Coronary stent technology: a narrative review

Daniel Chen, Nigel Jepson

 Percutaneous coronary intervention (PCI) is the most commonly performed therapeutic procedure in the contemporary management of significant coronary disease. In Australia, 170 PCI procedures per 100,000 population are performed through 4.3 PCI centres per million population. In 2015, over 47,000 procedures were performed nationally. Interventional technology has advanced drastically, from balloon angioplasty, to bare metal and drug-eluting stents, through to the recent development of fully bioresorbable stent scaffolds. Increasingly sophisticated platforms have sought to improve on the outcomes of the preceding generation of devices by refining their design, structure, and component materials. This review discusses the evolution of PCI technology, the efficacy and safety of currently available devices, and the rationale for new generation platforms.

A list of acronyms used is provided in Box 1 and a brief historical summary of coronary stent technology is given in Box 2.

This narrative review used a PubMed search of original and review articles from 1970 to 2016, as well as specialist society publications and guidelines from the European Society of Cardiology, American College of Cardiology, and the Cardiac Society of Australia and New Zealand to formulate an evidence-based overview of contemporary stent technology, as applied to clinical practice.

Plain old balloon angioplasty

The treatment of obstructive coronary disease was revolutionised when Andreas Gruntzig first performed coronary balloon angioplasty in 1977, providing an alternative to bypass surgery. However, the outcomes from plain old balloon angioplasty were compromised by high rates of restenosis in up to 30–50% of patients at 3–6 months, mediated by dissection, elastic recoil, late vascular remodelling, and neointimal proliferation. Additionally, abrupt vessel closure due to balloon-induced dissection or elastic recoil occurred in 5–10% of patients within minutes to hours of angioplasty, often resulting in acute myocardial infarction (MI) precipitating the need for urgent surgical revascularisation.

Bare metal stents

Stainless steel coronary stents, or bare metal stents (BMSs), were developed to overcome the issues posed by balloon angioplasty and maintain vessel patency, and Sigwart and colleagues heralded the second technological advance in interventional cardiology when they implanted the first coronary stent in a human coronary artery in 1986. Implantation of BMSs served to prevent acute vessel closure by sealing the balloon-induced dissection flaps, as well as to reduce the rate of restenosis by scaffolding the balloon-dilated artery and preventing late recoil. Consequently, coronary stents improved procedural safety and efficacy and rapidly eliminated the need for cardiothoracic surgical back-up. This led to stents being used in more than 85% of PCI procedures by the 1990s.

First generation drug-eluting stents

Although stent implantation represented an advance, a 20–30% incidence of restenosis with BMS persisted. The new entity of in-stent restenosis (ISR) was the result of stent-mediated arterial injury inducing neointimal hyperplasia (in-stent growth of smooth muscle cells and extracellular matrix) and led to the development of drug-eluting stents (DESs). This pathophysiology is shown in Box 3. These devices consisted of a metallic stainless steel frame, an anti-proliferative drug such as sirolimus or paclitaxel, and a permanent polymer that acted to control local drug release. The third paradigm shift of interventional cardiology was signalled when the first DES was implanted in 1999.

A pivotal study (the RAVEL trial) showed that the sirolimus-eluting stent (SES) significantly reduced the incidence of ISR (0 vs 26.6%; P < 0.001). This was closely followed by the development of the paclitaxel-eluting stent (PES).

Summary

- Coronary angioplasty and coronary artery stents have revolutionised interventional cardiology.
- Contemporary coronary stent technology continues to seek to improve on the outcomes of the preceding generation of devices by refining their design, structure and component materials.
- These technologies include new generations of drug-eluting stents, non-polymeric stents, bioresorbable polymer-coated stents, and fully bioresorbable scaffolds.
- This review discusses the evolution of coronary stent technology, the efficacy and safety of currently available devices, and the rationale for new generation platforms as efforts continue to design the ideal coronary stent technology.

