Renal Interventions

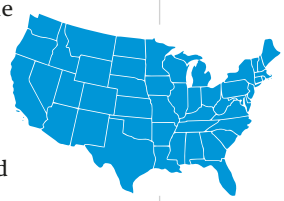
May 2022
Issue 03
www.renalinterventions.net

In this issue:

US end-stage kidney disease prevalence more than doubles

THE NUMBER OF PEOPLE LIVING with end-stage kidney disease (ESKD; prevalent cases) more than doubled between 2000 and 2019–increasing by 118.7%, from 358,247 to 783,594–according to data analysis from the United States Renal Data System (USRDS).

A 41.8% increase in new (incident) cases also occurred during the same period, from 92,660 to 131,422. Diabetes and hypertension were identified as primary causes driving higher percentage changes in prevalent and incident ESKD cases.



ESKD cases increased by 118.7% between 2000 and 2019

The analysis, which is published in a *Morbidity and Mortality Weekly Report* from the Centers for Disease Control and Prevention (CDC) also highlights racial and ethnic disparities in US ESKD rates.

Among Asian people, new ESKD cases increased from 2,507 cases in 2000 to 6,256 cases in 2019–a 149.5% increase that was the largest seen in any racial or ethnic group. During the study period, new cases increased from 25,917 to 33,700 among Black people (30% increase), from 11,297 to 20,790 among Hispanic people (84% increase), from 742 to 1,458 among Native Hawaiian or other Pacific Islander people (96.5% increase), and from 51,156 to 67,919 among white people (32.8% increase).

American Indian or Alaska Native people had the smallest increase in new cases, from 1,041 to 1,299, representing a 24.8% increase. The authors attribute the slowing of new cases in this population to targeted interventions funded by the Special Diabetes Program for Indians–a US$150 million annual grant programme established in 1997.

They anticipate that ESKD prevalence will continue to rise due to a growing and ageing population, high rates of hypertension and diabetes, and better survival of patients with ESKD. The continued increase in ESKD case numbers will compound the strain on the healthcare system and lead to higher costs, the authors write.

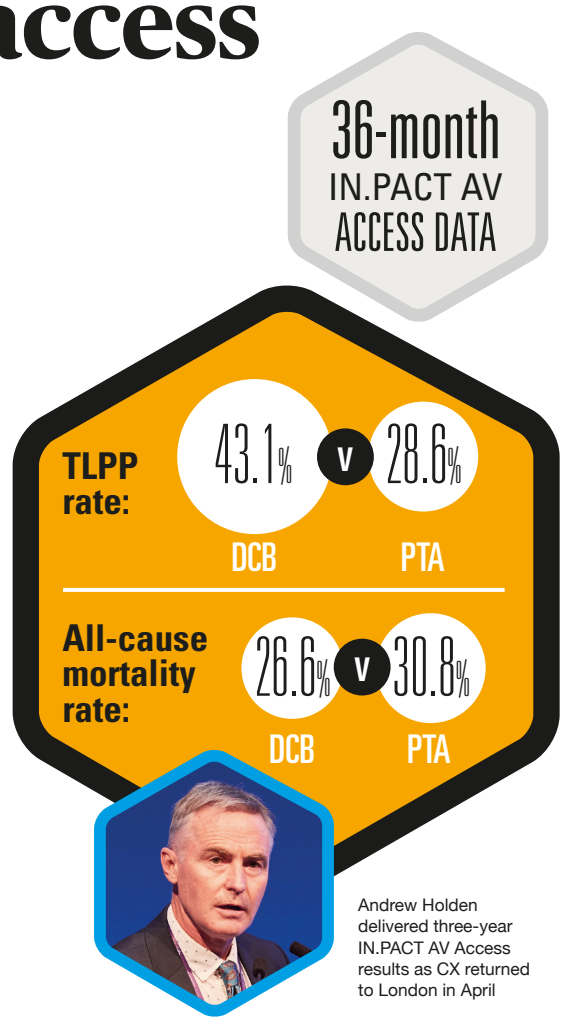
They note that, in 2019 alone, Medicare spent US$37.3 billion (7% of all paid claims costs) on ESKD, according to USRDS data.

Continued efforts to address risk factors, to prevent or delay ESKD onset, could stabilise or reverse these increasing numbers, the researchers conclude.

Follow *Renal Interventions* on all our social media platforms for the latest news, insight and events in kidney care

New drug-coated balloon data provide further encouragement in vascular access

Late-breaking data from clinical trials assessing drug-coated balloon (DCB) technologies have provided encouragement that these alternatives to plain-balloon angioplasty in vascular access care are safe, and can enable sustained freedom from reintervention over time. Findings from the IN.PACT AV Access (Medtronic) and ISABELLA (MedAlliance) trials were both delivered for the first time at the recent Charing Cross Symposium (CX 2022; 26–28 April, London, UK).



