The treatment of sepsis has come into focus in the last four weeks. As healthcare provision differs worldwide, our international experts respond from a global perspective. We appreciate your feedback on this. Sepsis must be recognised as global burden. Read what the Global Sepsis Alliance, our head organisation is doing and see the next steps for #wsd14.

**ProCESS trial: a word of caution**

In March, The New England Journal of Medicine finally published one of the most anticipated clinical studies in the sepsis field, the ProCESS trial. For the last 10 years we have been treating septic patients with hypoperfusion based on the results of the Rivers’ EGDT trial. The ProCESS trial was designed to test this strategy, and randomised 1341 patients in three arms. They compared the usual care arm with two protocolised therapy arms, one of them based on Rivers EGDT with SvO2 and CPV optimisation and the other one, named standard therapy, that did not require the placement of a central venous catheter. The investigators were not able to show any difference between the usual care and the protocolised care, neither the EGDT nor the standard arm.

Although this is a well-designed study, we need to be cautious. The initial sample size calculation was based on an expected mortality of 30-46%. However they ended up with 18% mortality in the usual care arm, which means that even the authors were surprised by their low mortality rates. These mortality rates are much lower than previously reported in other USA epidemiological studies, including the Rivers trial, even more so when we consider that only patients with hyperlactatemia or septic shock were included.

This low mortality reflects worldwide efforts to reduce the sepsis burden. These efforts, including initiatives like the Surviving Sepsis Campaign and the Global Sepsis Alliance, have resulted in increased sepsis awareness and improvement in treatment in the last few years. Unfortunately, this is not the reality in the major part of the world, nor in many developed countries and is certainly very far from the high mortality rates reported by emergent or limited-resource countries.

As clearly stated by the authors in their concluding paragraph, these results are only valid in settings with high-quality usual care, in which patients are identified early and receive adequate and prompt antibiotic treatment. In this scenario, the benefits of hemodynamic optimisation protocolised care could not be demonstrated.

In emerging and limited resource countries, the challenges are huge. Limitations in access to care, restricted public awareness among lay people and delays in searching for care, are among the major problems. The gap between scientific evidence and bedside, a frequent challenge even in developed nations, is probably greater. Such gaps are mainly explained by lack of adequate workflow prioritising, timely access of care for severely ill patients inside hospitals, resistance in following guidelines and lack of knowledge among staff.

We should not misinterpret these results. The optimisation of sepsis hemodynamic treatment is only required by the most severe septic patients. We should continue our efforts to implement protocolised strategies in the emergency department to enhance early detection and early antibiotic administration for septic patients.

It is also true that we are still awaiting the results of PROMISSE and ARISE, the two other studies aiming to test the EGDT strategy. However, we must keep in mind that they will also represent the scenario of high-income countries. We actually need a trial conduct in limited-resource or emerging countries to finally answer this question.
Regulatory mandates for sepsis care – no reason for caution but encouragement to promote and increase awareness for sepsis.

The report of the Centers for Disease Control and Prevention (CDC) which indicates that the incidence of sepsis has doubled between 2000 and 2008, is being challenged (Chanu Rhee et al NEJM 2014). To bolster their argument, the authors of this viewpoint article state that “this apparent explosion in sepsis is spurring high-profile initiatives to promote earlier recognition and better treatment” and lament “that policymakers are actively encouraging these efforts and that New York State now requires all hospitals to adopt sepsis protocols”. In reality the burden of sepsis is still under-recognised and the term sepsis is not known to most lay people, journalists or politicians. That is indeed why international and national initiatives like the Surviving Sepsis Campaign, the Global Sepsis Alliance, the Sepsis Alliance, the Rory Staunton Foundation and many more organisations and individuals over the past decade have worked diligently to increase public and policymaker awareness to the burden of sepsis which can be correctly labelled as a “hidden healthcare disaster”. Sepsis still only ranks 16 in the annual Burden of Disease Report of the WHO and World Bank as “sepsis in newborns and other infectious disorders”, whereas lower respiratory tract infections (LRTTs), a major cause of sepsis, is ranked as the second most common killer. Most people do not know that when someone dies from an acute infection such as LRTI, he or she actually dies of sepsis which is the common final pathway of infection, resulting in multiple organ failure and death.

