

## Priorities for Action on Thrombosis and Non-Communicable Diseases

ETHA statement on the EU Healthier Together Initiative

The European Thrombosis and Haemostasis Alliance (ETHA) supports the EU's efforts to prevent and treat non-communicable diseases through implementation of best practices across the Member States. These best practices should include systematic venous thromboembolism (VTE) risk assessment for all patients admitted to hospital in Europe, permitting preventative treatment for those at the highest risk.

VTE is a leading cause of hospital-related death, but not all people who could benefit from preventative treatment in Europe receive it. Additionally, non-communicable diseases – such as diabetes – can be risk factors for developing VTE.

Implementing VTE risk assessment and prophylaxis in a systematic and consistent manner across Europe, would help to reduce the risk of developing blood clots, safeguard patient quality of life, avoid preventable deaths, and reduce the health budget pressures arising from VTE incidents.

The European Thrombosis and Haemostasis Alliance's aim is to highlight the importance of venous thromboembolism (VTE) and stroke due to atrial fibrillation as diseases that have a potentially devastating, lifelong impact on quality of life, and which can frequently be deadly. This position paper relates to our suggested priorities and best practices, as submitted in the framework of the EU Healthier Together Initiative on non-communicable diseases.

### 1. Health Determinants

**EU research funding specifically allocated to developing and expanding knowledge about the impact of health determinants on patient outcomes, for conditions where the evidence base is lacking**

We do not have specific reported data for VTE – venous thromboembolism, an umbrella term for deep vein thrombosis (DVT) and pulmonary embolism (PE) – as a cause of death and disability, as the Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study does not report on VTE. What evidence we do have suggests that, across Europe, there are approximately 544,000 VTE-related deaths every year<sup>1</sup>. Data on secondary VTE prevention is particularly limited and more research is required to understand how health determinants affect long-term thrombosis prevention.

### **Collect data across Europe on incidence, death rate and long-term burden of venous thromboembolism (VTE)**

In order to create a Europe-wide basis for further research and health care actions, it is vital that the EU Member States collect consistent, interoperable data on the incidence, death rate, and long-term burden of VTE. This will establish a solid, common understanding on the impact VTE has in Europe – including its differential impact on people from socioeconomically disadvantaged backgrounds. Additionally, such data is essential for implementing best practice and assessing effectiveness of prevention measures across the EU.

### **Identify people at high risk of VTE**

VTE affects people from all walks of life. However, certain factors and situations, including common health determinants, can increase the risk of developing blood clots. Accordingly, identifying people at high risk of VTE – whether at the primary care level, or upon admission to hospital – can allow for early preventative advice and treatment where necessary. Where there is a lack of compliance with best practice guidelines on VTE risk assessment, research in New South Wales<sup>2</sup> has indicated that the incidence of hospital-associated VTE and timing of diagnosis can vary substantially between hospitals. Without shared European efforts on VTE risk assessment, there is a danger that some European citizens may be less likely to receive effective preventative measures for blood clots than others.

### **Raise awareness in the medical community about the importance of identifying and preventing VTE**

Although VTE guidelines exist, research<sup>3</sup> has shown that VTE risk assessments and appropriate prophylaxis measures are not always enacted, and that healthcare professionals have concerns about the clarity of such guidelines. Providing easy to use information at hand for risk situations

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<sup>1</sup> Cohen AT, Agnelli G, Anderson FA et al. “Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality.” *J Thromb Haemost*, 2007;98:756–764

<sup>2</sup> Stubbs J, Assareh H, Curnow J, Hitos K, Achat H. Variation in the incidence and timing of diagnosis of hospital-associated venous thromboembolism using linked administrative data. *Intern Med J*. 2018;48(9):1137-1141. doi:10.1111/imj.14019

<sup>3</sup> Abboud J, Rahman A, Shaikh N, Dempster M, Adair P. Physicians’ perceptions and preferences for implementing venous thromboembolism (VTE) clinical practice guidelines: a qualitative study using the Theoretical Domains Framework (TDF). *Archives of Public Health*. 2022;80(1). doi:10.1186/s13690-022-00820-7

and preventive strategies could go some way to alleviating these concerns, as well as concerns about whether to prescribe prophylaxis where bleeding risk is high.

### **Raise awareness of VTE among the general population**

The population should be enabled to recognise symptoms indicative of VTE, because blood clots can affect anyone at any time. Current public knowledge of thrombosis is low<sup>4</sup> – much lower than that of other conditions such as heart attack, stroke, hypertension, breast cancer, prostate cancer, and AIDS. 81%<sup>5</sup> of people would not know what a pulmonary embolism (PE) felt like if they experienced one, and around one-third of people with undiagnosed, untreated PE do not survive. When it is diagnosed and treated quickly, the number of deaths drops dramatically. As such, awareness-raising about the signs and symptoms of VTE is a life-saving measure.

### **Improve non-communicable disease prevention strategies, in turn improving VTE prevention**

EU Member States should take a holistic approach to preventive measures, encompassing lifestyle change, non-pharmaceutical therapies and medication. A cohort study showed that, among cancer patients readmitted to hospital within 90 days for VTE, higher number of comorbidities was a factor associated with readmission.<sup>6</sup> Additionally, higher scores on the Charlson Comorbidity Index<sup>7</sup> – a measure of severity and prognosis in patients with comorbid conditions – are associated with an increased risk of VTE. As such, improvements in overall prevention of non-communicable disease may also be associated with improvements in prevention of VTE.

