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CLINICAL RESEARCH

A Prospective Clinical Study to EvaluAte the AbiliTy of the CloudCath System to Detect Peritonitis During In-Home Peritoneal Dialysis (CATCH)

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Introduction: Peritonitis is the leading complication of peritoneal dialysis (PD). Patients are instructed to seek care promptly for signs (cloudy effluent) or symptoms (abdominal pain), and earlier treatment improves outcomes. The CloudCath Peritoneal Dialysis Drain Set Monitoring (CloudCath) system monitors turbidity in dialysis effluent and sends notifications of changes signaling possible peritonitis.

Methods: We conducted this single-arm, open-label, multicenter study of CloudCath system use during PD. We deactivated system notifications to participants and investigators, who followed standard-of-care for peritonitis signs and symptoms. Effectiveness endpoints measured time between CloudCath system notifications and peritonitis events using International Society of Peritoneal Dialysis (ISPD) criteria.

Results: Two hundred forty-three participants used the CloudCath system for 178.8 patient-years. Of 71 potential peritonitis events, 51 events (0.29 per patient-year) met ISPD white blood cell (WBC) count criteria. The system triggered notifications for 41 of 51 events (80.4%), with a median lead time of 2.6 days (10%–90% range, –1.0 to 15.7; $P < 0.0001$). Excluding 6 peritonitis events that occurred when the system was not in use, the system triggered notifications for 41 of 45 events (91.1%), with a median lead time of 3.0 days (10%–90% range, –0.5 to 18.8; $P < 0.0001$). Of the 0.78 notifications per patient-year, the majority were peritonitis events or nonperitonitis events such as exit site and tunnel infections or catheter/cycler issues.

Conclusion: The CloudCath system detected peritonitis events during PD several days earlier than the current standard-of-care and has the capacity to send notifications that could expedite peritonitis diagnosis and treatment.

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See Commentary on Page 749

More than 550,000 persons in the United States and nearly 3 million persons worldwide currently receive maintenance dialysis as treatment for kidney failure, and more than 120,000 persons in the United States begin dialysis each year.[1] In the US, the vast majority of patients with kidney failure requiring dialysis receive in-center hemodialysis. Approximately 12% receive at-home PD,[1] despite several advantages compared with in-center hemodialysis. Potential advantages of PD include slower, gentler removal of uremic solutes and extracellular fluids, hemodynamic stability, and generally, more liberal dietary allowances. Based in part on the advantages of PD with lower societal costs, the Advancing American Kidney Health 2019 Executive Order set a goal of 80% use for either home dialysis therapy or a kidney transplant among patients newly diagnosed with kidney failure by 2025.[2]

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Patients receiving PD generally report greater satisfaction with treatment relative to patients receiving in-center hemodialysis.[3,4] Unfortunately, patient fears of infectious complications such as peritonitis often preclude adoption of the modality.[5,6] Peritonitis with PD is the most common reason for patients to switch to hemodialysis[7] and peritonitis is associated with a higher risk of death.[8] Earlier detection and management of peritonitis may reduce its severity and clinical consequences.[9] Remote monitoring as an aid in identifying occult infection due to early stage peritonitis before the development of overt signs or symptoms could instill confidence in patients to choose PD upon dialysis initiation, maintain patients on PD as a bridge to kidney transplantation, preserve vascular access, and avoid procedures required for, and complications associated with, switching from PD to hemodialysis.

The CloudCath system uses an optical sensor placed around the drain line of a continuous cycling PD system (Supplementary Figure S1). The technology quantifies the cloudiness of PD effluent by measuring the physical property of turbidity. In comparison to standard-of-care visual inspection of PD effluent cloudiness (known as the "newspaper test") the technology of the CloudCath system is far more sensitive than the human eye in measuring the degree of cloudiness. The CloudCath system continuously monitors patients during each PD treatment and the system uses machine learning algorithms to analyze the measured data and creates actionable insights by transmitting notifications to both the healthcare provider and patient when the algorithm detects changes in the dialysate effluent. The algorithm assessed in this study was trained on measurements of 184 participants with a total of 14,314 individual PD exchange cycle measurements (hereafter referred to as the V1 algorithm). We undertook this study of the CloudCath system to assess the performance of the algorithm in routine PD practice and whether it detected peritonitis earlier than patient presentation with clinical signs and symptoms, as is the current standard-of-care. These insights could enable early interventions with the potential for improved health outcomes and reduced hospitalizations.

METHODS

Study Design and Oversight

CATCH (NCT04515498) was a multicenter, single-arm, open-label study to evaluate the safety and effectiveness of the CloudCath system and assess the ability of algorithms to identify the onset of peritonitis compared with standard-of-care. The study was performed at 19 sites in the United States in accordance with the US Food and Drug Administration regulations, the Declaration of Helsinki, and applicable local regulations. Approval was obtained from the institutional review boards and site management for each investigational site.

Participants

Eligible participants were aged ≥18 years, had kidney failure treated with automated PD employing at least 2 night-time cycle exchanges, had cellular data coverage at home, and signed informed consent. Patients were excluded if they had peritonitis (based on conventional ISPD diagnostic criteria[10]) within 30 days of study entry, had signs or symptoms of an active infection within 14 days of study entry, planned to use low recirculation sets with fill volumes <1000 ml, had an active malignancy or history of malignancy requiring chemotherapy within 6 months of study entry, or were participating in another research study involving an investigational device or drug that might affect study results.

Treatment

Each eligible participant received a CloudCath system and was trained on set-up, drain set insertion and removal, and system troubleshooting. Participants were instructed to use the CloudCath system during each PD exchange cycle for at least 12 continuous months and up to 18 months. Throughout the study, the CloudCath system sent data directly to a cloud-based portal. The notification capability of the CloudCath system was deactivated so that participants, investigators, other clinicians, and care partners were not notified of potential peritonitis events and were not aware of the system's measurements. To ensure notifications from the CloudCath system did not affect clinical outcomes, a minimum of 30 days was required for data collection related to each notification before there was any investigation into the potential cause. Thus, participants were instructed to follow standard practice for clinical evaluation if they suspected they had peritonitis, based on symptoms of abdominal pain or visible turbidity of effluent.

Procedures

In Supplementary Table S1, we show the routine schedule of events. Study visits occurred at 1, 3, 6, 9, and 12 months, and at the end of study (between 13 and 19 months). At these visits, we determined effluent cell count and differential, and collected information on other laboratory or imaging studies, any hospitalization or other adverse events, and participant responses on an 8-item questionnaire addressing usability of the CloudCath system (Supplementary Appendix). When a participant presented with suspected peritonitis, site personnel evaluated the participant for signs and

symptoms of peritonitis, vital signs, laboratory tests of cycler effluent samples (including but not limited to effluent cell counts and differential and cultures), and a PD exit site and tunnel examination. Site personnel repeated the evaluations per usual practice, including a final assessment 3 days after completion of antibiotics.

