Review

Fibrinaloid Microclots and Atrial Fibrillation

Douglas B Kell *, Gregory YH Lip, Etheresia Pretorius *

Posted Date: 29 January 2024

doi: 10.20944/preprints202401.1945.v1

Keywords: Atrial fibrillation; fibrinaloid; microclots; long Covid; inflammation; microthromboses

Review

Fibrinaloid Microclots and Atrial Fibrillation

Douglas B. Kell [1,2,3,*], Gregory Y. H. Lip [4] and Etheresia Pretorius [1,3,*]

[1] Department of Biochemistry, Cell and Systems Biology, Institute of Systems, Molecular and Integrative Biology, Faculty of Health and Life Sciences, University of Liverpool, Crown St, Liverpool L69 7ZB, UK. ORCID: 0000-0001-5838-7963

[2] The Novo Nordisk Foundation Center for Biosustainability, Building 220, Søltofts Plads, Technical University of Denmark, 2800 Kongens Lyngby, Denmark

[3] Department of Physiological Sciences, Faculty of Science, Stellenbosch University, Stellenbosch, Private Bag X1 Matieland, 7602, South Africa

[4] Liverpool Centre for Cardiovascular Science at University of Liverpool, Liverpool John Moores University and Liverpool Heart & Chest Hospital, Liverpool, United Kingdom; and Danish Center for Health Services Research, Department of Clinical Medicine, Aalborg University, Aalborg, Denmark. ORCID: 0000-0002-7566-1626.

* Correspondence: dbk@liv.ac.uk; resiap@sun.ac.za

Abstract: Atrial fibrillation (AF) is a comorbidity of a variety of other chronic, inflammatory diseases for which fibrinaloid microclots are a known accompaniment (and in some cases a cause, with a mechanistic basis). Clots are, of course, a well-known *consequence* of atrial fibrillation. We here ask the question as to whether the fibrinaloid microclots seen in plasma or serum may in fact also be a cause of (or contributor to) the development of AF. We consider known 'risk factors' for AF, and in particular exogenous stimuli such as infection and air pollution by particulates, both of which are known to cause AF. The external accompaniments of both bacterial (lipopolysaccharide and lipoteichoic acids) and viral (SARS-CoV-2 spike protein) infections are known to stimulate fibrinaloid microclots when added *in vitro*, and fibrinaloid microclots are cytotoxic by inducing hypoxia/reperfusion and other means. Strokes and thromboembolisms are also common consequences of AF. Consequently, taking a systems approach, we suggest that it is likely that microclots may well have an aetiological role in the development of AF. This has significant mechanistic and therapeutic implications.

Keywords: Atrial fibrillation; fibrinaloid; microclots; long Covid; inflammation; microthromboses

Introduction

Atrial fibrillation (AF) is at once the commonest heart arrhythmia (Chugh et al. 2014; Corica et al. 2023a; Zulkifly et al. 2018) and a chief cause of death therefrom (Benjamin et al. 1998; Staerk et al. 2017). Its global incidence amounts to millions of individuals (Chugh et al. 2014), possibly 1% of populations, and even 20 years ago its cost represented some 1% of the NHS budget, with all these numbers on a rising trend (Camacho and Lip 2023; Dai et al. 2021; Okafor et al. 2023; Sun et al. 2023), albeit with large regional differences of incidence and/or reporting (e.g. South Asia is said to be 12x lower than North America (Joseph et al. 2021)).

AF symptoms (virtually by definition) involve (Hindricks et al. 2021) "A supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction. Electrocardiographic characteristics of AF include:

- Irregular R-R intervals (when atrioventricular conduction is not impaired),
- Absence of distinct repeating P waves, and
- Irregular atrial activations." (Hindricks et al. 2021)

Within this there are, of course, AF subclasses with different levels of severity, especially as regards the various sequelae. AF is also associated with risk factors that rarely occur in isolation, and patients with AF are commonly associated with multimorbidity, polypharmacy and frailty, with

 doi:10.20944/preprints202401.1945.v1

major implications for treatment and outcomes (Lip et al. 2022a; Romiti et al. 2022b; Treewaree et al. 2024; Zheng et al. 2023).