### **Develop specific European guidelines for prevention and treatment of VTE**

Currently, European health care professionals use guidelines developed by American clinical societies to help them manage deep vein thrombosis (DVT)<sup>8</sup>, which is closely connected with pulmonary embolism (PE). In fact, PE arises from DVT. Due to differing epidemiological situations

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<sup>4</sup> Wendelboe A, McCumber M, Hylek E, Buller H, Weitz J, Raskob G. Global public awareness of venous thromboembolism. *Journal of Thrombosis and Haemostasis*. 2015;13(8):1365-1371. doi:10.1111/jth.13031

<sup>5</sup> Open Your Eyes to Pulmonary Embolism (PE), World Thrombosis Day. <https://www.worldthrombosisday.org/issue/vte/pe/>

<sup>6</sup> Mallick S, Aiken T, Varley P et al. Readmissions From Venous Thromboembolism After Complex Cancer Surgery. *JAMA Surg*. 2022;157(4):312. doi:10.1001/jamasurg.2021.7126

<sup>7</sup> Kalayci A, Gibson C, Hernandez A et al. Inverse relationship between body mass index and risk of venous thromboembolism among medically ill hospitalized patients: Observations from the APEX trial. *Thromb Res*. 2022;211:63-69. doi:10.1016/j.thromres.2022.01.016

<sup>8</sup> Schünemann H, Cushman M, Burnett A et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients. *Blood Adv*. 2018;2(22):3198-3225. doi:10.1182/bloodadvances.2018022954

in Europe, specific European guidelines<sup>9</sup> should be developed and implemented in a uniform manner across the European Union so that patient outcomes are not dependent on their Member State of residence.

### **Role of academia, industry, scientific societies & healthcare professionals: Conducting research**

Clinicians and researchers, such as those we represent, are well-aware of the gaps in the existing literature and well-placed to help close those knowledge gaps through research studies, potentially in cooperation with their colleagues from research societies in other Member States.

### **Role of healthcare systems: Developing data collection standards to support better information collection**

The level of detailed information collected on patient backgrounds and outcomes has a direct effect on the ability of researchers to draw links between health determinants and likelihood of thrombosis or responsiveness to treatment. In many cases better information can only be obtained when standards for data collection are changed.

## **2. Cardiovascular diseases**

### **Awareness of venous thromboembolism as a neglected cardiovascular disorder**

Thrombosis is the most common underlying pathology of the three major cardiovascular disorders: ischemic heart disease, stroke, and venous thromboembolism (VTE), and VTE is the third leading cardiovascular diagnosis after heart attack and stroke.<sup>10</sup> When accounting for indirect costs such as disability and productive life years lost, it has been estimated<sup>11</sup> that the total costs of VTE are as high as €13.2 billion each year.

Despite the severity and prevalence of VTE, public awareness remains low. A 2014 survey<sup>12</sup> showed that, while 88% of respondents were aware of heart attacks and 90% of high blood pressure, only 68% were aware of thrombosis and only 45% knew it was preventable. As such, there is much more work to be done on awareness-raising and prevention of thrombosis in the EU.

### **Prevention of venous thromboembolism**

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<sup>9</sup> Konstantinides S, Meyer G, Becattini C et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J*. 2019;41(4):543-603. doi:10.1093/eurheartj/ehz405

<sup>10</sup> ISTH Steering Committee for World Thrombosis Day. Thrombosis: a major contributor to the global disease burden. *J Thromb Haemost* 2014; 12: 1580–90.

<sup>11</sup> European Union-28: An annualised cost-of-illness model for venous thromboembolism. *J Thromb Haemost*, 2016 Apr;115(4):800-8.

<sup>12</sup> Wendelboe A, McCumber M, Hylek E, Buller H, Weitz J, Raskob G. Global public awareness of venous thromboembolism. *Journal of Thrombosis and Haemostasis*. 2015;13(8):1365-1371. doi:10.1111/jth.13031

Research suggests that many VTE cases are preventable, and that evidence-based prevention strategies can stop the development of clots in 'at-risk' individuals. Healthcare professionals should conduct VTE risk assessments to determine who is at risk – using tools or questionnaires to collect information about patients' ages, medical histories, medications and specific lifestyle factors<sup>13</sup>.

People identified as being at risk of developing blood clots in the legs or lungs should then be given appropriate preventative measures, which can involve anti-clotting medicines and mechanical devices. Hospital patients may also be instructed to move around or do exercises as soon and as often as possible. Up to 60% of VTE cases occur during or after hospitalisation, making it a leading preventable cause of hospital death<sup>14</sup>.

### **Inclusion of VTE in patient safety action plans**

Despite the World Health Organisation (WHO) Global Patient Safety Action Plan's<sup>15</sup> recommendation that healthcare facilities should implement clinical risk management activities to address venous thromboembolism, many health systems are yet to adopt systematic VTE risk assessment protocols that can have a significant impact on improving patient safety.

Governments should therefore include hospital-associated VTE in their patient safety improvement programmes, clinical risk management activities, risk assessment tools, and clinical guidance. VTE prevention should also be considered a priority in all Member State activities to promote patient safety.

### **EU plan for VTE/coordination of national plans on VTE**

Access to VTE risk assessment and prophylaxis, as well as medical outcomes, varies by country and region<sup>16</sup>. A variety of factors could explain<sup>17</sup> these disparities, including national guidelines, VTE awareness, health care standards, VTE prevalence differences, and

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<sup>13</sup> Open Your Eyes to Thrombosis, World Thrombosis Day.