Endpoints

Effectiveness endpoints were based on the timing of CloudCath system notifications for potential peritonitis relative to clinical detection of peritonitis events. Effectiveness of the CloudCath system was determined by the time interval from the CloudCath notification to detection by the current standard-of-care. The primary effectiveness endpoint considered peritonitis events based on ISPD WBC count criteria alone: effluent with WBC >100/μl and polymorphonuclear leukocytes (PMN) >50%.[10] A secondary effectiveness endpoint considered peritonitis events based on the conventional ISPD diagnostic criteria, wherein 2 of 3 of the following were present: (i) clinical features consistent with peritonitis (i.e., abdominal pain and/or cloudy dialysis effluent), (ii) effluent with WBC >100 cells/μl and PMN >50%, and (iii) positive effluent culture.[10] Other secondary effectiveness endpoints were based on participant responses about usability of the CloudCath system. An exploratory effectiveness endpoint examined the ability of the CloudCath system to detect resolution of peritonitis after initiation of treatment. We conducted an additional exploratory analysis examining the performance of an updated notification algorithm trained on the full CATCH dataset. The safety endpoint was reporting of CloudCath system-related adverse events.

Statistical Analysis

The full analysis population included all participants with at least 1 CloudCath system reading. The primary analysis population for effectiveness analyses excluded peritonitis events potentially affected by either protocol deviations or nonperitonitis events affecting optical characterization of effluent fluid. For the primary and secondary effectiveness endpoints, we analyzed the difference in distribution of time to peritonitis detection between the CloudCath system and standard-of-care using the Wilcoxon Signed Rank test. We considered 2-sided P-values <0.05 to be statistically significant. The null hypothesis was no difference in peritonitis detection times between the CloudCath system and standard-of-care. For instances where the CloudCath system detected peritonitis within 1 day after clinical presentation, we imputed a time to detection of −12 hours. For instances where the CloudCath system did not detect peritonitis within 1 day after clinical presentation, we imputed a time to detection of −24 hours. For peritonitis events after multiple notifications, the lead time was calculated from the first notification that was triggered. In cases of missing time for a laboratory report or participant-reported presentation time, we imputed 12:00 PM (noon).

For the sample size estimation, we assumed (with 90% probability) that the CloudCath system would detect peritonitis events before laboratory testing. We estimated that the CloudCath system would detect peritonitis a mean (SD) of 24 hours before confirmation with laboratory testing. We expected these times to follow a log normal distribution, limiting values at the lower end of the time scale to greater than 0, and allowing for some expected skewness. We assumed that the CloudCath system would detect peritonitis the day after laboratory testing in up to 5% of cases and would not detect infection at all in up to 5% of cases. Using simulation analysis, we determined that a minimum of 13 peritonitis events would be required to yield power of 87% to detect a peritonitis event at least 24 hours before laboratory testing. With an estimated peritonitis rate of 0.20 events per patient-year,[11] 130 participants needed to be followed for at least 6 months to identify 13 peritonitis events. To account for an estimated loss to follow-up or withdrawal rate of 30% at 6 months, we determined that a target sample size of 186 participants was required to identify 13 peritonitis events at 6 months. To increase the number of peritonitis events observed, the protocol was amended to allow up to 450 participants into the study.

RESULTS

Participants

From August 2020 through June 2022, 243 participants from 19 centers across the United States enrolled in the study (Table 1). The mean (SD) age of participants at baseline was 59.0 (13.7) years and the mean (SD) PD vintage was 16.4 (20.5) months (median, 9.4 months; 10% to 90% range, 1.4 to 41.1 months). Participants used the CloudCath system for 178.8 patient-years total and a median of 9.2 months (10% to 90% range, 1.1 to 17.4 months). The system analyzed 292,555 individual PD exchange cycles, or approximately 4.5 cycles per patient-day whereas the mean (SD) number of PD exchange cycles prescribed per night was 4.6 (1.2).

Detection of Peritonitis Based on ISPD WBC Count Criteria

For the primary effectiveness endpoint, 57 participants presented for clinical evaluation of 71 potential peritonitis events based on standard signs or symptoms. In

Table 1. Baseline characteristics

Baseline characteristics	All participants (N = 243)
Age, yr, mean (SD)	59.0 (13.7)
Sex, *n* (%)	
Male	143 (58.9)
Female	100 (41.2)
Race, *n* (%)[a]	
White	150 (61.7)
Black or African American	81 (33.3)
Other	13 (5.3)
Ethnicity, *n* (%)[a]	
Hispanic or Latino	34 (14.0)
Body mass index, kg/m^2, mean (SD)	31.0 (6.6)
Time on PD, months	
Mean (SD)	16.4 (20.5)
Median (10%–90%)	9.4 (1.4–41.1)
Prescribed PD exchanges per night, mean (SD)	4.6 (1.2)
Prescribed total volume of dialysate per night, l, mean (SD)	9.8 (3.4)
Prior PD catheter revision or replacement, *n* (%)	24 (9.9)
Any peritonitis event since starting PD, *n* (%)	15 (6.2)
Prior hemodialysis, *n* (%)	94 (38.7)
Relevant medical history, *n* (%)	
Cardiovascular disease	94 (38.8)
Hyperlipidemia	149 (61.3)
Hypertension	237 (97.5)
Diabetes mellitus	128 (52.7)
Cancer	38 (15.6)
Abdominal surgery	63 (25.9)
Liver disease	8 (3.3)

PD, peritoneal dialysis.
[a]Race/ethnicity were identified by the participant and assigned by the investigator to fixed categories in the case report form. More than 1 category for race could be selected.

the full analysis population, 51 events (0.29 events per patient-year) met the ISPD WBC count criteria for peritonitis. In this population, the CloudCath system triggered notifications for 41 of 51 events (80.4%; Figure 1). The median lead time between the notification and a peritonitis event based on ISPD WBC count criteria was 2.6 days (10% to 90% range, −1.0 to 15.7 days [negative lead times resulted from penalties applied for nonnotification]; $P < 0.0001$; Figure 2a).

Of these events, 45 events (0.25 events per patient-year) met ISPD WBC count criteria for peritonitis and were included in the primary analysis population. This population excluded 6 events due to nonuse of the CloudCath system in the days leading up to the event (Table 2). No event was excluded due to a non-peritonitis event that affected optical characterization of effluent fluid. The CloudCath system triggered notifications for 41 of 45 events (91.1%; Figure 1) in the primary analysis population, with a median lead time of 3.0 days (10% to 90% range, −0.5 to 18.8 days; p<0.0001; Figure 2b). In Table 3, we provide narrative descriptions of peritonitis events based on ISPD WBC count criteria that were evaluable for lead time but were not detected by the CloudCath system within 1 day after clinical presentation.

Detection of Peritonitis Based on Conventional ISPD Diagnostic Criteria

Of the 71 potential peritonitis events, 54 events (0.30 events per patient-year) met the conventional ISPD diagnostic criteria for peritonitis. In the full analysis population, the CloudCath system triggered notifications for 44 of 54 events (81.5%; Figure 3). The median lead time between the notification and a peritonitis event based on conventional ISPD diagnostic criteria was 3.0 days (10% to 90% range, −1.0 to 18.8 days; $P < 0.0001$; Figure 4a).