The chief fear is that AF leads to an increased likelihood of a clot forming or residing within the atrial chamber, from which it can then escape, and it is well recognised (e.g. (Tsao et al. 2023)) that those with AF are associated with mortality and morbidity from strokes (Alshehri 2019; Lip et al. 2022b; Marini et al. 2005; Ozdemir et al. 2023; Qureshi et al. 2022; Schnabel et al. 2019; Son et al. 2017; Wolf et al. 1991), coronary heart disease (Emdin et al. 2016; Kannel et al. 1983; Odutayo et al. 2016) (including myocardial infarction (Ruddox et al. 2017)) or both (Lip et al. 2023), and vice versa due to the build-up of blood-flow-occluding macro-clots in the relevant tissues. Note, however, that because AF is often asymptomatic, and until recently was rarely screened for, many/most of these studies are actually post hoc (Kalarus et al. 2023; Sposato et al. 2015; Thakur et al. 2023; Yang et al. 2019), i.e. they study the incidence of AF in people who have had cardiovascular events rather than the other way round (i.e., for our present purposes, the incidence of heart attacks and strokes in those with known, pre-existing AF).

Our purpose here is to recognise that a certain kind of 'fibrinaloid' microclot that we discovered (Pretorius et al. 2016c), despite being in many ways a 'conventional' blood clot formed by the polymerisation of fibrinogen to fibrin (albeit containing other proteins (Kruger et al. 2022; Pretorius et al. 2021)), is by virtue of its amyloid nature (Kell and Pretorius 2023, 2017), rather resistant to fibrinolysis and can persist in the circulation. The presence of these microclots, commonly in the range 2-100 mm, is known to occur in a variety of conditions that may lead to or accompany AF (see below), and some of the molecules that catalyse their production such as bacterial cell wall substances (de Waal et al. 2018; Pretorius et al. 2018a; Pretorius et al. 2016c; Pretorius et al. 2018c; Pretorius et al. 2018d) or the spike protein of SARS-CoV-2 (Grobbelaar et al. 2022; Grobbelaar et al. 2021) are also known. The widespread existence of these fibrinaloid microclots also led us to wonder whether they might thus contribute to the actual genesis of AF. Recognising this as a problem of systems biology (Alon 2006; Kell and Knowles 2006; Klipp et al. 2005; Palsson 2006), the present overview sets out what is actually the considerable evidence for this view. We summarise our review in the form of a 'mind map' (Buzan 2002; Hull et al. 2008).

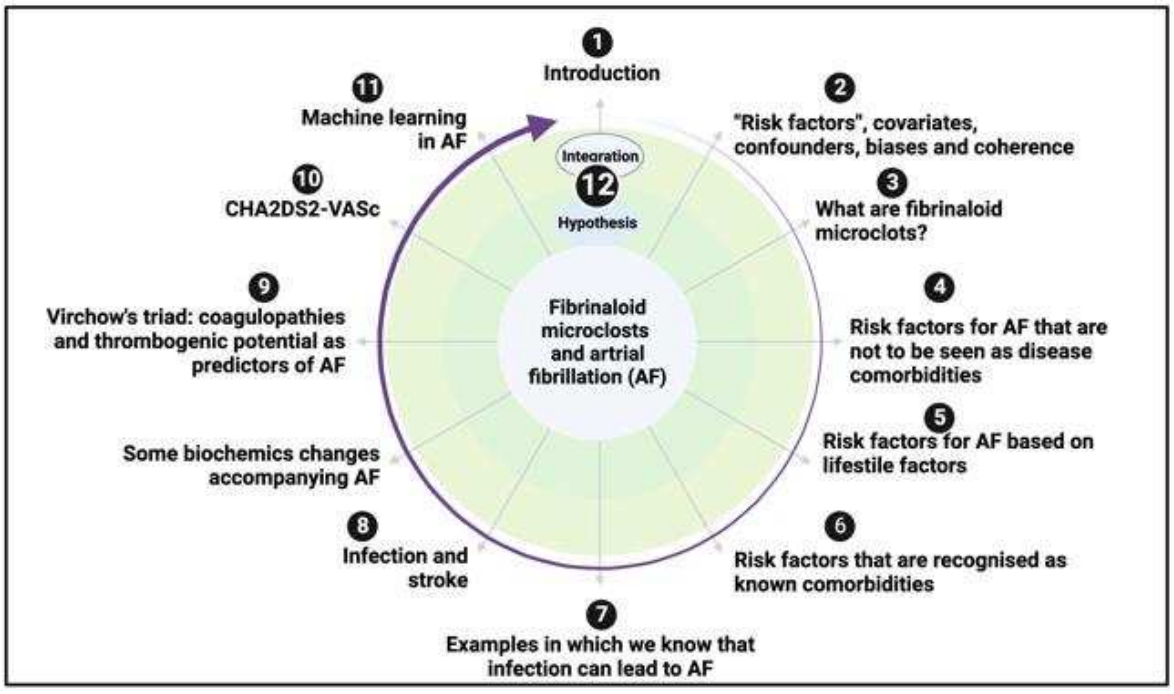

Figure 1. A 'mind map' (Buzan 2002) setting out this review. Created with Biorender.com.