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2 Historical summary of coronary stent technology

<table>
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<th>Stent Type</th>
<th>First Developed</th>
<th>Description</th>
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<tr>
<td>Balloon angioplasty</td>
<td>First performed by Andreas Gruntzig in 1977</td>
<td>First performed by Andreas Gruntzig in 1977 to prevent acute vessel closure following balloon angioplasty.</td>
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<tr>
<td>Bare metal stents</td>
<td>First implanted by Sigwart in 1986</td>
<td>Prevent acute vessel closure using balloon angioplasty.</td>
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<td>First generation DES</td>
<td>Sirolimus-eluting stents and paclitaxel-eluting stents were the first drug-eluting stents coated with an anti-proliferative drug to prevent in-stent restenosis.</td>
<td></td>
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<tr>
<td>Second generation DES</td>
<td>Zotarolimus-eluting stents and everolimus-eluting stents were next generation DES that were developed to improve on the safety profile of first generation devices.</td>
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<tr>
<td>Bioresorbable polymer DES</td>
<td>DES coated with bioresorbable polymers, developed to prevent late adverse events implicated with polymer coating.</td>
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<tr>
<td>Polymer-free DES</td>
<td>DES without a polymer coat, developed to avoid polymer-mediated late adverse events.</td>
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<tr>
<td>Fully bioresorbable scaffolds</td>
<td>These devices completely resorb after providing mechanical support and local drug delivery in the first 12 months of implantation, removing the nidus for late adverse events.</td>
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DES = drug-eluting stent. 

The efficacy of these first generation DESs compared with BMSs has been confirmed in randomised trials and registry databases. A 2007 meta-analysis examined 38 randomised trials of 18,023 patients comparing SESs and PESs with BMSs. Over a follow-up period of 1–4 years, there was a significant reduction in target lesion revascularisation (TLR) seen with both SESs (hazard ratio [HR] 0.40; 95% CI 0.32–0.51) and PESs (HR 0.58; 95% CI 0.46–0.72) compared with BMS. A registry analysis of 3,751 propensity-matched pairs of patients who either received a first-generation DES or a BMS also confirmed the superior efficacy of DESs, with a significant reduction in TLR at 2 years (7.4% v 10.7%; P < 0.001). In particular, the benefit was seen in high-risk patients with two or three risk factors for restenosis — presence of diabetes, small vessels and long lesions.

Registry data confirmed the safety and efficacy of first generation DESs in an Australian context, demonstrating significant reductions in major adverse cardiovascular events compared with BMS (odds ratio [OR], 0.68; 95% CI, 0.56–0.81). These significant reductions in incidence of vessel restenosis with DESs allowed for stent implantation in more complex coronary anatomy, previously untreated due to prohibitive restenosis rates. Subsequent uptake of this technology was so widespread that by 2005, 95% of PCI in the Australian private sector was with first generation DES. However, this optimism was shaken in 2006 by the release of a pooled analysis of findings from randomised trials of DESs by Camenzind and colleagues that showed a significantly increased risk of death and Q-wave MI at late follow-up in patients receiving an SES compared with those implanted with a BMS (6.3% v 3.9%; P = 0.03). The analysis also identified a distinct entity of very late stent thrombosis (VLST) beyond 1-year following DES implantation, with a steady annual risk of 0.3%–0.6% up to 5 years.

Subsequently, several large meta-analyses provided reassurance by demonstrating comparable outcomes with DESs and BMSs. The largest of these revealed a similar risk of death at both short and long term follow-up. This was further supported by the largest registry data of 262,700 patients that found lower rates of death (12.9% v 17.9%; P < 0.0001), MI (7.3% v 10.0%; P < 0.0001) and repeat revascularisation (23.0% v 24.5%; P = 0.007) with a DES compared with a BMS over a 30-month follow-up.

The discrepancy between the later data and the initial results by Camenzind and colleagues is multifactorial. First, the use of dual antiplatelet therapy (DAPT) differed between trials, with patients receiving just 8 weeks of DAPT in the RAVEL study, while the protocol in later trials involved up to 12 months of DAPT. Second, while Camenzind and colleagues examined only Q-wave MI as an endpoint, most other studies demonstrating the safety of DESs examined all MI as an endpoint. Third, Camenzind and colleagues produced a study-based meta-analysis that examined aggregate data from published reports rather than data from individual patients, which is susceptible to inter-study heterogeneity. Fourth, before the standardised definitions by the Academic Research Consortium in 2007, the initial definitions and adjudication of stent thrombosis (ST) between studies were not uniform. Last, the incidences of death, MI, and ST are still relatively infrequent and subsequently some small trials are not powered to detect small differences in event rates, leading to a difference in outcomes between studies.