Excluding the 6 events described in Table 2, 48 events (0.27 events per patient-year) met conventional ISPD diagnostic criteria and were included in the primary analysis population. The CloudCath system triggered notifications for 44 of 48 events (91.7%; Figure 3) in the primary analysis population, with a median lead

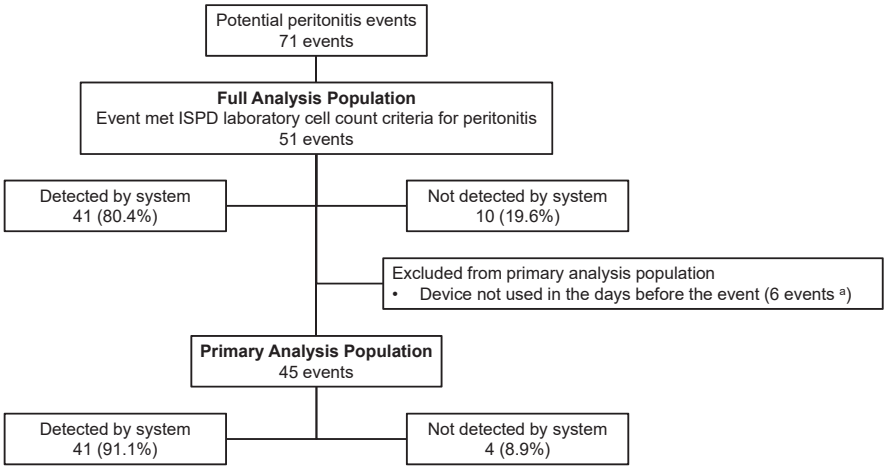


Figure 1. CloudCath system notifications (V1 algorithm) for peritonitis events based on ISPD WBC count criteria (WBC >100 cells/μl and PMN >50%). ISPD, International Society of Peritoneal Dialysis; PMN, and polymorphonuclear leukocytes; WBC, white blood cell [a]See Table 2 for descriptions of these events.

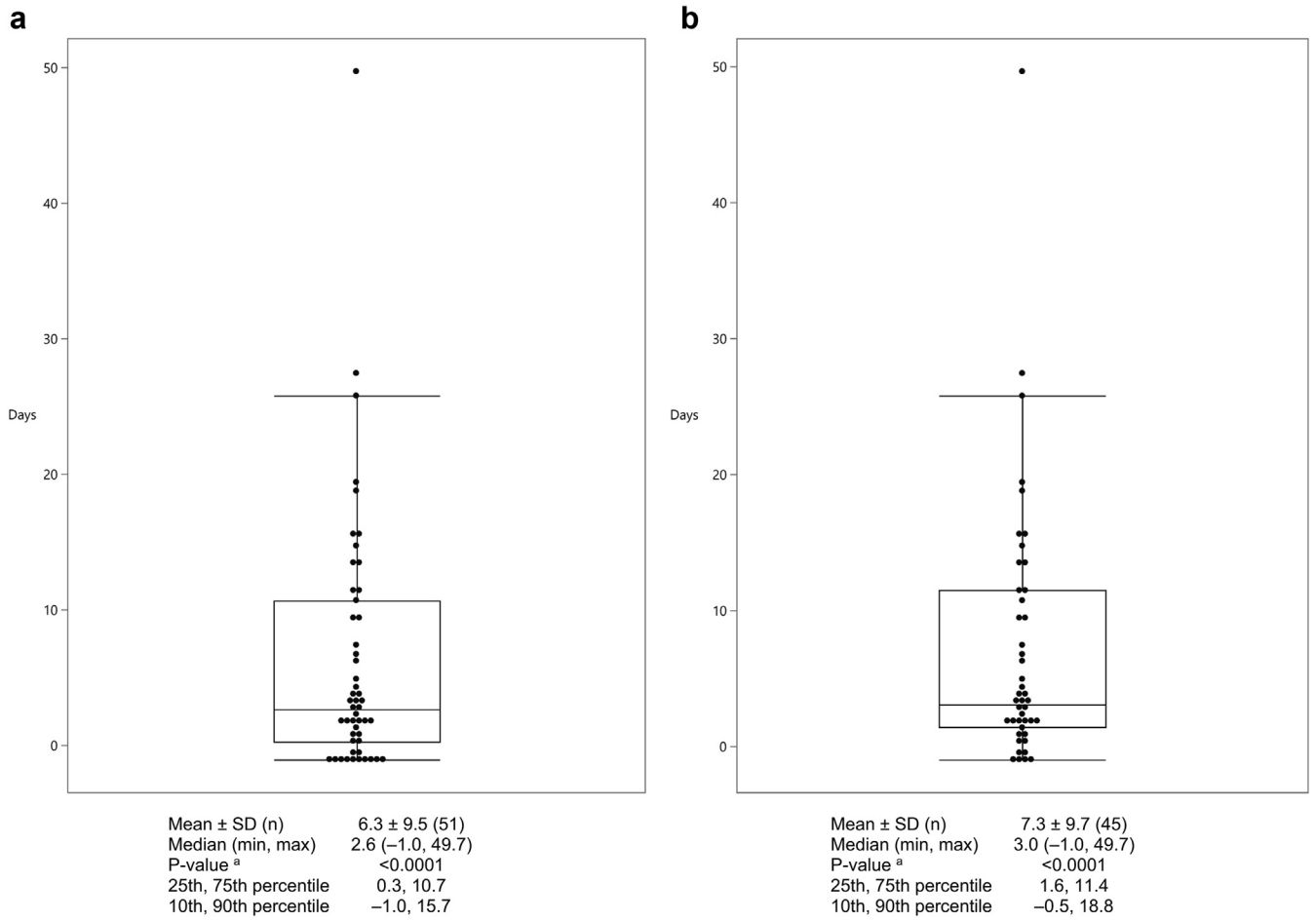


Figure 2. Lead time between CloudCath system notification (V1 algorithm) and confirmation of peritonitis event based on ISPD WBC count criteria: (a) full analysis population; (b) primary analysis population. ISPD, International Society of Peritoneal Dialysis; WBC, white blood cell [a]*P*-values were calculated using Wilcoxon Signed Rank test.

time of 4.1 days (10% to 90% range, −0.5 to 19.4 days; $P < 0.0001$; Figure 4b).

We calculated lead times between CloudCath system notifications and when participants presented for signs or symptoms of possible peritonitis. In the full analysis population, the median lead time was 2.2 days (10% to 90% range, −1.0 to 17.2 days; $P < 0.0001$; Figure 5a). In the primary analysis population, the median lead time was 3.1 days (10% to 90% range, –0.5 to 17.7 days; $P < 0.0001$; Figure 5b).

Table 2. Events excluded from the primary analysis population

Event	Notes
1	Ultrafiltration issues on day –2. No CCPD exchanges on day –1
2	CloudCath system used only once, and ultrafiltration issues on day – 1
3	Only 3 system measurements in the 14 days before presentation and no measurements on day –1; CCPD slow-flow alarms, catheter issues, and ultrafiltration issues during this period
4	System not used for 4 days before presentation
5	System not used for 8 days before presentation; no CCPD exchanges on day –3 and day –2; fill issues occurred on day –1
6	System not used for 6 days before presentation; multiple cycler alarms related to drainage and ultrafiltration issues during this period

CCPD, continuous cycling peritoneal dialysis.
Days are numbered relative to peritonitis presentation.