<https://www.worldthrombosisday.org/issue/thrombosis/>

<sup>14</sup> Open Your Eyes to Venous Thromboembolism (VTE), World Thrombosis Day.

<https://www.worldthrombosisday.org/issue/vte/>

<sup>15</sup> Global patient safety action plan 2021–2030: towards eliminating avoidable harm in health care. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO.

<sup>16</sup> Global Solutions to Minimize the Impact of Social Determinants of Health in the Management of Extended Anticoagulation? - Stefano Barco, MD, PhD, FESC

<https://www.mededonthego.com/Video/program/834/module/6382>

<sup>17</sup> Forgo G, Micieli E, Ageno W et al. An update on the global use of risk assessment models and thromboprophylaxis in hospitalized patients with medical illnesses from the World Thrombosis Day steering committee: Systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis*. 2021;20(2):409-421. doi:10.1111/jth.15607

reimbursement systems. Data from 123 countries<sup>18</sup> show that reported PE-related death figures varied substantially between regions and states – likely due to different ways of reporting deaths and diagnosing PE. As such, EU Member States should develop plans to monitor and report VTE-related disability and death in a consistent manner.

Additionally, PE-related mortality is likely to increase as a result of COVID-19 due to its potential blood clot-related complications. As such, it is important for Member States to have plans in place to address the risk of a reverse in the decline of PE-related mortality rates in the European Region. Although VTE risk assessment<sup>19</sup> is often used or mandated in European countries, very few (Belgium, North Macedonia, United Kingdom) have national guidelines in place recommending the use of VTE risk assessment.

### **Raising awareness of atrial fibrillation and the necessity of screening for it**

Atrial fibrillation (AFib) is a common type of irregular heartbeat, which can cause slowed blood flow and therefore the formation of a blood clot. AFib-caused blood clots (arterial thromboembolism) develop in the arteries and can break free and travel to the brain – potentially resulting in a stroke.<sup>20</sup> Diabetes is one of the risk factors of AFib, but only 20% of the respondents to a global survey<sup>21</sup> were aware that this is the case. Additionally, only 36%<sup>22</sup> of the respondents to a global survey knew that AFib could lead to stroke.

AFib can be present without signs or symptoms<sup>23</sup>, and so proactive screening is required to detect and treat it. As such, it is important that people living with diabetes know that they can and should ask their healthcare professional to have their pulse checked for an irregular heartbeat in order to reduce their risk of stroke.

Effective policies, best practices, promising approaches or innovative actions

### **Preventative anticoagulation measures in hospitals & Systematic VTE risk assessment**

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<sup>18</sup> Barco S, Valerio L, Gallo A et al. Global reporting of pulmonary embolism-related deaths in the World Health Organization mortality database: Vital registration data from 123 countries. *Res Pract Thromb Haemost.* 2021;5(5). doi:10.1002/rth2.12520

<sup>19</sup> Wendelboe A, Langenfeld H, Ageno W et al. Current practices of standardized risk assessment for venous thromboembolism: Results from a global survey from the World Thrombosis Day steering committee. *Journal of Thrombosis and Haemostasis.* 2021;20(2):532-535. doi:10.1111/jth.15608

<sup>20</sup> Open Your Eyes to Atrial Fibrillation, World Thrombosis Day. <https://www.worldthrombosisday.org/issue/AFib/>

<sup>21</sup> Wendelboe AM, Raskob GE, Angchaisuksiri P, Blanco AN, Büller H, Ddungu H, Dvorak JD, Hunt BJ, Hylek EM, Kakkar A, Konstantinides SV, McCumber M, McLintock C, Urano T, Weitz JI. Global public awareness about atrial fibrillation. *Res Pract Thromb Haemost.* 2017 Oct 25;2(1):49-57. doi: 10.1002/rth2.12051. PMID: 30046706; PMCID: PMC6055485.

<sup>22</sup> Ibid.

<sup>23</sup> Patient Education Handouts – Atrial Fibrillation, Centers for Disease Control and Prevention. [https://www.cdc.gov/heartdisease/atrial\\_fibrillation.htm](https://www.cdc.gov/heartdisease/atrial_fibrillation.htm)

Up to 60%<sup>24</sup> of all VTE cases happen during or within 90 days of hospitalisation, making it a leading preventable cause of hospital-related deaths<sup>25</sup>. However, only 66.8%<sup>26</sup> of medically ill patients with an indication for thromboprophylaxis receive adequate thromboprophylaxis in Europe.

In the UK, risk assessment for VTE has been included as a National Quality Requirement<sup>27</sup> – requiring acute providers to carry out VTE risk assessments<sup>28</sup> for at least 95% of inpatients each month. This target has been exceeded since 2013/14 Q1, and deaths from VTE within 90 days of discharge per 100,000 adult hospital admissions have fallen from 72 in 2007/08 to 60 in 2019/20<sup>29</sup>. A retrospective database study showed a reduction of 9% in deaths due to VTE as a result of these mandated risk assessments<sup>30</sup>.

Additionally, UK National Institute for Health and Care Excellence guidance<sup>31</sup> requires discussion about VTE prevention and prophylaxis with all patients admitted to hospital who are at increased risk of VTE. This could also help reduce costs to Member State healthcare systems, as the overall annual cost of VTE<sup>32</sup> is estimated to be between 1.5 and 2.2 billion EUR for the EU-27 and the UK.