Rhee et al also express concerns that “protocols that force physician behavior risk promoting inappropriate prescribing of broad-spectrum antibiotics, unnecessary testing, overuse of invasive catheters, diversion of scarce ICU capacity, and delayed identification of nonsepsis diagnoses.” However, the opposite is also true. It has been estimated that if the US as a whole achieved earlier sepsis identification and evidence-based treatment, there would be 92,000 fewer deaths annually, 1.25 million fewer hospital days annually, and reductions in hospital expenditures of over $1.5 billion (Shorr et al CCM 2007). That is why the national and international initiatives and healthcare providers in many parts of the world promoted numerous quality improvement projects that demonstrated the benefits of recognition, early fluid resuscitation and broad-spectrum antibiotics in reducing sepsis mortality significantly. Most recently, the efficacy of early recognition and sepsis therapy with antibiotics and fluids was demonstrated in the ProCESS trial in which the mortality rate of patients with severe sepsis and septic shock admitted to the emergency department was only 20% (Angus et al NEJM 2014). The accompanying editorial correctly concluded: “The publication of the ProCESS trial launched the era of early recognition and treatment in the management of sepsis” (Lilly CM, NEJM 2014).

Rhee et al also argued that the observed decrease in sepsis mortality may not only be due to improvements in sepsis care but might rather be related to progressively more sensitive coding by capturing a larger but less severely ill group of patients over time. To support this opinion they point to the fact that the increase in sepsis incidence observed in the US is much higher than the modest increases in hospital admissions of patients with infections such as urinary tract infections, abdominal infections and bacteremia, or a decrease in pneumonia over the same time period. However, this observation may well result from the fact that in the past only the underlying infection that caused sepsis was coded rather than sepsis itself, despite the presence of signs of systemic inflammation and organ dysfunction which qualifies for the diagnosis of sepsis, severe sepsis and septic shock. It may well be that in the US the coding habits have changed over the last decade because of increased awareness and also because the revised ICD9 and the ICD10 coding system more easily permitted the coding to be based on consensus definitions. This does not support the opinion that sepsis is overcoded today, but rather that for a long time the true incidence of sepsis was hidden by lack of awareness and inadequate coding. It is for these reasons that from a patient and healthcare provider perspective, early sepsis recognition, before multi-organ failure and septic shock are present and may become irreversible, is exactly what is needed. The fact that real improvements in the quality of sepsis care occurred over the last decade is also supported by the finding of decreased mortality rates in the
WHO:
Recognition of sepsis as Global Burden

All medical professionals should code diseases according to the ‘International Code of Diseases’ by the WHO. The results of this coding forms the basis for the ‘Global Disease’ Report and other World Health related publications – which provide the basic decision-making documents for governments world-wide. In these reports, sepsis is only listed as neonates or maternal sepsis – despite the fact that sepsis is the most common pathway to death following an infection – and the incidence and mortality could be reduced easily. Many countries in the world do not adequately document sepsis – possibly on the basis of the ICD 9 or ICD 10. Moreover when it is documented it is done only as a primary diagnosis which accounts for less than 50% of all sepsis cases. This is a major hurdle and reflected in the fact that sepsis is not mentioned in the A-Z list of the WHO description of diseases. The Global Sepsis Alliance executive board has targeted this for change in a joint effort with leading world federations and medical scientists.

CDC took the first steps:
Thanks to the relentless efforts of the Rory Staunton Foundation, the CDC as a leading American academic institution, has begun to recognise sepsis for what it is – both a global and local issue. Dr Tom Frieden, Director at the CDC – Centers for Disease Control and Prevention and thus one of the top public health officials in the United States, supports the initiative of World Sepsis Day. As new Ambassador he states the importance of increasing public awareness for sepsis and his willingness to help spread the word.

“Sepsis can be devastating to patients and their families. Even survivors of sepsis can suffer life-long impacts of their illness,” said CDC Director Tom Frieden, M.D., M.P.H.