Notifications Not Associated with Peritonitis Events

During 178.8 patient-years of use, the CloudCath system triggered 140 total notifications (0.78 notifications per patient-year; Figure 6). As documented above, 44 notifications (0.25 notifications per patient-year) were triggered for peritonitis events based on conventional ISPD diagnostic criteria. Forty-one notifications (0.23 notifications per patient-year) were triggered for other clinical events, most frequently nonperitonitis infections (13 events, such as exit site and tunnel infections) or catheter dysfunction/drainage issues (9 events); the fourth most frequent nonperitonitis event was bleeding (6 events), usually after participants underwent catheter revisions. Fifty-five notifications (0.31 notifications per patient-year) were triggered without a known connection between the notification and a temporal clinical event, based on participant recall at least 30 days after the notification. Of the 96 total

Table 3. Peritonitis events (WBC >100/μl and PMN >50%) that did not trigger a system notification

Event	Clinical narrative
1	The participant had a gynecologic procedure 2 days before presentation. It was unknown if an antibiotic was administered at the time of the procedure. In this case of a possible sudden inoculum of bacteria, it is likely the turbidity rose too quickly and the number of drain cycles with elevated turbidity did not meet the device notification algorithm before the participant presented to the hospital with symptoms.
2	The participant presented to the clinic with abdominal pain and tenderness over the tunnel and purulent drainage at the exit site. The PD fluid culture was positive for *Staphylococcus epidermidis*. Gram stain of the exit site revealed no WBC and no organisms but culture positive for *Neisseria sicca*. Given that the device notification algorithm requires a certain number of drain cycles with elevated turbidity before alerting, the participant may have presented early in the course of peritonitis, likely due to an exit site or tunnel infection, before the obligatory number of elevated turbidity measures were met. Another possibility is that the participant had impaired initial cell reaction, as has been described to occur in 6% of peritonitis episodes.[12]
3	The participant presented to the hospital with worsening abdominal pain and catheter dysfunction; the catheter would not drain or fill. Effluent was obtained from the catheter lumen with a syringe. Gram stain was positive for gram-negative coccobacilli but cultures were ultimately negative. i.v. antibiotics were initiated. The catheter was removed 6 days later due to dysfunction (omentum wrapped around the catheter confirmed at surgery). After catheter removal, the participant stated the pain that had been present since the catheter was placed 6 months prior, was gone. The catheter culture at the time of removal was positive for *Acinetobacter baumannii*. This case was complicated by the cell count being obtained from the catheter lumen due to the catheter dysfunction and therefore may not represent the true intraperitoneal cell count.
4	The participant presented to the hospital with peritonitis-related symptoms and ultimately negative cultures. The CloudCath device notification algorithm, which depends on continuous, longitudinal measurements, did not trigger a notification, suggesting that the participant presented early in the course of peritonitis before the obligatory number of elevated turbidity measures was met.

PD, peritoneal dialysis; WBC, white blood cell.

notifications unassociated with peritonitis, 191 participants contributed 0 notifications; 30 participants contributed 1 notification; 22 participants contributed the remainder of the 66 notifications (Figure 7). The largest contribution came from 1 participant who contributed 14 notifications unassociated with peritonitis. Future studies can determine underlying clinical characteristics that contribute to consistently elevated turbidity.

Detection of Peritonitis Resolution

Examples of CloudCath system turbidity scores over time are illustrated in Figure 8. In Figure 8a, the CloudCath system identified turbidity above the participant's baseline levels and triggered an internal notification because the notifications to the participant and health care team were deactivated. Four days later, the participant presented to the dialysis care facility with abdominal pain and cloudy effluent. The participant had peritonitis with WBC of 260/μl, PMN of 85%, and a positive culture. Antimicrobial treatment was initiated, and the CloudCath system measured the participant's declining turbidity as it returned to baseline levels through resolution of peritonitis.

In Figure 8b, the CloudCath system measured the participant's turbidity at consistently low levels from baseline until elevated turbidity triggered an internal notification; the participant was hospitalized 14 days later with abdominal pain. Effluent cell count was WBC of 676/μl and PMN of 95%, with negative cultures. After hospital discharge, the dialysis care facility determined that the infection was resolved based on laboratory assessment of effluent (WBC of 158/μl and PMN of 26%). However, the CloudCath system measured an elevated turbidity score during this time that rose steadily above baseline levels after the initial

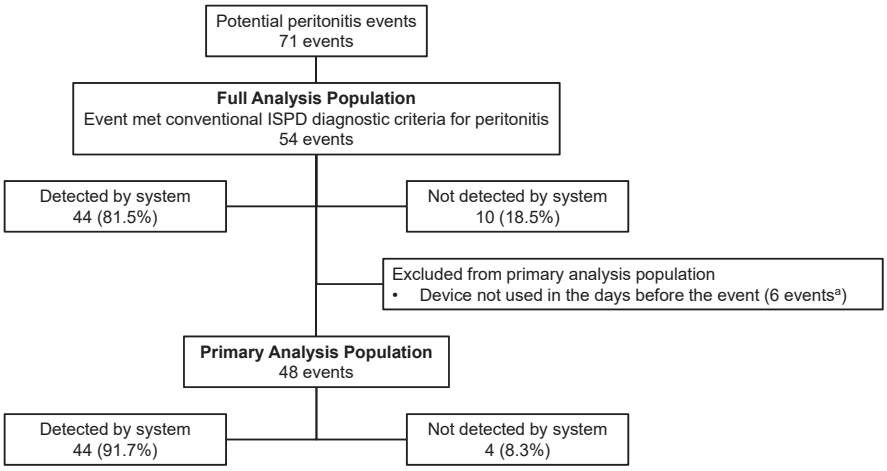


Figure 3. CloudCath system notifications (V1 algorithm) for peritonitis events based on conventional ISPD diagnostic criteria, wherein 2 of 3 of the following were present: (i) clinical features consistent with peritonitis (i.e., abdominal pain and/or cloudy dialysis effluent), (ii) dialysis effluent with WBC >100 cells/μl and PMN >50%, and (iii) identification of positive dialysis effluent culture. ISPD, International Society of Peritoneal Dialysis; PMN, and polymorphonuclear leukocytes; WBC, white blood cell. [a]See Table 2 for descriptions of these events.