In view of its success, we recommend<sup>33</sup> mandated VTE risk assessment for all hospital patients in Europe. We would therefore propose that Member State authorities replicate the NHS England risk assessment tool in all hospitals throughout each Member State.

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<sup>24</sup> Jha AK, Larizgoitia I, Audera-Lopez C, Prasopa-Plaisier N, Waters H, Bates DW. The global burden of unsafe medical care: analytic modeling of observational studies. *BMJ Qual Saf* 2013; 22;809-15. Retrieved from: <http://qualitysafety.bmj.com/content/22/10/809.full.pdf+html>

<sup>25</sup> Open Your Eyes to Hospital-Associated VTE, World Thrombosis Day <https://www.worldthrombosisday.org/issue/hospital-associated-vte/>

<sup>26</sup> Forgo G, Micieli E, Ageno W et al. An update on the global use of risk assessment models and thromboprophylaxis in hospitalized patients with medical illnesses from the World Thrombosis Day steering committee: Systematic review and meta-analysis. *Journal of Thrombosis and Haemostasis*. 2021;20(2):409-421. doi:10.1111/jth.15607

<sup>27</sup> Venous thromboembolism. The Nuffield Trust. <https://www.nuffieldtrust.org.uk/resource/venous-thromboembolism#background>.

<sup>28</sup> Department of Health VTE risk assessment tool, National Institute for Health and Care Excellence (NICE), UK <https://www.nice.org.uk/guidance/ng89/resources/department-of-health-vte-risk-assessment-tool-pdf-4787149213>

<sup>29</sup> Ibid.

<sup>30</sup> Catterick D, Hunt BJ. Impact of the national venous thromboembolism risk assessment tool in secondary care in England: retrospective population-based database study. *Blood Coagul Fibrinolysis*. 2014 Sep;25(6):571-6. doi: 10.1097/MBC.000000000000100. PMID: 24686103; PMCID: PMC4162339.

<sup>31</sup> Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism: NICE guideline [NG89] <https://www.nice.org.uk/guidance/ng89>

<sup>32</sup> Barco S, Woerschling A, Spyropoulos A, Piovella F, Mahan C. European Union-28: An annualised cost-of-illness model for venous thromboembolism. *Thromb Haemost*. 2016;115(04):800-808. doi:10.1160/th15-08-0670

<sup>33</sup> ISTH Response to the Web-based consultation of the WHO Independent High-Level Commission on NCDs

## **Digital tools for treatment decision making**

Patients with VTE and their doctors make shared decisions about whether to discontinue anticoagulation measures for VTE after three months, and patient education is vital to assist them in decision making. A Dutch study<sup>34</sup> showed that, alongside the hospital-specific standard of care, an app providing patients with daily videos on VTE and anticoagulation can increase patient satisfaction with information provision and reduce uncertainty in treatment decision making. As such, apps could have an important role in assisting patients to make informed decisions, together with healthcare professionals, regarding their treatment process for VTE and other NCDs.

## **Strengthen research on anticoagulation in patients with AFib**

Easy to use, effective and safe anticoagulation - and thus prevention of stroke - is the most important treatment goal in AFib. There are several groups that cannot be treated with anticoagulation medication despite a very high risk of stroke – e.g., those with end stage renal disease<sup>35</sup>. In addition, every medication that is currently used for stroke prevention comes with an increased risk of bleeding. As such, it is imperative to strengthen research with the goal of developing treatments for AFib patients that adequately address the risks<sup>36</sup> of both stroke and bleeding.

## **Role of healthcare professionals, patient organisations: Awareness raising around VTE**

Healthcare professionals and patient organisations have a vital role in ensuring people are aware of the signs and symptoms of thrombosis – and that they have the right<sup>37</sup> to ask their healthcare providers to assess their risk of VTE. This is particularly vital upon admission to hospital.

## **Role of patient organisations: Promoting information among their members about the need for assessment, diagnosis and treatment of AFib**

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<https://web.archive.org/web/20220120202504/https://www.who.int/ncds/governance/high-level-commission/International-Society-for-Thrombosis-and-Haemostasis.pdf>

<sup>34</sup> de Winter MA, Timmers T, Hovens MMC, Iglesias Del Sol A, Mairuhu ATA, Kaasjager HAH, Nijkeuter M. Effect of an interactive, educational app about venous thromboembolism and anticoagulation on patient satisfaction: A randomized controlled trial. *Thromb Res.* 2022 Jan;209:86-93. doi: 10.1016/j.thromres.2021.11.028. Epub 2021 Dec 7. PMID: 34896916.

<sup>35</sup> Königsbrügge O, Ay C. Atrial fibrillation in patients with end-stage renal disease on hemodialysis: Magnitude of the problem and new approach to oral anticoagulation. *Res Pract Thromb Haemost.* 2019;3(4):578-588. Published 2019 Aug 18. doi:10.1002/rth2.12250

<sup>36</sup> Lip G, Keshishian A, Li X et al. Effectiveness and Safety of Oral Anticoagulants Among Nonvalvular Atrial Fibrillation Patients. *Stroke.* 2018;49(12):2933-2944. doi:10.1161/strokeaha.118.020232

<sup>37</sup> Patients' Bill of Rights, European Thrombosis and Haemostasis Alliance <https://etha.eu/wp-content/uploads/2018/03/Patients-Bill-of-Rights.pdf>

Early identification and management are essential, given the tendency of AFib to present without signs or symptoms<sup>38</sup>. Patients, particularly those with risk factors for AFib, should ask their doctors to check their pulse for an irregular heartbeat, and patient organisations have a role to play in spreading this potentially lifesaving information within their communities.