Andrew Holden delivered three-year IN.PACT AV Access results as CX returned to London in April

The former was presented by Andrew Holden (Auckland City Hospital, Auckland, New Zealand), who disclosed 36-month data from a global randomised controlled trial (RCT) assessing the IN.PACT AV DCB (Medtronic) as part of the CX 2022 Vascular Access Masterclass. In a Podium 1st presentation, Holden told audiences that end-stage kidney disease (ESKD) patients treated with the IN.PACT AV DCB remained intervention-free for longer than those who received a standard percutaneous transluminal angioplasty (PTA). He noted that a "significant difference" in target-lesion primary patency (TLPP) between the trial's DCB and PTA treatment groups was seen through the three-year follow-up timepoint, maintaining the trend observed in the 24-month IN.PACT AV Access data, which Holden delivered virtually at last year's CX Symposium.

The investigational device exemption (IDE) trial is seeking to assess the safety and efficacy of the IN.PACT AV DCB, which delivers the antiproliferative drug paclitaxel to inhibit neointimal hyperplasia and treat this leading cause of arteriovenous fistula (AVF) stenosis in ESKD patients. Specifically, the trial is comparing the use of the IN.PACT AV DCB in a treatment group to standard PTA in a control group, and enrolled 330 patients with a *de novo* or non-stented restenotic native fistula undergoing haemodialysis.

Three-year data from IN.PACT AV Access

Building on positive results seen at previous timepoints in this prospective, single-blinded, randomised IDE trial, Holden relayed a TLPP rate of 43.1% in the DCB group, compared to 28.6% in the PTA group, through 36 months. He also reported that a 21.3% reduction in reinterventions was associated with DCB use, with 255 reinterventions to maintain TLPP being required through 36 months in the DCB group versus 324 in the PTA group.

Holden then moved on to detail 36-month access circuit primary patency (ACPP) rates–stating that a "similar trend" was observed here, with a rate of 26.4% in the DCB group and 16.6% in the PTA group. He labelled this difference as being "significant" too, and noted a similar reduction (20.7%) in the number of reinterventions required to maintain ACPP within the DCB group. There were 311 necessary reinterventions in the DCB group and 392 in the PTA group.

After briefly alluding to mortality-related safety concerns that have been raised regarding paclitaxel in the past,

Continued on page 2

New drug-coated balloon data provide further encouragement in vascular access

Continued from page 1

Holden reported all-cause mortality findings–following a vital status update–that did not represent a statistically significant difference between the two treatment groups. He noted an all-cause mortality rate of 26.6% in the DCB group and 30.8% in the PTA group, and highlighted the fact that the mortality rate among "all-comer" haemodialysis patients from the United States Renal Data System (USRDS) through three years is higher than in both groups, at 41.9%.

Holden also stated that these findings compare favourably to those seen in the Lutonix AV IDE trial (BD) too, but noted that direct comparisons are difficult to draw because this trial concluded after 24 months. Having shown a sustained and superior performance with DCB versus PTA, IN.PACT AV Access is now "the only randomised pivotal trial of a device treating dysfunctional AVFs to demonstrate consistent and sustained clinical benefit through 36 months", according to Holden. Summarising the data, he added that ESKD patients in IN.PACT AV Access had a median time to reintervention that was 14.7 months longer when they were treated with DCB compared to PTA. As such, Holden concluded that these findings represent durable, long-term data supporting the use of the IN.PACT AV DCB as "a standard of care" for AVF maintenance in this patient population.

Encouragement in spite of "potentially disappointing" results

A second Podium 1st presentation at CX 2022 saw Tjun Tang (Singapore General Hospital, Singapore) deliver late-breaking data from a small-scale pilot trial that indicate "potentially disappointing" results–but, according to Tang, still offer encouragement in the treatment of dysfunctional dialysis accesses with DCBs.

Tang presented 12-month findings from the prospective, single-centre ISABELLA trial, which assessed the safety and feasibility of the Selution SLR sirolimus-eluting balloon (MedAlliance) for minimising the effect of neointimal hyperplasia. While its goal of treating AVF stenosis, and ultimately preventing fistula failure, is broadly the same as that of IN.PACT AV Access, a key difference is that the DCB being evaluated in ISABELLA uses sirolimus–an alternative anti-restenotic drug to paclitaxel–to reduce neointimal hyperplasia.

A total of 34 patients were ultimately evaluated at the 12-month follow-up timepoint in ISABELLA, Tang detailed, with the most common indication for intervening being a drop in access flow (61.5% of cases). Moving on to 12-month trial data, he reported a TLPP rate of 44% (16/36 lesions) and an ACPP rate of 31% (10/32 lesions), which represented decreases from 72% and 63%, respectively, at six months. In addition, he stated that the overall rate of secondary patency–defined as freedom from access circuit abandonment–was 94.1% (32/34 patients) at 12 months compared to the 97.2% (35/36 patients) observed at six months.

Tang, who was awarded the CX 2022 Senior Clinician Abstract Prize for this presentation, concluded by highlighting "excellent" technical and clinical success rates of 100%, and positive safety outcomes, in the ISABELLA trial. He also relayed that the use of Selution SLR in patients with AVF stenosis appears safe, with no serious adverse events, such as pulmonary embolism or bronchopneumonia, being associated with its use in the trial. And, in terms of efficacy, Tang added that, while the results are "potentially disappointing", this is a small, exploratory investigation and alluded to possible confounding factors within its findings.

