example, the collection of a urine culture may be indicated for a resident with sepsis, whether or not a positive result represents a UTI or asymptomatic bacteriuria. The generalizability of results among VA CLCs to community non-VA LTCFs may be limited. The residents of VA CLCs have more complex medical needs and the staffing levels in are higher than in non-VA LTCFs.[31] Finally, while many facilities ensure that cultures results obtained from outside the VA system are captured within the electronic medical record, it is impossible to ascertain if all cultures collected at outside laboratories are included in this analysis. Finally, our categorization of cultures by source and organism are based on the ordering, interpretation, and reporting of the providers and microbiology laboratory that ordered and handled the clinical culture. Additionally, the specificity of the culture collection site varies, and we cannot always identify the specific body sites where cultures were collected (for example sputum versus endotracheal among respiratory cultures, or skin swab versus lesion aspirate among skin cultures). As such, we used used broad culture type categories (e.g. urine, blood, skin and soft tissue, or respiratory).

We did not assess whether changes in culture collection corresponded with changes in antibiotic use, resource utilization and costs, or resident outcomes, such as hospitalizations, which should be explored further.

CONCLUSIONS AND IMPLICATIONS

Our data revealed a significant reduction in the number of cultures collected among VA CLCs nationally over an 8-year period, with a large reduction in urine cultures. This reduction in cultures likely reflects a reduction in collection of unnecessary cultures in VA CLCs nationally and may be driven by increased awareness for over-testing and over-treatment of presumed urinary tract infection. Moreover, this reduction may have had important clinical and economic impact through reduction of additional unnecessary testing and antibiotic use, reduced resource utilization and costs, and improved overall resident care and outcomes.

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Table 1. Annual rates (per admission) and trends in cultures collected at VA Community Living Centers nationally from 2010-2017

Year	**Overall cultures**	**Urine cultures**	**Blood cultures**	**Skin cultures**	**Respiratory cultures**
2010	1.6	0.692	0.389	0.125	0.052
2011	1.4	0.648	0.373	0.111	0.049
2012	1.2	0.613	0.342	0.105	0.040
2013	1.1	0.577	0.315	0.097	0.040
2014	1.1	0.538	0.304	0.090	0.039
2015	1.0	0.505	0.300	0.094	0.036
2016	0.9	0.474	0.276	0.086	0.034
2017	0.9	0.429	0.262	0.080	0.034
AAPC (95% CI)	-8.3% (-9.6 – -6.9)*	-6.4 (-6.8 – -6.0)*	-5.4 (-6.2 – -4.7)*	-5.6 (-6.9 – -4.2)*	-5.9 (-7.8 – -4.0)*

The Joinpoint Regression Program was used to calculate average annual percent change (AAPC) and 95% confidence intervals (95% CI). AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment.

*Indicates significant trend at $p<0.05$.

CLC= Community Living Center

Table 2. Annual rates (per 1,000 bed days) and trends in cultures collected at VA Community Living Centers nationally from 2011-2017

Year	Overall cultures	Urine cultures	Blood cultures	Skin cultures	Respiratory cultures
2011	14.3	6.8	3.9	1.2	0.5
2012	13.4	6.6	3.7	1.1	0.4
2013	12.8	6.5	3.6	1.1	0.5
2014	12.0	6.1	3.4	1.0	0.4
2015	11.7	5.8	3.5	1.1	0.4
2016	10.5	5.3	3.1	1.0	0.4
2017	9.3	4.6	2.8	0.9	0.4
AAPC (95% CI)	-6.0% (-8.7 – -3.2)*	-6.3% (-8.2 – -4.4)*	-5.0% (-5.8 – -4.3)*	-4.4% (-6.6 – -2.3)*	-4.9% (-6.9 – -2.7)*

The Joinpoint Regression Program was used to calculate average annual percent change (AAPC) and 95% confidence intervals (95% CI). AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment.

*Indicates significant trend at p<0.05.

CLC= Community Living Center

Table 3. Annual distribution and trends in positive cultures collected at VA Community Living Centers nationally from 2011-2017

Year	**Proportion of positive cultures**	**Positive cultures per 1,000 CLC bed days**
2011	43.3%	6.2
2012	42.3%	5.7
2013	42.8%	5.5
2014	41.8%	5.0
2015	41.2%	4.8
2016	40.6%	4.3
2017	40.1%	3.8
AAPC (95% CI)	-0.9 (-1.4 – - 0.4)*[a]	-7.0 (-9.7 – -4.2)*[b]

The Joinpoint Regression Program was used to calculate average annual percent change (AAPC) and 95% confidence intervals (95% CI). AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment.

* Indicates significant trend at p<0.05.

CLC= Community Living Center

[a]AAPC presented for change in proportion of positive cultures collected from 2010 to 2017. The proportion of positive cultures in 2010 was 42.2%.

[b]AAPC presented for change in rate of positive cultures per 1,000 bed days of care. Similar results were observed for rate per admission (data not presented in table).