### **Healthcare professionals: Proactive efforts to systematically evaluate patients for AFib risk and start treatment where necessary**

Healthcare professionals should take the initiative to evaluate their patients for AFib risk. The rate of stroke in AFib is dependent on the presence of comorbid conditions and the use of antithrombotic therapy, and so it is important to ensure people with AFib are diagnosed and treated to reduce their risk of stroke.

## **3. Diabetes**

### **Raising awareness among people living with diabetes that it is a risk factor for VTE**

Metabolic syndrome (a combination of diabetes, high blood pressure, and obesity<sup>39</sup>) is a frequent risk factor for both first incidence of VTE<sup>40</sup> and its reoccurrence<sup>41 42</sup>. As such, people with diabetes should be informed about their increased risk of developing VTE, what its signs and symptoms<sup>43</sup> are, and that they have the right<sup>44</sup> to ask their healthcare professionals to conduct a VTE risk assessment.

### **Evaluation for AFib as part of diabetes management**

Many people who have AFib don't know they have it and don't have any symptoms. Global public awareness of AFib is low - 48%<sup>45</sup> - and so people are unlikely to present specifically to seek treatment for it. However, a cardiac exam or electrocardiogram as part of diabetes follow-

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<sup>38</sup> Open Your Eyes to Atrial Fibrillation, World Thrombosis Day. <https://www.worldthrombosisday.org/issue/AFib/>

<sup>39</sup> Metabolic syndrome. National Health Service (UK). <https://www.nhs.uk/conditions/metabolic-syndrome/>.

<sup>40</sup> Ageno W, Dentali F, Grandi A. New evidence on the potential role of the metabolic syndrome as a risk factor for venous thromboembolism. *Journal of Thrombosis and Haemostasis*. 2009;7(5):736-738. doi:10.1111/j.1538-7836.2009.03327.x

<sup>41</sup> Ay C, Tengler T, Vormittag R et al. Venous thromboembolism a manifestation of the metabolic syndrome. *Haematologica*. 2007;92(3):374-380. doi:10.3324/haematol.10828

<sup>42</sup> Stewart L, Kline J. Metabolic syndrome increases risk of venous thromboembolism recurrence after acute deep vein thrombosis. *Blood Adv*. 2020;4(1):127-135. doi:10.1182/bloodadvances.2019000561

<sup>43</sup> Open Your Eyes to Venous Thromboembolism (VTE), World Thrombosis Day. <https://www.worldthrombosisday.org/issue/vte/>

<sup>44</sup> Patients' Bill of Rights, European Thrombosis and Haemostasis Alliance <https://etha.eu/wp-content/uploads/2018/03/Patients-Bill-of-Rights.pdf>

<sup>45</sup> Wendelboe AM, Raskob GE, Angchaisuksiri P, Blanco AN, Büller H, Ddungu H, Dvorak JD, Hunt BJ, Hylek EM, Kakkar A, Konstantinides SV, McCumber M, McLintock C, Urano T, Weitz JI. Global public awareness about atrial fibrillation. *Res Pract Thromb Haemost*. 2017 Oct 25;2(1):49-57. doi: 10.1002/rth2.12051. PMID: 30046706; PMCID: PMC6055485

up could help detect or confirm AFib. Treating it is essential in order to prevent blood clots from forming and reduce stroke risk, as is regular follow-up care. For people living with diabetes and AFib, this could most efficiently be done as part of their usual medical appointments.

### **Diagnosis of Diabetes**

Early diagnosis of diabetes permits people living with the condition to proactively address potential comorbidities – including venous thromboembolism – to prevent the development of additional health conditions. In the case of VTE, the earlier someone is diagnosed with diabetes, the earlier they will be aware of the need to undergo a VTE risk assessment<sup>46</sup> because of their increased risk status.

### **Diagnosis of metabolic syndrome**

Improved diagnosis of metabolic syndrome could help to reduce cardiovascular and other complications of metabolic syndrome. In turn, this would help to address costs to the health care system<sup>47</sup> and to the individual<sup>48</sup>. Earlier diagnosis results in earlier intervention, which may be able to prevent the development of metabolic syndrome or reduce its impact, which would in turn reduce the risk of VTE (re)occurrence<sup>49</sup>. This would also therefore reduce future health costs.