### 3 Schematic representation of late adverse events following stent implantation

![Schematic diagram](image)

Section 1 shows delayed healing with incomplete endothelialisation of stent struts and protruding stent struts, which present a potential nidus for thrombus formation. Section 2 shows physiological arterial healing with smooth and homogeneous coverage of stent struts by smooth muscle cells and extracellular matrix, which is described as benign neointimal hyperplasia (NIH). Section 3 shows in-stent neointimal hyperplasia, which is susceptible to subsequent plaque rupture and thrombotic luminal stenosis. Section 4 demonstrates excessive neointimal hyperplasia leading to in-stent restenosis. Section 5 shows stent malapposition, which results in exposed stent struts, which also present as a potential nidus for thrombus formation.

procedural factors and suboptimal platelet inhibition. Late and very late ST is seen more frequently with first generation DES compared with BMS, and has been related to incomplete strut re-endothelialisation, polymer-induced chronic inflammation and hypersensitivity reaction, stent malapposition, and accelerated neatherosclerosis.\textsuperscript{21,23}

Newer platforms (second generation DESs) include the zotarolimus-eluting stent (ZES) and the everolimus-eluting stent (EES). These were developed to overcome the late safety and efficacy concerns with SESs and PESs, using less toxic anti-proliferative drugs, more biocompatible polymer coatings, and thinner and more flexible metal alloy struts.\textsuperscript{24} Optical coherence tomography has been used to demonstrate vascular healing over time (Box 4).

EESs have become the most widely used DES worldwide.\textsuperscript{25,26} They are implanted in more than 500,000 patients every year in the United States\textsuperscript{27} and are used in 80–90% of all PCI procedures in Australia.

Pooled analysis of the 2-year results from pivotal randomised trials showed improved outcomes with the EES, with significant reductions in rates of MI (relative risk [RR], 0.57; 95% CI, 0.45–0.73), TLR (RR, 0.59; 95% CI, 0.47–0.73) and ST (RR, 0.35; 95% CI, 0.21–0.60) compared with first generation PESs.\textsuperscript{28} The ZES was compared with the first generation PES in the ENDEAVOR IV trial, demonstrating non-inferiority based on 9-month follow-up data of IFR (13.3% vs 6.7%; P = 0.075) and TLR (6.6% vs 7.1%; P = 0.01).\textsuperscript{29} At 5-year follow-up, the rates of target vessel failure (defined as a composite of cardiac death, MI and clinically driven target vessel revascularisation) (17.3% vs 21.3%; P = 0.061) were similar, but there were significantly fewer target vessel MI and cardiac deaths with the ZES (6.4% vs 9.2%; P = 0.049).\textsuperscript{30}

Second generation DESs have also been compared head-to-head in large randomised trials. The RESOLUTE All-Comers and TWENTE trials compared the EES with the ZES in real-world broad patient populations, demonstrating comparable outcomes between the two stents in terms of TLR (defined as the composite of cardiac death), target vessel MI, or clinically indicated TLR (8.3% vs 8.2%; P for non-inferiority < 0.001), and 12-month mortality (2.8% vs 1.6%; P = 0.08).\textsuperscript{31,32} Optical coherence tomography has been used to demonstrate vascular healing over time (Box 4).

Given these clinical advances, second generation DESs are widely accepted as the percutaneous treatment of choice for obstructive coronary disease and have replaced SESs and PESs globally.\textsuperscript{33}

Despite the clinical improvements of second generation DESs, issues with long term safety and efficacy persist. The Bern–Rotterdam cohort of 4212 real-world patients who received an EES experienced a definite or probable ST rate of 6.3% and a VLSH rate of 2.0% over a 4-year follow-up period. Although the VLSH rate was significantly lower compared with that for first generation PESs (4.0%; P < 0.0001) and SESs (2.8%; P = 0.02), it nonetheless represents an ongoing 0.67% annual risk of ST beyond 1 year.\textsuperscript{34} Further, there remains an associated annual TLR incidence rate of 1.3% beyond 1 year.\textsuperscript{34} Several large scale randomised trials demonstrate an accrual of adverse events arising from the treated target lesion after implantation of a contemporary second generation metallic DES at a rate of 2–3% per year for at least 5 years with no apparent plateau evident.\textsuperscript{34–36} Significant advantages have been achieved with second generation DESs. However, the persistence and accrual of late events, thought to result largely from the presence of a permanent metallic implant, have further prompted a new generation of devices. These include biocompatible polymer and polymer-free DESs, and fully bioresorbable scaffolds.