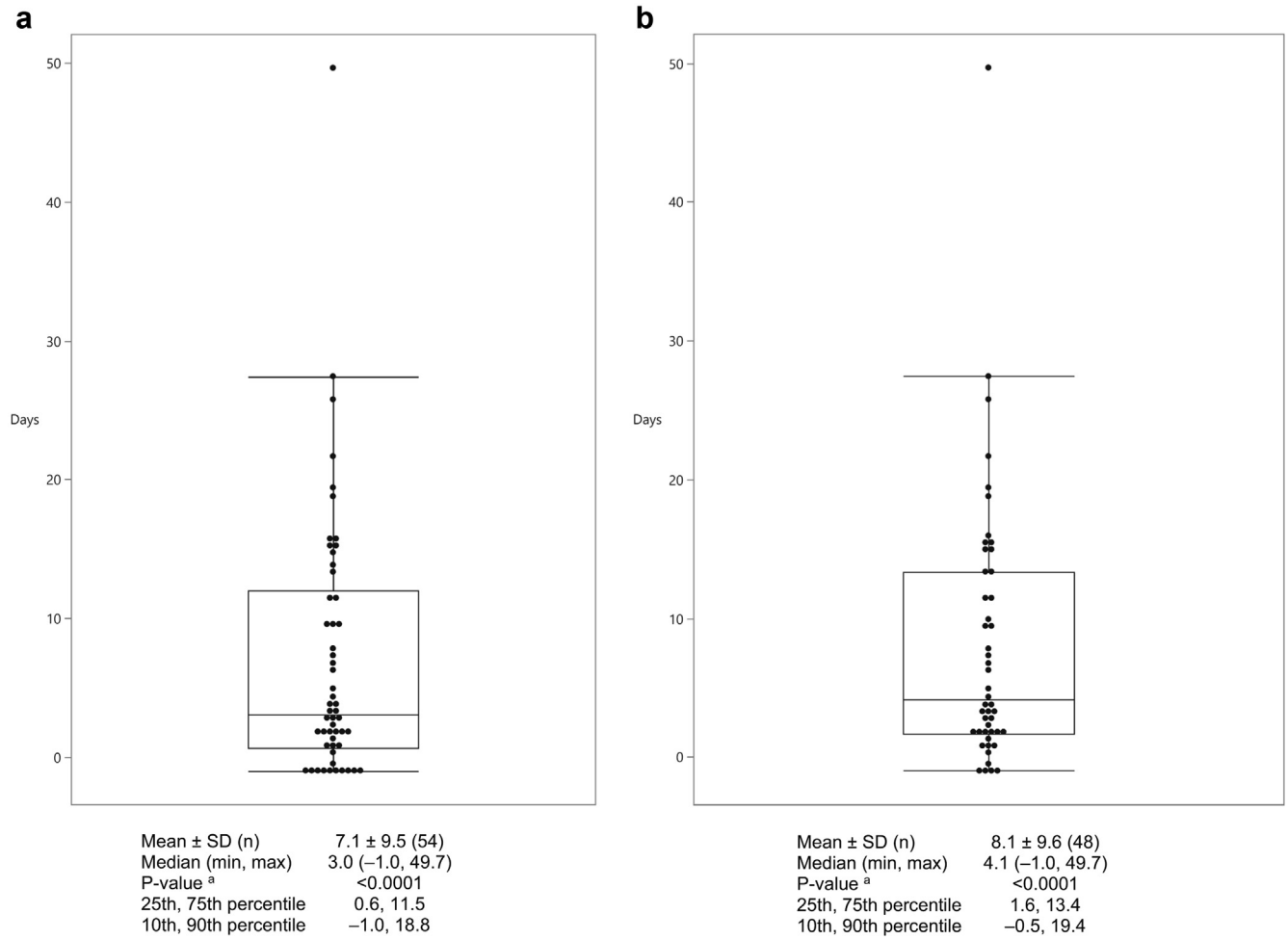


Figure 4. Lead time between CloudCath system notification and confirmation of peritonitis event based on conventional ISPD diagnostic criteria (V1 algorithm): (a) full analysis population; (b) primary analysis population. ISPD, International Society of Peritoneal Dialysis. [a]*P*-values were calculated using Wilcoxon Signed Rank test.

antimicrobial treatment regimen was completed. The participant's symptoms returned, which resulted in a second hospitalization. Cultures yielded *Candida parapsilosis* and effluent with WBC of 915/μl and PMN of 65%, and the participant's PD catheter was removed.

Updated Notification Algorithm Performance

The CloudCath notification algorithm was updated and trained utilizing the CATCH data set with a total of 298,009 individual PD exchange cycle measurements across 243 participants. We utilized bootstrap aggregation to train 5 models on different random subsets of the CATCH data set, where the subset was resampled by random selection from a list of participant IDs, with replacement.

The updated algorithm yielded 93 total notifications (0.52 notifications per patient-year; Figure 9). Forty-four notifications (0.25 notifications per patient-year) were triggered for peritonitis events based on conventional ISPD diagnostic criteria. Sixteen notifications (0.09 notifications per patient-year) were triggered for nonperitonitis events. Thirty-three notifications (0.18 notifications per patient-year) were triggered without a known connection between the notification and a temporal clinical event, based on participant recall at least 30 days after the notification. The median lead time between the notification and a peritonitis event based on ISPD WBC count criteria was 2.4 days.

Participant Experience

Most participants reported that they were able to set up the CloudCath system in 3 minutes or less, including 74% of participants at the first follow-up visit at 1 month, 88% by 6 months, and 81% across all study visits (Supplementary Figure S2A). Using 5-point Likert scales ranging from 1 (strongly disagree) to 5 (strongly agree), participants reported average scores for CloudCath system usability at 1 month that ranged from 4.70 to 4.83. Participants continued to report high average scores for usability across all study visits (Supplementary Figure S2B).