## **4. Chronic respiratory diseases**

### **Prevention and management of venous thromboembolism among patients with COVID-19 pneumonia**

Emerging research<sup>50</sup> indicates that people with COVID-19, particularly those who are hospitalised with moderate and severe COVID-19 pneumonia, have a high incidence of venous thromboembolism (VTE). COVID-19 pneumonia is also associated with an increased tendency for blood to clot (hypercoagulability) and with the development of micro-clots in the lungs. Recent

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<sup>46</sup> Open Your Eyes to Venous Thromboembolism (VTE), World Thrombosis Day.  
<https://www.worldthrombosisday.org/issue/vte>

<sup>47</sup> Boudreau D, Malone D, Raebel M et al. Health Care Utilization and Costs by Metabolic Syndrome Risk Factors. *Metab Syndr Relat Disord.* 2009;7(4):305-314. doi:10.1089/met.2008.0070

<sup>48</sup> Burton W, Chen C, Li X, Schultz A, Abrahamsson H. The Association of Self-Reported Employee Physical Activity With Metabolic Syndrome, Health Care Costs, Absenteeism, and Presenteeism. *Journal of Occupational & Environmental Medicine.* 2014;56(9):919-926. doi:10.1097/jom.0000000000000257

<sup>49</sup> Stewart L, Kline J. Metabolic syndrome increases risk of venous thromboembolism recurrence after acute deep vein thrombosis. *Blood Adv.* 2020;4(1):127-135. doi:10.1182/bloodadvances.2019000561

<sup>50</sup> Masten A. A Systematic Approach for Managing Venous Thromboembolism in Patients with COVID-19. International Society for Thrombosis and Haemostasis. <https://www.isth.org/news/517212/A-Systematic-Approach-for-Managing-Venous-Thromboembolism-in-Patients-with-COVID-19.htm>. Published 2020.

findings published in the British Medical Journal<sup>51</sup> also suggest that catching COVID-19 is associated with a fivefold increase in the risk of deep vein thrombosis and a 33-fold increase in risk of pulmonary embolism in the 30 days after becoming infected – with increased risk persisting for up to six months. As such, it is important to ensure a systematic approach to preventing, diagnosing and treating VTE among patients with COVID-19. WHO guidelines<sup>52</sup> on the clinical management of COVID-19 patients advocate for consistent monitoring for symptoms of thromboembolism, setting out substantial guidance for thromboprophylaxis if thromboembolism is suspected.

Furthermore, as we learn more about COVID-19 and VTE, such information needs to be included in health worker education on COVID-19. Collection of data on COVID-19 and VTE is also vital for research purposes and informing updated evidence-based clinical recommendations.

### **Improve awareness of prevention and management of VTE among patients with chronic obstructive pulmonary disease**

Patients with COPD with VTE have a fatality risk twice<sup>53</sup> as high as those with normal airflow, and COPD is an independent risk factor of PE. Acute exacerbation of COPD (AECOPD) is also associated<sup>54</sup> with a prethrombotic state. It is difficult<sup>55</sup> to differentiate between PE and AECOPD because of the similarity of clinical symptoms, and the failure of clinicians to rapidly begin anticoagulation therapy worsens the prognosis. The public have little awareness<sup>56</sup> about the signs, symptoms and risk factors of VTE, and improving such understanding would facilitate VTE risk assessment and prevention among people at high risk – including those with (AE)COPD. Such public understanding is vital for preventing VTE and reducing its prevalence, as patients with COPD that have had anticoagulant treatment do not have significantly different risk levels of recurrent VTE than patients without COPD<sup>57</sup>.

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<sup>51</sup> Geddes L. Covid linked to 33-fold increase in risk of potentially fatal blood clot. The Guardian. [https://www.theguardian.com/world/2022/apr/06/covid-linked-33-fold-increase-risk-pulmonary-embolism-dvt?CMP=fb\\_gu&utm\\_medium=Social&utm\\_source=Facebook&fbclid=IwAR0TtG9Q3FJNRIbz0yBftMpdtTa9ykMzPilaBbNLKVgFj0qTYhrnPZC99g#Echobox=1649315060](https://www.theguardian.com/world/2022/apr/06/covid-linked-33-fold-increase-risk-pulmonary-embolism-dvt?CMP=fb_gu&utm_medium=Social&utm_source=Facebook&fbclid=IwAR0TtG9Q3FJNRIbz0yBftMpdtTa9ykMzPilaBbNLKVgFj0qTYhrnPZC99g#Echobox=1649315060). Published 2022.

<sup>52</sup> Living guidance for clinical management of COVID-19. World Health Organization. <https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2>

<sup>53</sup> Han W, Wang M, Xie Y, Ruan H, Zhao H, Li J. Prevalence of Pulmonary Embolism and Deep Venous Thromboembolism in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *Front Cardiovasc Med.* 2022;9. doi:10.3389/fcvm.2022.732855–90.

<sup>54</sup> Ibid.

<sup>55</sup> Ibid.

<sup>56</sup> Wendelboe A, McCumber M, Hylek E, Buller H, Weitz J, Raskob G. Global public awareness of venous thromboembolism. *Journal of Thrombosis and Haemostasis.* 2015;13(8):1365-1371. doi:10.1111/jth.13031

<sup>57</sup> Han W, Wang M, Xie Y, Ruan H, Zhao H, Li J. Prevalence of Pulmonary Embolism and Deep Venous Thromboembolism in Patients With Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis. *Front Cardiovasc Med.* 2022;9. doi:10.3389/fcvm.2022.732855–90.

## **Signpost to accredited evidence based clinical information portals on VTE related COVID-19 clinical guidance**

Front-line clinicians caring for patients with COVID-19 should have access to emerging clinical guidance to ensure quality care. The ISTH COVID-19 Resource Page<sup>58</sup> collates information about VTE in COVID-19 management.

## **Role of healthcare professionals: Proactive efforts to systematically evaluate COVID-19 patients for VTE risk and start treatment where necessary**

Healthcare professionals should take the initiative to evaluate COVID-19 patients for VTE risk. The WHO recommends routine monitoring and (where necessary) treatment for VTE as part its guidance<sup>59</sup> on the clinical management of COVID-19.