"Risk factors", covariates, confounders, biases and coherence

 doi:10.20944/preprints202401.1945.v1

Much of modern analytics in medicine is concerned with identifying 'risk factors', most of which are really in fact covariates (Figure 2). To illustrate this point, we take a different cardiovascular disease (pre-eclampsia) (Kell and Kenny 2016; Kenny and Kell 2018), where because this is a disorder of pregnancy we do at least know the time and nature of the origin (of the pregnancy). Thus, we know that the likelihood of developing pre-eclampsia (equivalent to B in Figure 1) increases with certain pre-conditions (first pregnancy with the father, existing diabetes, maternal age, BMI, blood pressure at first visit, infection, etc) (e.g. (Allotey et al. 2020; Bartsch et al. 2016; Bilano et al. 2014; Elawad et al. 2024; Giannakou et al. 2018; Kell and Kenny 2016; Lee et al. 2022; Machano and Joho 2020; Xue et al. 2023), but *a priori* there is no way of knowing whether any of the above conditions are truly on a causal pathway or simply covariates (and caused by other factors such as those labelled X and Y in Figure 2). The infeasibility of establishing causality solely from measurements of variables is widely encapsulated in the mantra 'correlation does not equal causation', although any co-variation has the potential to contain useful information. Unravelling such relationships by causal inferencing either requires good longitudinal data and/or (better) affecting them as independent variables.

Thus the fact that the long-term use of antibiotics following a toxoplasma infection lowers the risk of pre-eclampsia by a massive 11-fold (Todros et al. 2006), along with a mass of other evidence, strongly implies an infectious origin for pre-eclampsia (Kell and Kenny 2016; Kenny and Kell 2018; Todros et al. 2007), but because these are not always even recognised they do not appear in most lists of risk factors.

Overall, we find useful the principle of *coherence*, which indicates that if a variety of nominally orthogonal lines of evidence point towards the same mechanism then that mechanism is more likely to be true (Thagard 2012, 2007, 1999). Similarly, we consider that an understanding of comorbidities, where the knowledge available from sets of related diseases may be brought to bear, must enhance the understanding of the disease of particular intellectual interest (Petsko 2009). As Petsko (Petsko 2009) notes, this strategy is well-established e.g. in functional genomics (where it is often called 'guilt by association' (e.g. (Gillis and Pavlidis 2012; Oliver 2000; Tian et al. 2008; Voy et al. 2006)), where it uses the idea that the co-expression of genes of unknown function with genes of known function implies a contributory role for the 'unknown' genes in the known function. Especially when the associations are between genetic polymorphisms and diseases the activity – then known as genome-wide association studies or GWAS – is seen as entirely respectable (Alsheikh et al. 2022; Baker 2010; Lappalainen et al. 2019). Nowadays, because the statistical risks of false positives are quite considerable when the number of variables (such as SNPs) is large (Benjamini and Hochberg 1995; Broadhurst and Kell 2006; Gunning and Pavlidis 2021; van den Oord 2008), the basis for any co-variation or correlation has to be very well established, and include separate validation sets.

Consequently, although our ultimate aims are mechanistic, we shall start by looking at known 'risk factors' and comorbidities of AF, where the term 'guilt-by-association' has itself been used (Al-Falahi et al. 2017). We simply note here that the terms 'bias' and 'confounder' should really just be applied in studies in which relevant and knowable covariates (e.g. gender or pre-existing pill consumption) are inadvertently distributed differently between two populations of interest (such as 'diseased' and 'control') (Broadhurst and Kell 2006). Other kinds of 'biases', such as a focus on particular sets of gene products leading to models that use them, are in fact a significant feature of the now-commonplace large language models (Bommasani et al. 2021) based on transformers (Vaswani et al. 2017).