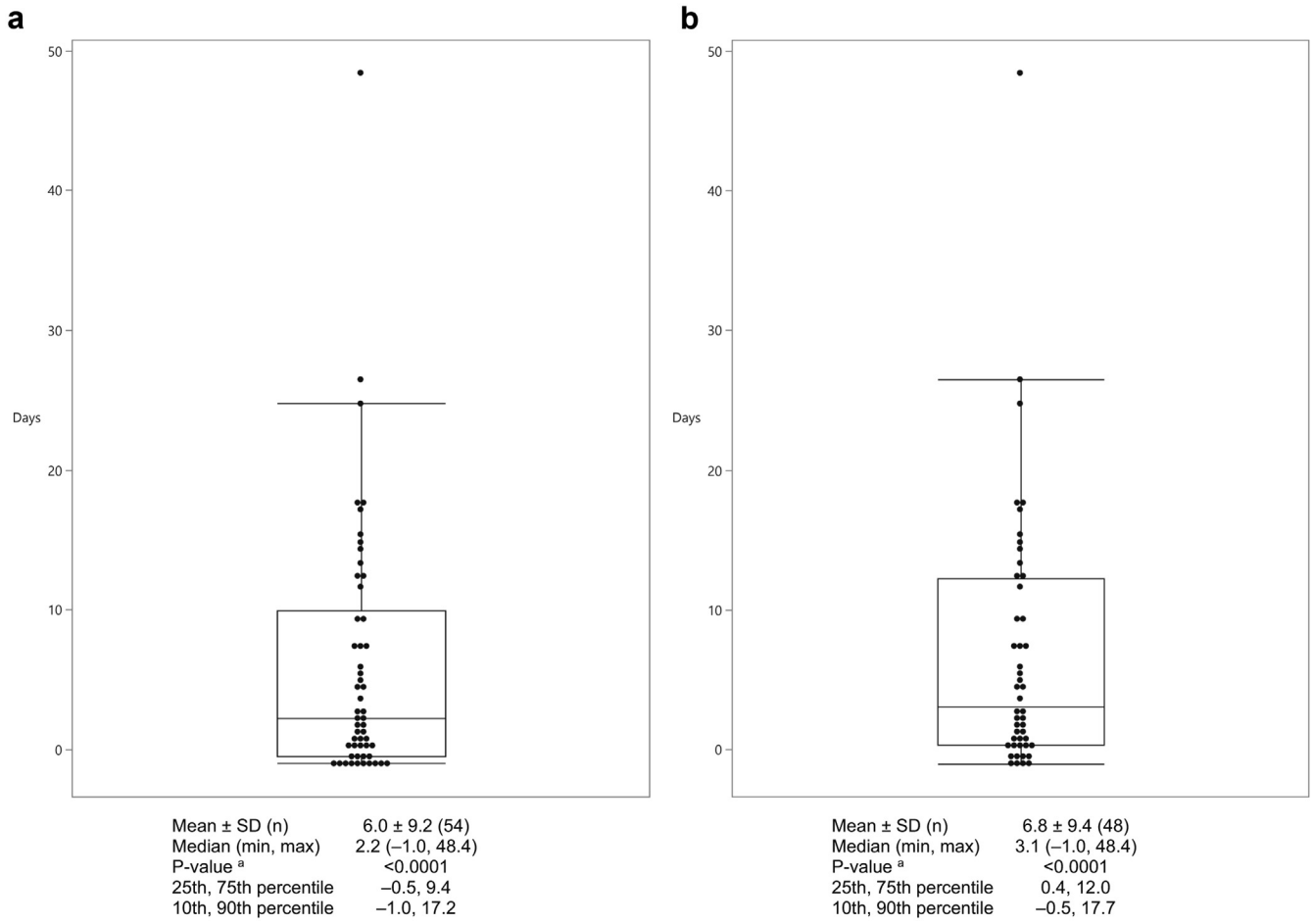


Figure 5. Lead time between CloudCath system notification and presentation for signs or symptoms of potential peritonitis (V1 algorithm): (a) full analysis population; (b) primary analysis population. [a]*P*-values were calculated using Wilcoxon Signed Rank test.

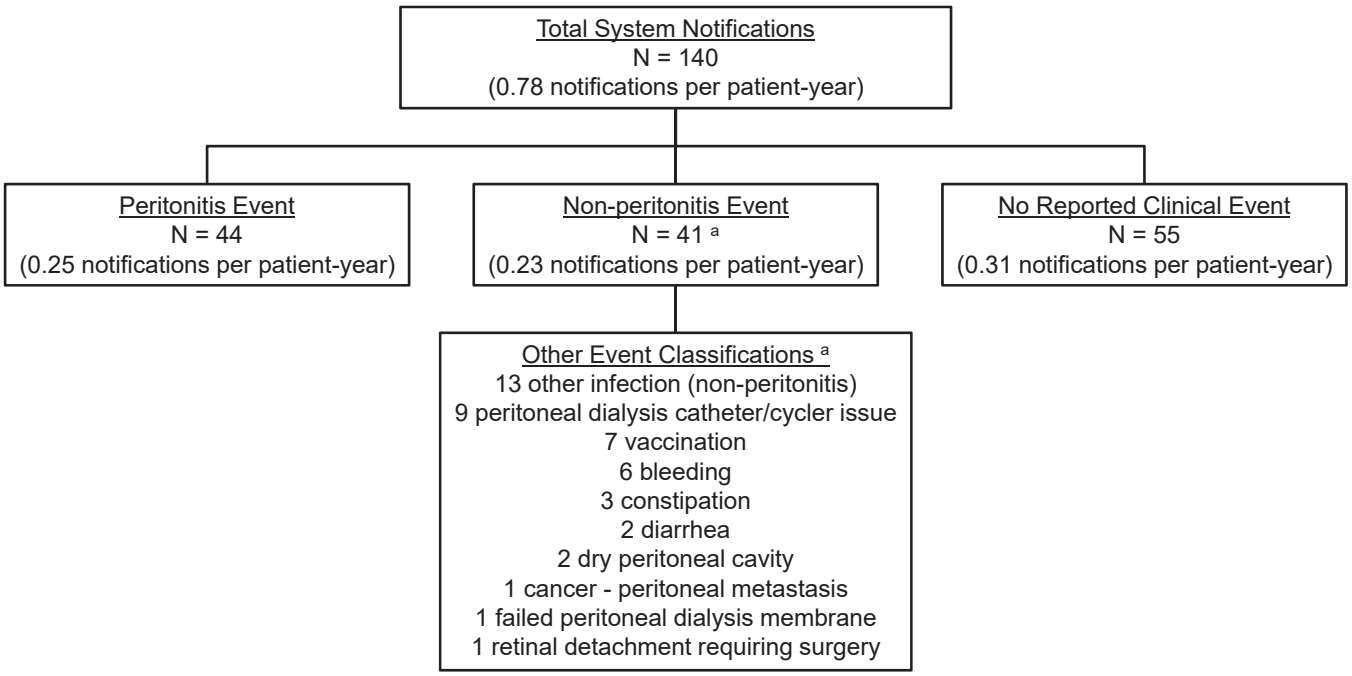
Safety

No participants reported CloudCath system-related adverse events during the study.

DISCUSSION

In this study, 243 participants with kidney failure who were treated with PD used the extracorporeal CloudCath system nightly, for a total of 178.8 patient-years. By analyzing the turbidity of effluent during each PD treatment and using the notification algorithm that is currently applied for use of the device in clinical practice, the system detected most peritonitis events early. The system triggered notifications for more than 80% of all peritonitis events. When the CloudCath system was used as intended, it triggered notifications for 91% and 92% of peritonitis events based on ISPD WBC count criteria or conventional ISPD diagnostic criteria, respectively.[10] In the primary analysis, notifications were triggered a median of 3.0 days before peritonitis events. In other effectiveness analyses, notifications were triggered a median of 2.6 to 4.1 days before peritonitis events and a median of 2.2 to 3.1 days before a participant presented with signs or symptoms of possible peritonitis.

In modern dialysis practice, there are no strategies in place to detect peritonitis before the development of overt signs and symptoms. Patients are presently instructed to be vigilant for abdominal pain and cloudy dialysate for diagnosis of peritonitis and to inform professional care providers (i.e., dialysis nursing staff or nephrologists) if newspaper print cannot be deciphered through spent dialysate. A sizeable fraction of patients with kidney failure has impaired visual acuity. Moreover, abdominal pain is typically a relatively late manifestation of peritonitis and can be caused by a wide variety of inflammatory and noninflammatory disorders. An automated system that tracks changes in the turbidity of spent dialysate could be advantageous to a broad range of patients receiving PD. Those who may experience the greatest benefit include patients with cognitive or visual impairment, those living alone, and those residing in rural or less well-resourced communities, where access to medical staff with PD



[a]The sum of individual events listed (N = 45) is greater than the number of associated notifications (N = 41) because 4 patients each had 2 separate non-peritonitis events that had the potential to affect the turbidity of peritoneal dialysis effluent

Figure 6. Flowchart of CloudCath system notification events (V1 algorithm). [a]The sum of individual events listed ($n = 45$) is greater than the number of associated notifications ($n = 41$) because 4 participants each had 2 separate nonperitonitis events that had the potential to affect the turbidity of peritoneal dialysis effluent.

experience is limited. An automated monitoring system could also facilitate ongoing use of PD in patients transferred to acute rehabilitation units and skilled nursing facilities, admission to which often obligates the unnecessary and undesirable urgent transition to in-center hemodialysis.