### Biodegradable polymer drug-eluting stents

As a polymer coat is implicated in the pathogenesis of late adverse events (Box 3) after DES implantation (especially VLST) by providing a potential chronic inflammatory stimulus,\textsuperscript{37} DESs coated with biocompatible polymers (such as polylactic acid glycolide or polylactic acid) have been developed. Degradation of the polymer occurs simultaneously with controlled release of the anti-proliferative drug. Following completion of drug elution, only the stent platform remains in the coronary artery. Biodegradable polymer EESs and SESs are approved for implantation in Australia. A biolimus-eluting stent (BES) is also commercially available. However, despite extensive research\textsuperscript{38} and subsequent Therapeutic Goods Administration approval of the BES, there has been minimal uptake within the Australian context. Several other biodegradable polymer DESs have been trialled and used clinically outside Australia.

The EVOLVE II trial found that when compared with an EES with a permanent polymer, the biostable polymer DES has similar efficacy and safety up to 12 months, as measured by the primary endpoint of TLR (6.7% vs 6.5%; P for non-inferiority = 0.0005), as well as definite or probable ST (0.4% vs 0.6%; P = 0.50).\textsuperscript{39} Recent data from the randomised BIOSCIENCE trial established non-inferiority of a biodegradable polymer SES compared with a contemporary permanent polymer EES, with similar rates of TLR (RR, 0.99; 95% CI, 0.71–1.38; P = 0.95 and P for non-inferiority = 0.0004).\textsuperscript{40} Despite theoretical advantages, biodegradable polymer DESs have yet to deliver decreased late events when compared with second generation permanent polymer DESs and longer term data are still needed.

### Polymer-free drug-eluting stents

An alternative strategy to eliminate polymer-mediated chronic inflammation has been the development of the polymer-free DES. The challenge in this class of devices has been achieving adequate levels of anti-proliferative drug without the polymer vehicle to ensure neointimal hyperplasia and ISR is inhibited.

In the randomised LEADERS FREE trial, which recruited 2466 patients who were at high risk of bleeding, the composite primary safety endpoint of cardiac death, MI or ST (9.4% vs 12.9%; HR, 0.71; CI 95%, 0.56–0.91; P = 0.005) and the primary efficacy endpoint of TLR (5.1% vs 9.8%; HR, 0.50; 95% CI, 0.37–0.69; P < 0.001) occurred less frequently in patients treated with a polymer-free umilimus-eluting stent than in those treated with the BMS.\textsuperscript{41} Patients were only treated with 1 month of DAPT. This represents promising data for patients who are considered high risk for bleeding, and deemed unsuitable for prolonged use of DAPT. However, this polymer-free umilimus-eluting stent has yet to be approved for use in Australia, and the shorter duration of DAPT in this patient population cannot be extrapolated to other devices in the absence of further data and research.

### Fully bioresorbable scaffolds

While there have been considerable efforts to eliminate the use of permanent polymers, contemporary second generation DESs remain the default device for PCI. However, concerns over late adverse events (particularly VLST) after permanent metallic prostheses have led to interest in fully bioresorbable stent technology in the past decade, potentially representing a fourth technological paradigm in interventional cardiology.

Referred to as scaffolds, these devices provide the local drug delivery and mechanical support of metallic DES in the first
4 Optical coherence tomography evaluation of a second generation drug-eluting stent

Optical coherence tomography evaluation of stent efficacy and vascular healing over time at 6 months (A), 9 months (B), and 12 months (C), as shown by good strut coverage by endothelialisation, and good apposition against the vascular wall. There are no protruding strut struts as schematically illustrated in Box 1, and there is benign neointimal hyperplasia without in-stent restenosis.

Source: Image courtesy of Abbott Vascular.

5 Optical coherence tomography evaluation of an everolimus-eluting bioresorbable vascular scaffold

Stent struts are shown at baseline. At 6 months and 2 years, there are progressively fewer struts, indicating gradual resorption. At 5 years, no struts remain, showing that the scaffold has been completely bioresorbed.

Source: Image courtesy of Abbott Vascular.

12 months and completely resorb 3 years after implantation (Box 5). As the scaffold struts resorb, they are replaced by cellular and connective tissue, allowing restoration of normal vasomotor function and increased luminal dimensions over 5 years due to compensatory vascular remodelling and plaque regression. These permanent changes are not possible with metallic stents, which permanently cage the vessel and serve as a substrate for persistent inflammation, neointimal hyperplasia and strut fracture. The theoretical rationale for bioresorbable scaffolds is that these provide improved long term outcomes compared with DESs, as they remove any nidus for late adverse events (ISR and VLST). Additional potential benefits may include avoidance of exceptionally long segment metallic stenting ("full metal-jacket"), thereby maintaining later surgical and percutaneous revascularisation options, and compatibility with non-invasive computed tomography angiographic imaging (limited by metallic stents), and restricting very long term reliance on long term DAPT.