Table 4. Annual rates (per 1,000 bed days) and trends in positive cultures by organism collected at VA Community Living Centers nationally from 2011-2017

Year	*Staphylococcus aureus*	*Enterococcus spp.*	*Streptococcus pneumoniae*	*Escherichia coli*	*Proteus mirabilis*	*Pesudomonas aeurginosa*	*Klebsiella spp.*	*Enterobacter spp.*	*Morganella morganii*	*Citrobacter spp.*	*Serratia marcescens*
2011	0.989	0.743	0.011	0.997	0.908	0.564	0.535	0.139	0.114	0.078	0.050
2012	0.841	0.750	0.014	0.930	0.819	0.535	0.493	0.143	0.117	0.078	0.047
2013	0.802	0.752	0.011	0.947	0.826	0.534	0.543	0.140	0.114	0.081	0.043
2014	0.738	0.625	0.007	0.881	0.759	0.451	0.511	0.140	0.099	0.074	0.042
2015	0.651	0.619	0.008	0.856	0.713	0.456	0.511	0.110	0.093	0.075	0.044
2016	0.593	0.533	0.011	0.771	0.684	0.462	0.479	0.114	0.074	0.064	0.040
2017	0.520	0.484	0.010	0.758	0.596	0.379	0.395	0.120	0.076	0.065	0.038
AAPC (95% CI)	-9.6 (-10.8 – -8.5)*	-7.4 (-10.2 – -4.6)*	-3.8 (-14.2 – 7.8)	-4.5 (-5.8 – -3.2)*	-6.1 (-7.6 – -4.6)*	-5.7 (-8.3 – -3.0)*	-3.6 (-7.2 – 0.1)	-4.0 (-7.5 – -0.3)*	-8.0 (-11.2 – -4.6)*	-3.6 (-6.0 – -1.1)*	-3.9 (-5.7 – -2.2)*

The Joinpoint Regression Program was used to calculate average annual percent change (AAPC) and 95% confidence intervals (95% CI). AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment. *Indicates significant trend at p<0.05.

AAPC presented for change in rates per 1,000 bed days of care. Similar results were observed for rates per admission (data not presented in table).

CLC= Community Living Center; spp.= species

Table 5. Trends in rates (per 1,000 bed days) of positive cultures by organism and culture type collected at VA Community Living Centers nationally from 2011-2017

	Staphylococcus aureus	*Enterococcus spp.*	*Escherichia coli*	*Proteus mirabilis*	*Pesudomonas aeurginosa*	*Klebsiella spp.*	*Enterobacter spp.*	*Morganella morganii*	*Citrobacter spp.*	*Serratia marcescens*
Urine AAPC (95% CI)	-8.0 (-9.8 – -6.1)*	-7.5 (-11.3 – -3.5)*	-4.9 (-6.3 – -3.5)*	-6.8 (-8.9 – -4.8)*	-5.7 (-8.1 – -3.3)*	-3.7 (-7.1 – -0.1)*	-4.5 (-10.0 – 1.3)	-8.3 (-11.6 – -4.9)*	-4.3 (-6.8 – -1.7)*	-3.7 (-10.0 – 3.1)
Blood AAPC (95% CI)	-6.0 (-11.5 – -0.2)*	-8.2 (-14.7 – -1.3)*	-2.7 (-8.2 – 3.1)	-2.3 (-11.1 – 7.4)	-10.9 (-23.4 – 3.6)	-0.4 (-11.7 – 12.3)	-6.6 (-18.7 – 7.2)	-1.2 (-33.4 – 46.4)	-1.2 (-48.6 – 90.0)	-15.7 (-38.5 – 15.6)
Skin AAPC (95% CI)	-6.7 (-8.6 – -4.7)*	-3.7 (-6.2 – -1.1)*	-0.6 (-3.1 – 1.9)	-2.4 (-4.6 – -0.2)*	-2.6 (-6.9 – 1.9)	-1.6 (-8.8 – 6.1)	2.8 (-3.2 – 9.2)	-10.2 (-15.8 – -4.2)*	3.8 (-4.5 – 12.8)	-0.9 (-9.0 – 7.9)
Respiratory AAPC (95% CI)	-9.8 (-12.7 – -6.7)*	-11.0 (-41.4 – 35.3)	-11.3 (-18.7 – -3.2)*	-16.4 (-24.3 – -7.7)*	-10.4 (-14.8 – -5.7)*	-10.2 (-12.8 – -7.5)*	-17.6 (-21.8 – -13.1)*	-10.1 (-38.4 – 31.2)	-17.9 (-32.9 – 0.4)	-8.0 (-19.7 – 5.4)

The Joinpoint Regression Program was used to calculate average annual percent change (AAPC) and 95% confidence intervals (95% CI). AAPC is calculated as a weighted average of the average percent change (APC) segments from a joinpoint model with the weights equal to the duration of each APC segment. *Indicates significant trend at $p<0.05$.

AAPC presented for change in rates per 1,000 bed days of care. Similar results were observed for rates per admission (data not presented in table).