## **5. Mental health and neurological disorders**

### **AFib awareness and thromboembolic stroke**

Every year, people with AFib are estimated to account for 15%<sup>60</sup> of the 15 million strokes that occur worldwide. Many people who have AFib don't know they have it and don't have any symptoms. Global public awareness of AF is low - 48%<sup>61</sup> - and so people are unlikely to present specifically to seek treatment for it. However, treating it is essential in order to prevent blood clots from forming and reduce stroke risk, as is regular follow-up care.

### **Stroke prevention methods for people with AFib**

AFib-related stroke can be particularly dangerous – patients are twice as likely to be bedridden and more likely to die than patients with non-AFib related stroke<sup>62</sup>. Early identification and management are essential, given the tendency of AFib to present without signs or symptoms. Patients, particularly those with risk factors for AFib, should ask to have their pulses checked, and healthcare professionals should take the initiative to evaluate their patients for AFib risk. The rate of stroke in AFib is dependent<sup>63</sup> on the presence of comorbid conditions and the use of

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<sup>58</sup> International Society of Thrombosis and Haemostasis COVID-19 Resource Page:

[https://academy.isth.org/isth/#!\\*menu=8\\*browseby=2\\*sortby=1\\*label=19794](https://academy.isth.org/isth/#!*menu=8*browseby=2*sortby=1*label=19794)

<sup>59</sup> Living guidance for clinical management of COVID-19. World Health Organization.

<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-2>

<sup>60</sup> Know Afib, European Thrombosis and Haemostasis Alliance. <https://etha.eu/wp-content/uploads/2018/03/Know-AFib-Infographic.pdf>

<sup>61</sup> Wendelboe AM, Raskob GE, Angchaisuksiri P, Blanco AN, Büller H, Ddungu H, Dvorak JD, Hunt BJ, Hylek EM, Kakkar A, Konstantinides SV, McCumber M, McLintock C, Urano T, Weitz JI. Global public awareness about atrial fibrillation. *Res Pract Thromb Haemost.* 2017 Oct 25;2(1):49-57. doi: 10.1002/rth2.12051. PMID: 30046706; PMCID: PMC6055485.

<sup>62</sup> Open Your Eyes to Atrial Fibrillation, World Thrombosis Day. <https://www.worldthrombosisday.org/issue/AFib/>

<sup>63</sup> Gage B, van Walraven C, Pearce L et al. Selecting Patients With Atrial Fibrillation for Anticoagulation. *Circulation.* 2004;110(16):2287-2292. doi:10.1161/01.cir.0000145172.55640.93

antithrombotic therapy, and so it is important to ensure people with AFib are diagnosed and treated to reduce their risk of stroke.

### **Monitoring of patients at follow up appointments for decline in quality of life, to facilitate early intervention**

Although scarcity of evidence makes it difficult to generalise research findings, estimates from a German study<sup>64</sup> into quality of life 3 and 12 months following acute PE that 7.7% of patients who experienced a pulmonary embolism experience disease-specific quality of life decreases could suggest a need to identify patients experiencing difficulties at follow-up treatment appointments. This study also found that, although quality of life increases over time, women, older people, and people with a history of VTE may experience a more persistent decreased quality of life.

Experiencing VTE is a difficult, worrying time in a patient's life, and they may require social/emotional support and psychotherapy<sup>65</sup>. Including quality of life in follow-up care discussions could help identify patients who could benefit from this kind of additional support.

Effective policies, best practices, promising approaches or innovative actions

### **Early diagnosis of AFib**

AFib is a very important risk factor for ischemic stroke<sup>66</sup>. Anticoagulation reduces the risk of stroke dramatically and is, at present, the most important therapeutic intervention in patients with AFib. The rate of stroke in AFib depends on the presence of comorbid conditions and the use of antithrombotic therapy<sup>67</sup>, and, as such, patients with AFib that have a certain risk level of stroke require anticoagulation treatment. AFib can be present without any signs and symptoms, and, therefore, both patients and health care professionals must be proactive<sup>68</sup> about requesting and conducting (respectively) evaluations of AFib risk.

### **Improve risk factor definitions for stroke in AFib**

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<sup>64</sup> Valerio L, Barco S, Jankowski M, Rosenkranz S, Lankeit M, Held M, Gerhardt F, Bruch L, Ewert R, Faehling M, Freise J, Ghofrani HA, Grünig E, Halank M, Hoepfer MM, Klok FA, Leuchte HH, Mayer E, Meyer FJ, Neurohr C, Opitz C, Schmidt KH, Seyfarth HJ, Trudzinski F, Wachter R, Wilkens H, Wild PS, Konstantinides SV. Quality of Life 3 and 12 Months Following Acute Pulmonary Embolism: Analysis From a Prospective Multicenter Cohort Study. *Chest*. 2021 Jun;159(6):2428-2438. doi: 10.1016/j.chest.2021.01.071. Epub 2021 Feb 3. PMID: 33548221.