The first non-drug-eluting bioresorbable scaffold was implanted in a patient in 2000. Since then, a significant number of bioresorbable scaffolds have been developed. However, only the everolimus-eluting bioresorbable vascular scaffold (BVS) is available commercially in Australia.

The ABSORB III trial, in which 2008 patients were assigned in a 2:1 ratio to treatment with either a BVS or an EES, demonstrated similar rates of the primary outcome of TLF (7.8% vs 6.1%; P for non-inferiority = 0.007) as well as of ST at 1 year (1.5% vs 0.7%; P = 0.13). A meta-analysis of pooled data for 3389 patients comparing BVS with EES implantation similarly showed equivalent rates of TLF (RR, 1.22; 95% CI, 0.91–1.64; P = 0.17) and the composite outcome of death, MI and revascularisation (RR, 1.09; 95% CI, 0.89–1.34; P = 0.38). Prospective Australian registry data of 100 patients treated with a BVS also demonstrated good outcomes in the local context. Procedural success was high (95.3%), with no mortality, 1% scaffold thrombosis and 4% TLR within the 12-month follow-up period.

Despite early optimism, challenges exist for the current first generation BVS. The device has a thick strut (a design feature necessary to maintain radial strength) and higher crossing profile resulting in a significantly lower procedural success rate (94.9% vs 97%; P = 0.003) compared with that of the EES. Additionally, the meta-analysis by Stone and colleagues demonstrated a safety concern with higher rates of device thrombosis at 1 year (1.3% vs 0.6%; HR, 2.11; 95% CI, 0.92–4.83; P = 0.08) and MI (5.7% vs 4.0%; RR, 1.34; 95% CI, 0.97–1.85; P = 0.08) with the BVS, but neither of these were statistically significant. More recently, Lipinski and colleagues presented an expanded meta-analysis that found no significant difference in all-cause mortality with a BVS compared with a DES (OR, 0.40; 95% CI, 0.15–1.06; P = 0.06); but an increase in definite or probable ST (OR, 1.91; 95% CI, 0.82–4.46; P = 0.03). The observation of increased scaffold thrombosis is also supported by a large clinical registry.

Available evidence has shown equivalent efficacy of the BVS against the current best-in-class DES at 12 months. Significantly, users in these trials were still learning the optimal BVS implantation techniques; meticulous attention to device sizing, vessel preparation and routine high pressure post-dilatation may further improve early and 12-month outcomes. Regardless, longer term results (up to 5 years), particularly in trials involving real-world patients, are needed before generalisation adoption of BVSs can be recommended in routine clinical practice. Separately, the broader challenge to BVS technology and engineering will be the transition to second generation devices with thinner struts, increased expansile capacity, improved delivery and shorter biodegradation times.

Conclusion

The ideal coronary stent technology is one that can achieve optimal efficacy without compromising long term patient safety. It must be easy and predictable to deliver, applicable to a broad range of clinical and anatomical settings, meet the needs of future imaging and revascularisation options, permit the restoration of normal vascular function, and limit the requirement for prolonged DAPT. Despite the established excellent efficacy and safety profile of current gold standard second generation DESs, the narrative of PCI continues to evolve in a bid to build on previous successes. The emerging third generation of DESs has the potential to improve on the performance of current DESs. However, it remains to be seen if the novel bioresorbable scaffolds will truly represent a new paradigm of coronary intervention and become a mainstream PCI device.

Competing Interests: Nigel Jaffé has provided consultative support for Abbott Vascular and served as a proctor for BVS implantation training program. No grants, financial support, technical support or other assistance was received for this narrative review.

Provenance: Commissioned; externally peer reviewed.
Integrative medicine: more than the promotion of unproven treatments?

TO THE EDITOR: We believe that Ernst is out of touch with international medical leadership and patient behaviour.

The Australian Medical Association, the Royal Australian College of General Practitioners and the Australasian Integrative Medicine Association acknowledge the growing popularity of complementary and integrative medicine, the high practice rates among doctors themselves (about 30% of Australian general practitioners), and the increasing demand for better education, information, regulation and dialogue by GPs.