“While we need to increase awareness and early detection of sepsis to protect patients and save lives, we also need to understand the causes of sepsis so that we can prevent it whenever possible.”
www.world-sepsis-day.org
www.rorystaunton.com

placebo groups of recent sepsis trials such as the PROWESS shock trial compared to sepsis trials that used similar definitions for sepsis as earlier trials that were conducted ten years ago. Likewise, the recent report from Australia and New Zealand demonstrates a decrease in hospital mortality of ICU treated patients with severe sepsis between 2000 and 2012, from 35% to 18%. Just as important is the fact that the proportion of severe sepsis or septic shock among all ICU admissions has increased every year, from 7.2% in 2000 to 11.1%, despite no change in the sepsis criteria used over this period and the decline in mortality rate remained after adjustments for illness severity and other potential confounders. (Kaukonen et al JAMA 2104)

...but rather that for a long time the true incidence of sepsis was hidden by lack of awareness and inadequate coding.

As careful sensitivity analysis was performed to control changes in coding habits, the editorial accompanying this study came to the conclusion that “this suggests that the true incidence of severe sepsis throughout the community actually increased.” (Iwashyna and Angus JAMA 2014). These findings contradict the notion of Rhee et al that the increase in the incidence of severe sepsis may result only from changes in coding habits. Indeed, undercoding of sepsis may have been very common in the US a decade ago and undercoding still is very likely to occur in many parts of the world.

However, lack of awareness and delayed diagnosis may cost thousands of lives and will perpetuate the fact that the general public and health authorities including WHO and funding agencies, are aware of the real and increasing burden of sepsis. These reasons dictate that we should continue to encourage successful quality improvement initiatives but also forge ahead with concerted political and public awareness campaigns to ensure sustainability of these efforts.

Konrad Reinhart
Niranjan Kissoon
Ron Daniels
Getting it right: Antibiotic Stewardship
The increase of antibiotic resistant bacteria (ARB) over the last two decades is a known fact– and finally recognised as a global threat by the WHO. Increased mobility, overuse of antibiotics and the decrease in research has lead to a situation where more and more ARB are known. Realistic steps against the rise of ARB are needed in order to maintain the current status of treatments available for sepsis patients. An adequate and optimised use of antibiotics is required to survive sepsis. Together with two of our supporting organisations we are taking action to enhance antibiotic stewardship.

WAAAR World Alliance against Antibiotic Resistance
The World Alliance against Antibiotic Resistance is an effort to raise global professional awareness by Prof. Jean Carlet. WAAAR advocates the 5 following actions:
• Cautious, controlled and surveyed approaches to the use of antibiotics
• Informational and educational efforts for change
• Prevention
• Basic and applied research, and drug development
• Query to the UNESCO to include the “lives saved by antibiotics” in the list of the world immaterial heritage.
As a group of 700 individuals from 55 different countries representing all the key stakeholders (physicians, veterinarians, microbiologists, pharmacists, nurses, evolutionary biologists, ecologists, environmentalists, and including patient advocacy groups) WAAAR strikes out to enhance Antibiotic Stewardship on a global level.
For more information: Click here

The Alliance to Save Our Antibiotics
The Alliance to Save Our Antibiotics was founded in 2013 by Compassion in World Farming, the Soil Association and Sustain, and is supported by the Jeremy Coller Foundation. The Alliance exists to highlight the danger of antibiotic overuse in intensive farming to the health of people and farm animals and to be part of the solution to the problem of growing antimicrobial resistance. Its vision is a world in which human and animal health and well-being are protected by food and farming systems that do not rely routinely on antibiotics and related drugs. If you want to join their fight: Click Here

Creating awareness
Sepsis is always occurring after an infection. To prevent, spot and treat it early and with the best possible measures, will ensure the survival of many and reduce the risk of Post Traumatic Stress Disorder. This is the reason why we, as World Sepsis Day Headquarters, continue to inform on the most infectious diseases which are the major causes of sepsis. Pneumonia, urinary tract infections, Malaria, Cancer and Aids are major infections which may lead to sepsis. Please feel free to use this information in your social media activities! Send us an e-mail and we will provide you with images as soon as they are available.
Contact: office@world-sepsis-day.org