In this study, the CloudCath system triggered only 0.78 notifications per patient-year. The majority of these notifications (0.48 per patient-year) were triggered within 14 days before either a peritonitis event or a clinically relevant nonperitonitis event, including other infections or catheter or cycler issues. A minority of notifications (0.31 per patient-year) in this study were unassociated with clinical events. Although cloudy effluent is most commonly due to bacterial peritonitis, not all instances of cloudy dialysate are due to infection.[10] Cloudy dialysate may also be due to pathologic increases of either cellular or noncellular constituents of peritoneal fluid, including due to allergic response to the catheter, bleeding, or clotting response.[13] In addition, drugs, including calcium channel blockers, can result in chyloperitoneum and high triglyceride concentrations in patients on PD.[14] We are unable to precisely measure specificity, although it can be assumed that nearly all exchanges performed by patients whose CloudCath system did not trigger a notification did not have peritonitis (i.e., "true negatives"); thus, the specificity of the CloudCath system exceeds 99%.

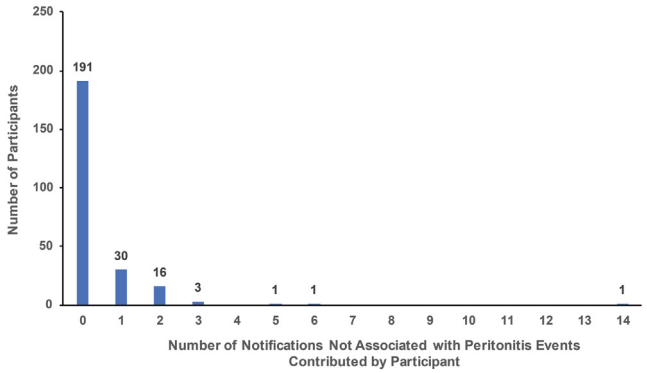


Figure 7. Histogram of participant contribution to CloudCath system notifications not associated with peritonitis events (V1 Algorithm).

This was a blinded study in which the CloudCath system notifications were not visible to the participant or healthcare providers, and we required a minimum follow-up of 30 days after each notification before we determined the potential cause of the notification. This delay may have rendered participants subject to recall bias that, in turn, may have diminished the ability to establish a connection between CloudCath system notifications and clinical events. Regardless of whether some of these notifications were associated

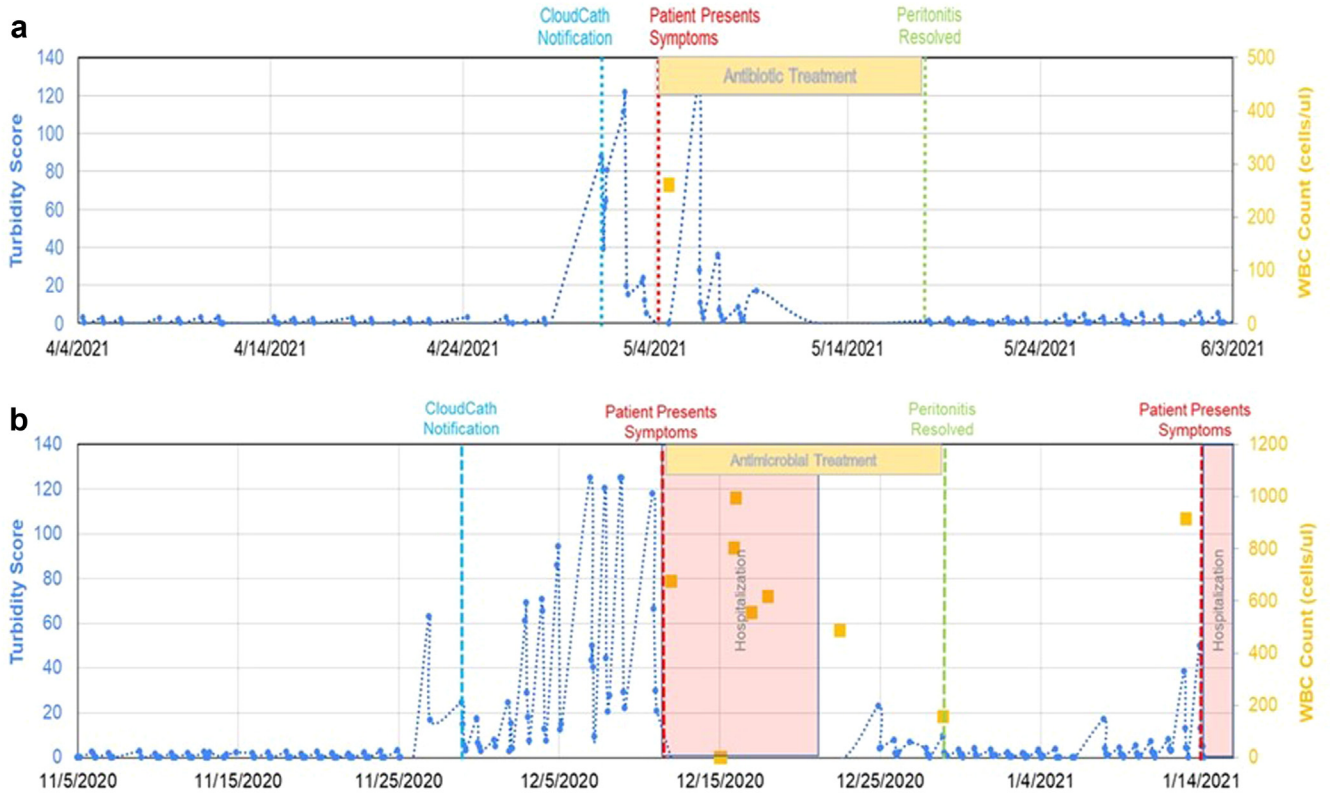


Figure 8. Examples of changes in effluent detected by the CloudCath system before and after peritonitis events. (a) The CloudCath system triggered a notification before the participant presented with symptoms; turbidity scores deceased with antibiotic treatment and remained low after peritonitis resolved. (b) The CloudCath system triggered a notification before the participant presented with symptoms; after peritonitis resolved, turbidity scores increased until the participant was hospitalized with symptoms and the catheter was removed.

with forgotten clinical events, receiving fewer than 1 notification per patient-year may be a reasonable tradeoff for the possible benefits of early detection of peritonitis events.