In response, medical leaders worldwide have formed the Academic Consortium for Integrative Medicine and Health. The top ten North American universities in medicine identified by the 2015-16 QS World University Rankings — including universities such as Harvard, Johns Hopkins, Stanford and Yale — are all members of this consortium, confirming an executive commitment to integrative medicine through established research, education and clinical programs. Over 60 academic institutes in North America undertake research and provide services in integrative medicine, and eight of the world’s top ten medical schools are involved in teaching or clinical activity in integrative medicine.

Evidence of treatment effectiveness is critical, but to polarise the debate — medicine is evidence based and integrative medicine is not — is inappropriate. The MJA itself has published extensively on the shortfalls of scientific evidence in conventional medical care, and the current review of the Medicare Benefits Schedule is premised on the fact that many tax-funded medical interventions are not well justified by evidence. While the body of evidence in support of particular integrative medicine interventions is growing, more is needed.

We look forward to a balanced perspective on these issues to assist a clear dialogue and research in an important area of health care that is widely used by our community.

Avoiding debate over terminology will help us identify those evidence-based therapies that can be safely and effectively integrated into clinical practice for the broader benefit.

Alan Bensoussan
Keryn Phelps
Vicki Kotsirilos
Penny Caldicott
Jennifer Hunter


TO THE EDITOR: Si and colleagues are committed for reporting on the bloodstream infection (BSI) surveillance in 23 Queensland public hospitals via the Centre for Healthcare Related Infection Surveillance and Prevention (2008–2012). Bloodstream infections are significant in terms of the need for intravenous antibiotics and hospitalisation, and estimating the burden of illness can reflect emerging trends. However, our experience of targeted BSI monitoring in Victorian hospitals indicates that health care-associated infection surveillance should also provide meaningful data to inform prevention programs. We note that Si and colleagues reported some data that appear reliant on non-standardised surveillance methodology, and some measures that may not facilitate action at the hospital level.

First, the inclusion of common skin commensals identified in a single blood culture, even in a patient commenced on empirical antibiotics, can be problematical. Such events are unlikely to represent a true infection and will comprise a significant portion of all observed pathogens. Inclusion of these infections will, therefore, affect the reported relative incidence of other more pathogenic organisms.

Second, we note that catheter tip cultures were employed as one method for defining device-associated BSIs. These are variably requested at the discretion of health care providers for clinical diagnosis, together with other tests such as differential time to positivity of central versus peripheral blood cultures. In contrast, standardised surveillance criteria are required for device-associated infections to ensure reliability and reproducibility of data. Estimates of disease burden are therefore not comparable with other programs, and inferences regarding ward or site of infection should be interpreted cautiously.

We also question the value of data concerning neutropenic patients with gram-negative BSIs. In the setting of chemotherapy-induced mucositis, such infections may arise in both community and inpatient settings, do not reflect breaches in aseptic technique or best clinical practice, and are not amenable to prevention activities. More likely, these infections reflect the intensity of cancer therapies and presence of comorbidities in cancer populations.

Quality improvement programs in health care must focus on modifiable factors and systems to mitigate risk, and should be underpinned by reliable, reproducible and valid data. We believe that the reported data are valuable, but suggest that additional clinical and epidemiological elements and standardised methodology would enhance the strategy.

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IN REPLY: We appreciate the comments by Worth and colleagues on our article and agree that bloodstream infection (BSI) surveillance should occur with the goal of informing initiatives to prevent infection.

With regard to positive blood cultures caused by common skin commensals, in 2013, the surveillance definition from the Centre for Healthcare Related Infection Surveillance and Prevention (CHRISP) was updated in line with that of the United States National Healthcare Safety Network (NHSN). The updated CHRISP definition, which required two positive cultures for a common skin commensal if treatment was initiated, was developed to coincide with the newly deployed Multiplicare health care-associated infection surveillance system in Queensland public hospitals. Our article acknowledged the impact of the use of the older definition.

Although the CHRISP surveillance definition of neutropenic sepsis is imperfect and includes reference to catheter tip cultures, it was implemented to create a distinction between BSI due to bacterial translocation across the gut in neutropenic patients and central line-associated BSI. The CHRISP definition was developed over a decade before the NHSN developed its classification of the mucosal barrier injury laboratory-confirmed bloodstream infection (MBI-LCBI). The data collection period reported in our article predates the inclusion of the MBI-LCBI definition into the central line-associated BSI surveillance definition from the Australian Commission on Safety and Quality in Health Care. We do not advocate the comparison of specific rates of infection collected with different surveillance systems; however, our