<sup>65</sup> Global Solutions to Minimize the Impact of Social Determinants of Health in the Management of Extended Anticoagulation? - Stefano Barco, MD, PhD, FESC  
<https://www.mededonthegeo.com/Video/program/834/module/6382>

<sup>66</sup> Open Your Eyes to Atrial Fibrillation, World Thrombosis Day. <https://www.worldthrombosisday.org/issue/AFib/>

<sup>67</sup> Gage B, van Walraven C, Pearce L et al. Selecting Patients With Atrial Fibrillation for Anticoagulation. *Circulation*. 2004;110(16):2287-2292. doi:10.1161/01.cir.0000145172.55640.93

<sup>68</sup> Know Afib, European Thrombosis and Haemostasis Alliance. <https://etha.eu/wp-content/uploads/2018/03/Know-AFib-Infographic.pdf>

Although anticoagulation treatment can be essential in preventing strokes among people with AFib, patients require accurate, reliable assessments<sup>69</sup> balancing the risks of bleeding against the benefits of anticoagulation to permit informed decision-making about when to prescribe antithrombotic treatments. The three main guidelines<sup>70</sup> on AFib management are in broad agreement, although contain some differences in the detail of what constitutes a high-risk patient in need of anticoagulation treatment. Therefore, it is necessary to improve risk-factor definitions in a manner that supports consistent assessments and ensures patients at very low risk of stroke are not exposed to potentially unnecessary heightened risk of bleeding.

### **Define patients at high risk of bleeding and assess risk of stroke after bleeding**

Patients at high risk of bleeding (particularly in the brain) during anticoagulation treatment must be carefully assessed in relation to stroke prevention. People with AFib who have survived such bleeds on the brain are at high risk of subsequent stroke, and the current medications available to treat them are not optimal<sup>71</sup>. Further research and careful assessment are necessary when considering how to proceed in preventing stroke and other vascular events among people with AFib who have experienced anticoagulation-associated brain bleeds, in order to identify which subgroups will benefit and which may be harmed by restarting anticoagulation treatment following bleeding incidents.

### **Role of patient organisations: Promoting information among their members about the need for assessment, diagnosis and treatment of AFib**

Early identification and management are essential, given the tendency of AFib to present without signs or symptoms. Patients, particularly those with risk factors for AFib, should ask their doctors to check their pulse<sup>72</sup> for an irregular heartbeat, and patient organisations have a role to play in spreading this potentially lifesaving information within their communities.

### **Role of healthcare professionals: Proactive efforts to systematically evaluate patients for AFib risk and start treatment where necessary**

Healthcare professionals should take the initiative<sup>73</sup> to evaluate their patients for AFib risk. The rate of stroke in AFib is dependent on the presence of comorbid conditions and the use of

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<sup>69</sup> Gage B, van Walraven C, Pearce L et al. Selecting Patients With Atrial Fibrillation for Anticoagulation. *Circulation*. 2004;110(16):2287-2292. doi:10.1161/01.cir.0000145172.55640.93

<sup>70</sup> Wolfes J, Ellermann C, Frommeyer G, Eckardt L. Evidence-based treatment of atrial fibrillation around the globe: comparison of the latest ESC, AHA/ACC/HRS, and CCS guidelines on the management of atrial fibrillation. *Rev Cardiovasc Med*. 2022;23(2):056. doi:10.31083/j.rcm2302056

<sup>71</sup> Schreuder F, van Nieuwenhuizen K, Hofmeijer J et al. Apixaban versus no anticoagulation after anticoagulation-associated intracerebral haemorrhage in patients with atrial fibrillation in the Netherlands (APACHE-AF): a randomised, open-label, phase 2 trial. *The Lancet Neurology*. 2021;20(11):907-916. doi:10.1016/s1474-4422(21)00298-2

<sup>72</sup> Open Your Eyes to Atrial Fibrillation, World Thrombosis Day. <https://www.worldthrombosisday.org/issue/AFib/>

<sup>73</sup> Ibid.

antithrombotic therapy<sup>74</sup>, and so it is important to ensure people with AFib are diagnosed and treated to reduce their risk of stroke.

**Role of healthcare professionals: Conducting quality of life assessment and monitoring mental health after VTE**

Healthcare professionals who see patients following incidents of deep vein thrombosis and/or pulmonary embolism are well-placed to check on mental as well as physical health. In the course of appointments focused on initiating or adjusting anticoagulation measures, they should also speak with their patients about their wellbeing and quality of life.

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<sup>74</sup> Gage B, van Walraven C, Pearce L et al. Selecting Patients With Atrial Fibrillation for Anticoagulation. *Circulation*. 2004;110(16):2287-2292. doi:10.1161/01.cir.0000145172.55640.93

**About ETHA:**

*The European Thrombosis and Haemostasis Alliance (ETHA) is made up of eminent clinicians and researchers from European national and international societies representing those working in the field of thrombotic and bleeding disorders. We have come together to give the European thrombosis and haemostasis community an allied voice and provide input to EU health and patient safety strategies; make recommendations on EU research programme funding and encourage sharing and adoption of best practices in the treatment and prevention of thrombotic and bleeding disorders across Member States. Learn more at [etha.eu](http://etha.eu).*

**About Thrombosis:**

*Thrombosis, also known as blood clots, is the formation of potentially deadly blood clots in an artery (arterial thrombosis) or vein (venous thrombosis). It is the underlying cause of heart attack, thromboembolic stroke, and venous thromboembolism (VTE), the top three cardiovascular killers.*

**About Atrial Fibrillation:**

*Atrial fibrillation (AFib) is a common type of irregular heartbeat in which blood flow slows or pools and can cause the formation of a blood clot. People with AFib are at higher risk of stroke, and AFib-related stroke can be particularly dangerous in terms of death and disability.*

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