"We do need longer-term data and randomised controlled studies [...] if we are going to move forward seriously within this field, and with this technology," he added. And, speaking to *Renal Interventions*, Tang noted the importance of being careful when interpreting the results of an exploratory pilot trial–especially one designed to power a future RCT.

"I do not think it is actually a setback at all," he continued. "In fact, I think it is very encouraging. I think the fact we are not getting any serious adverse events with the balloon [...] is reassuring." Tang also told *Renal Interventions* that, with the exception of the IN.PACT AV Access trial, a similar drop-off in patency rates between six and 12 months had been observed in several previous studies using paclitaxel to treat dysfunctional dialysis access.

"I do not think it is actually a setback at all. In fact, I think it is very encouraging."
Tjun Tang

Do the data stack up?

In a discussion at CX 2022, Ounali Jaffer (Barts Health NHS Trust, London, UK)–while clarifying that the IN.PACT AV Access trial was not adequately powered for the information he was seeking–enquired as to whether there was a signal for different areas within the access circuit that may benefit the most from DCB therapy. "The numbers are going to be smaller at three years, but we would say that restenotic lesions certainly have a higher response; the arteriovenous anastomosis and cephalic arch [are observed to benefit most]," Holden responded. "For people who want to start introducing DCB into their practice, these would be lesions that we would be able to support [for DCB treatment]." Following up with a question on the different populations outside of the USA treated in IN.PACT AV Access, Jaffer said: "You had more radiocephalic fistulas, and one of the findings is that there is more neointimal hyperplasia within that area. Do you think that had a profound effect?"

"I was pleasantly surprised because I think, while we know that, with radiocephalic fistulas, the patency is often better than with upper-arm fistulas, the focal stenoses–particularly at the arteriovenous anastomosis with smaller calibre vessels–are the worst performing," Holden noted. "And, we found that it is a group that actually differentially did the best. The smaller the calibre of the vessel, the better the drug-coated effect, so it was reassuring to see that." Here, CX executive board member Nicholas Inston (Queen Elizabeth Hospital, Birmingham, UK) highlighted that the safety signal with paclitaxel-coated balloons seen in the trial was particularly reassuring too.

When asked by Peter Gaines (Sheffield Hallam University, Sheffield, UK) to compare the ISABELLA data with results from IN.PACT AV Access, Tang said that the "all-comer" population of dialysis patients in his trial reflects everyday practice in Singapore–also noting that the lesions observed in patient populations from Asia tend to be greater in number and longer than those seen in European and US studies. "I think the IN.PACT [AV Access] data are fantastic and it is a unique trial in terms of showing a positive effect in its primary endpoint," Tang continued, but added that the IN.PACT AV Access dataset may be more "sanitised" and stems from a randomised trial as well. ISABELLA is promising, and demonstrated safety, but is still only exploratory, he concluded, stating a belief that, as such, this may be akin to "comparing apples and oranges".

Robert Jones (Queen Elizabeth Hospital, Birmingham, UK) then pressed Tang on which of the two leading drugs he favours in his everyday practice–paclitaxel or sirolimus. Tang said that, when it comes to AVFs specifically, "all the data there are with paclitaxel". He noted that he has access to all the established DCBs in his centre, including the MagicTouch sirolimus-coated balloon (Concept Medical), and stated: "My personal feeling would be to just use paclitaxel for the time being–I think there needs to be more data with sirolimus, but the signal we are getting is better." Tang said this belief is also supported by encouraging results from the MATILDA trial of the MagicTouch device.

For more insight on DCBs, including lessons from the DeVA trial (Boston Scientific), which Jones himself presented at CX 2022, *turn to pages 6-7*.

Editor-in-chief: Nicholas Inston | **Editorial Board:** Ziv Haskal, Stephen Hohmann, Robert Jones
Publisher: Roger Greenhalgh | **Content Director:** Urmila Kerslake | **Editor:** Jamie Bell *jamie@bibamedical.com* | **Design:** Terry Hawes, Wes Mitchell
Editorial contribution: Jocelyn Hudson, Will Date and Clare Tierney
Advertising (EU): Shilpa Suthar *shilpa@bibamedical.com* | **Advertising (US):** Nicole Schmitz *nicole@bibamedical.com*
Subscriptions: *subscriptions@bibamedical.com* | **News or advertising queries:** Tel: +44 (0)20 7736 8788

Published by: BIBA Publishing, which is a subsidiary of BIBA Medical Ltd BIBA Medical, Europe, 526 Fulham Road, Fulham, London, SW6 5NR, United Kingdom
Tel: +44 (0) 20 7736 8788 | BIBA Medical, North America, 155 North Wacker Drive, Suite 4250, Chicago, IL 60606, United States Tel: +1 708-770-7323
Printed by: Micropress Printers Ltd. Reprint requests and all correspondence regarding the newspaper should be addressed to the editor at the United Kingdom address.

If you have comments on this issue or suggestions for upcoming editions, write to jamie@bibamedical.com

Renal Interventions

Renal Interventions linkedin.com/company/renal-interventions/ @Renal_Ints