#5moments
Watch out for the #5Moments discussion on #handhygiene on 5th May with Didier Pittet Iyes, the famous one), Jules Storr (Manager of Clean Care is Saver Care, WHO), Ron Daniels (The UK Sepsis Trust), Luciano Azavedo (Brazil, Latin American Sepsis Society) Claire Kilpatrick (UK, Clean Care is Saver Care/Patient Safety Project Manager WHO)
The Twitter Chat: twitter.com/WorldSepsisDay
4pm-6pm CEST
3pm-5pm UTC
10am-12pm EDT
Event 2014: Pink Picnic

We invite everyone to hold a Pink Picnic or BBQ in celebration of every single sepsis hero and sepsis survivor. Pink Picnic is the World Sepsis Day fundraising event for 2014, starting on May 15. Pink Picnics are social events where pink is used to signify relation to World Sepsis Day. This can include pink salads or cupcakes, BBQ treats, beverages, plates, other table decor...and whatever you can think of! You can hold an event on World Sepsis Day: 13 September 2014 or whatever day you prefer.

Set up a pink picnic – it doesn’t matter if you are an organisation, a company or a family. Adapt the idea to your needs and invite your business partners to a Pink Dinner, employees to a Pink Picnic TGIF, colleagues, friends, family or whoever you think should be informed about sepsis.

Make your Pink Picnic a visible event: Pink shirts & other merchandise with the icons and the ‘stop sepsis save lives’ logo will be available online. They are simple, eye-catching symbols and signs, applicable for female, male, or children. We will communicate and establish a wide range of items.

The Pink Picnic Competition:
Pink dishes, cakes, drinks: Take a photo of your favourite Pink Picnic food or drink and add a selfie along with your creation! Post it on Facebook or tweet it and e-mail us your post with your receipt. The 10 best, chosen by the GSA-Executive Board & WSD HQ, will get their pick of a Pink Picnic shirt and Pocket Cards to inform colleagues, friends or relatives about sepsis! With the receipts and images, we will create a Pink Picnic receipt & idea booklet and publish it on the World Sepsis Day website and social media.

The Competition will start: Mid-May
Watch out @:
Facebook/worldsepsisday
Twitter/worldsepsisday

Raise funds:
Invite your friends, relatives or colleagues to a great day out. Do a Pink Picnic wherever you like – we will do ours in front of the Parliament. Ask everyone to bring a pink drink or food item and put up a donation basket. Donate the money online and your efforts will fund the fight against sepsis.

Should you wish to discuss any of the above
office@world-sepsis-day.org

ALSO – the long-awaited store for the US will be open to reduce shipping costs.
Publish your event on World Sepsis Day

Our event portal is open for 2014! Just log in and upload your event. All you need is an image and information such as venue, location, and contact details. About 30 events were featured on the World Sepsis Day website in 2013. With over 200 events world-wide in 2013, we will be able to feature at least 50 events this year – but we need your help. Inform us!

Patient Empowerment:

We are sorry to inform you that some material we announced in the last newsletter is delayed. Due to limited funding, the need to copy existing material as well as enhance and deepen our know-how about sepsis, we have to refrain from providing another patient brochure. You can access local patient information material here:

UK: [http://sepsistrust.org/](http://sepsistrust.org/)
USA: [http://www.sepsisalliance.org/](http://www.sepsisalliance.org/)
Brazil: [http://www.sepsisnet.org/](http://www.sepsisnet.org/)
Spain: [http://www.edusepsis.org](http://www.edusepsis.org)

Please share this newsletter and inform us about your activities.

Have a good read: Do you know the inventor of the alcoholic hand rub? New book: ‘Clean hands saves lives’

Thierry Crouzet

Prof. Didier Pittet developed this life-saving measure and donated this gift free of patents or licenses to the WHO, saving thousands of lives. His crusade is recounted in a book that promises to be a major event. Translated into seven languages, it is being published by Editions L’Âge de l’Homme to mark the occasion of World Hand Hygiene Day on 5 May 2014.

We invite you to download the newsletter and use these key messages for your own bulletins, website, Facebook, and Twitter or disseminate it to your colleagues /other organizations or friends in your area.

Stay connected

Twitter: twitter.com/WorldSepsisDay
#sepsis: information related to sepsis
#wsd14: Events around World Sepsis Day 2014
#5moments: Handhygiene
#pic: pink picnic (Starts 15 May)
Facebook: facebook.com/WorldSepsisDay

Our sponsors

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