Assessment of the updated algorithm performance demonstrates the value of training data in optimizing the system's performance. Increasing the training data set to 298,009 measurements from 243 participants for

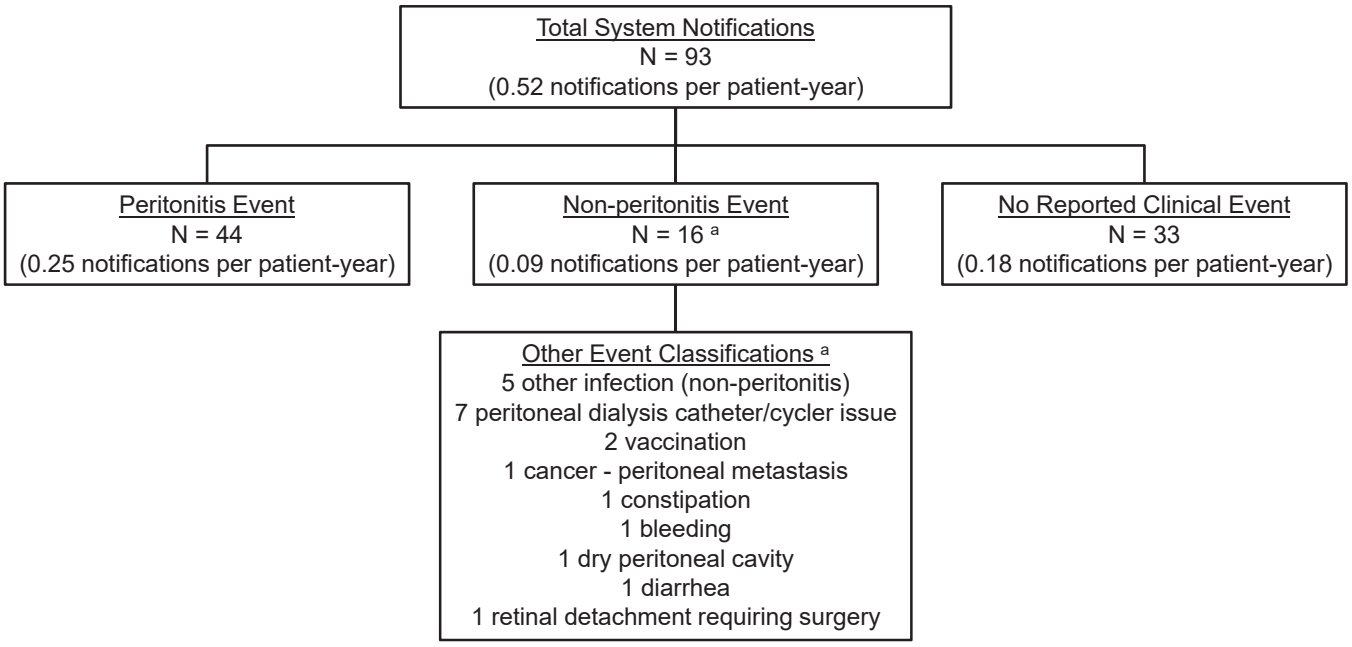


Figure 9. Flowchart of CloudCath system notification events (Updated Algorithm). [a]The sum of individual events listed ($n = 20$) is greater than the number of associated notifications ($n = 16$) because 4 participants each had 2 separate events that had the potential to affect the turbidity of peritoneal dialysis effluent.

the updated algorithm (vs. 14,134 measurements from 184 participants for the V1 algorithm) reduced notification for nonperitonitis events by nearly 50% (from 96 to 49). The median lead time between the notification and a peritonitis event based on ISPD WBC count criteria decreased slightly (from 2.6 days to 2.4 days). The Expansion of the training data set with additional patient-months of dialysis exchanges is likely to further improve algorithm performance.

Although there are few adequately powered clinical trials to compare clinically meaningful outcomes with PD or home hemodialysis and in-center hemodialysis, ample evidence suggests patients benefit from home-based therapies.[15,16] Performing dialysis at home provides patients with more flexibility in their schedule, irrespective of their life stage. Whether as young students, full-time workers, caretakers of children or older adults, or retirees, home-based dialysis therapies allow patients to work dialysis into their schedules, rather than to arrange their schedules around in-center hemodialysis. On a practical note, labor shortages at dialysis centers, which are anticipated to persist over the coming several years, threaten the ability to provide in-center hemodialysis to a growing population of patients with kidney failure.[17]

Remote in-home monitoring has become the norm in recent years to improve the safety of other therapies, including remote monitoring for the management of arrhythmia, heart failure complications, diabetes, and obstructive sleep apnea. Remote monitoring has already been extended to home dialysis, with the introduction of cyclers that transmit therapy-related data to dialysis units.[18–20] The CloudCath technology has the potential to build on remote monitoring of home dialysis by providing early identification of the most common and consequential complication of PD.

Our study has several strengths. We followed participants for a median of more than 9 months. The study sample was diverse by age, sex, designated race and ethnicity, PD vintage, and geography. We compared the time to detection of presumed peritonitis using the CloudCath system versus standard care, including participant symptoms and determination of the number of leukocytes and the proportion of PMN in spent dialysate. Study weaknesses included the modest sample size and the fact that participant and provider notifications were not activated.

The CATCH study was not designed to show that early detection of peritonitis with the CloudCath system versus standard-of-care improves clinical outcomes. The prospective, multicenter PROMPT study of 159 peritonitis events during PD demonstrated the potential benefits of early detection and treatment. In that study, each hour of delay in administering antibacterial therapy was associated with a 5.5% higher risk of transfer off PD or death.[9] Future studies will examine if CloudCath System notifications lead to less severe episodes of peritonitis, reduced complications, reduced hospitalizations, and extended time that patients can remain on PD, where appropriate.

In summary, we demonstrated that use of the CloudCath system during cycler-based PD treatment for up to 18 months remotely identified episodes of peritonitis with high sensitivity and a median lead time of approximately 3 to 4 days. Real-time monitoring of turbidity during PD may reassure the patient and healthcare team that most events of peritonitis will be detected early. After initiation of peritonitis treatment, the CloudCath system may also be used to monitor turbidity and alert the healthcare team if it does not decline during the first 3 to 5 days to identify refractory peritonitis.[21] These capabilities collectively could allow for earlier diagnosis, earlier treatment, and successful treatment of peritonitis in patients undergoing PD, which in turn may mitigate the health consequences of peritonitis in this patient population.

DISCLOSURE

RM reports serving as a consultant to Lightline Medical and Editor-in-Chief of the Clinical Journal of the American Society of Nephrology. He served as a site investigator for the CATCH study at the University of Washington. DEW, EY, AE-B, and BF are employees of, and have ownership interests in CloudCath, Inc. BAG reports serving on a Data Safety Monitoring Board via George Clinical for ongoing ProKidney studies. PDM reports serving as a consultant to CloudCath, Inc. BB reports serving as an advisor to CloudCath. He is the Chief Medical Officer of CosmosID. GMC reports serving as an advisor to CloudCath. He has served on the Board of Directors of Satellite Healthcare, a nonprofit dialysis provider. He has served as Chair or Co-Chair of Trial Steering Committees with Akebia, AstraZeneca, CSL Behring, Sanifit, and Vertex. He has also served as an Advisor to Durect, Eliaz Therapeutics, Miromatrix, Outset, Physiowave, Renibus, and Unicycive. He has served on Data Safety Monitoring Boards with Bayer, Mineralys, and ReCor. CRB declared no competing interests.

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DATA AVAILABILITY STATEMENT

Requests for data will be reviewed on a case-by-case basis to allow for confirmation of results without sharing of proprietary algorithms or other proprietary information.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. CloudCath system.

Figure S2. Participant usability assessment.

Table S1. Schedule of events.

CloudCath System Use Questionnaire.

CONSORT statement.

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