 doi:10.20944/preprints202401.1945.v1

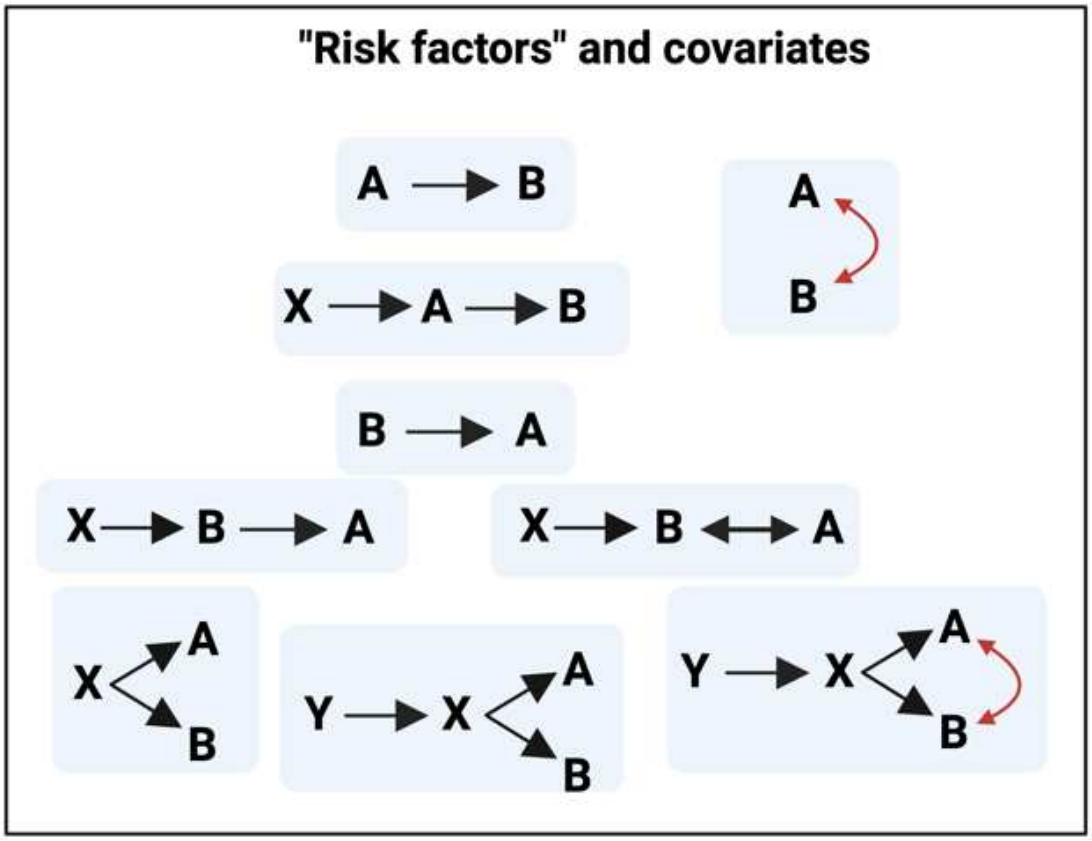

Figure 2. Risk factors, observables, causes and covariates.

It is common that observables A and B are seen to covary. There can be many reasons for this, e.g. that A causes B, that B causes A, that something else X causes them both whether sequentially or in parallel, and/or there may be a positive feedback cycle in which A causes B and B causes A. Often we can only measure variables but it is the parameters ('causes') that we seek. Since we cannot always influence the parameters directly, one job of systems biology or systems medicine is to seek to reconstruct the causal relations by measurements of the variables. Longitudinal methods can here be especially powerful as a later event cannot directly influence an earlier one. Created with BioRender.com

We begin by rehearsing what we know about fibrinaloid microclots.

What are fibrinaloid microclots?

Clotting and clot removal happen all the time, so that the body is 'primed' for any desirable clotting to be initiated rapidly in response say to a wound. At a high level (Figure 3) soluble fibrinogen, typically as a 5 x 45nm complex of three different polypeptides ($a_2\beta_2\gamma_2$) (MW ~ 340 kDa) (Kollman et al. 2009) https://www.rcsb.org/structure/3ghg plus internal fibrinopeptides A and B and one of the most abundant proteins in plasma (present at typically 2-4 $g.L^{-1}$ (Weisel 2005; Weisel and Litvinov 2017)), is acted upon by the serine protease thrombin. This action removes two fibrinopeptides, exposing 'knobs' and 'holes' and leading to a remarkable self-assembly in which fibrin monomers polymerise to make staggered oligomers, that themselves lengthen into protofibrils that aggregate laterally to make fibres, finally branching to create a three-dimensional network which represents the clots. Typical fibre diameters are a few hundred nm (say 100-400 nm (Belcher et al. 2023; Collet et al. 2000; Ferri et al. 2011; Li et al. 2016)), with a fractal morphology (Guthold et al. 2004), meaning that a 'unit' of fibrin fibre contains many hundreds of fibrinogen monomers contributing to its diameter at any point. Clots are then degraded by plasmin, which itself has a variety of activators and inhibitors (Figure 3). For our purposes, we note that the clots may not be fully formed, that they form anomalous conformations (see below) and that their rate of degradation is in many cases

 doi:10.20944/preprints202401.1945.v1

unusually low. This means that there may be, in certain diseases, a standing crop of fibrinaloid microclots.

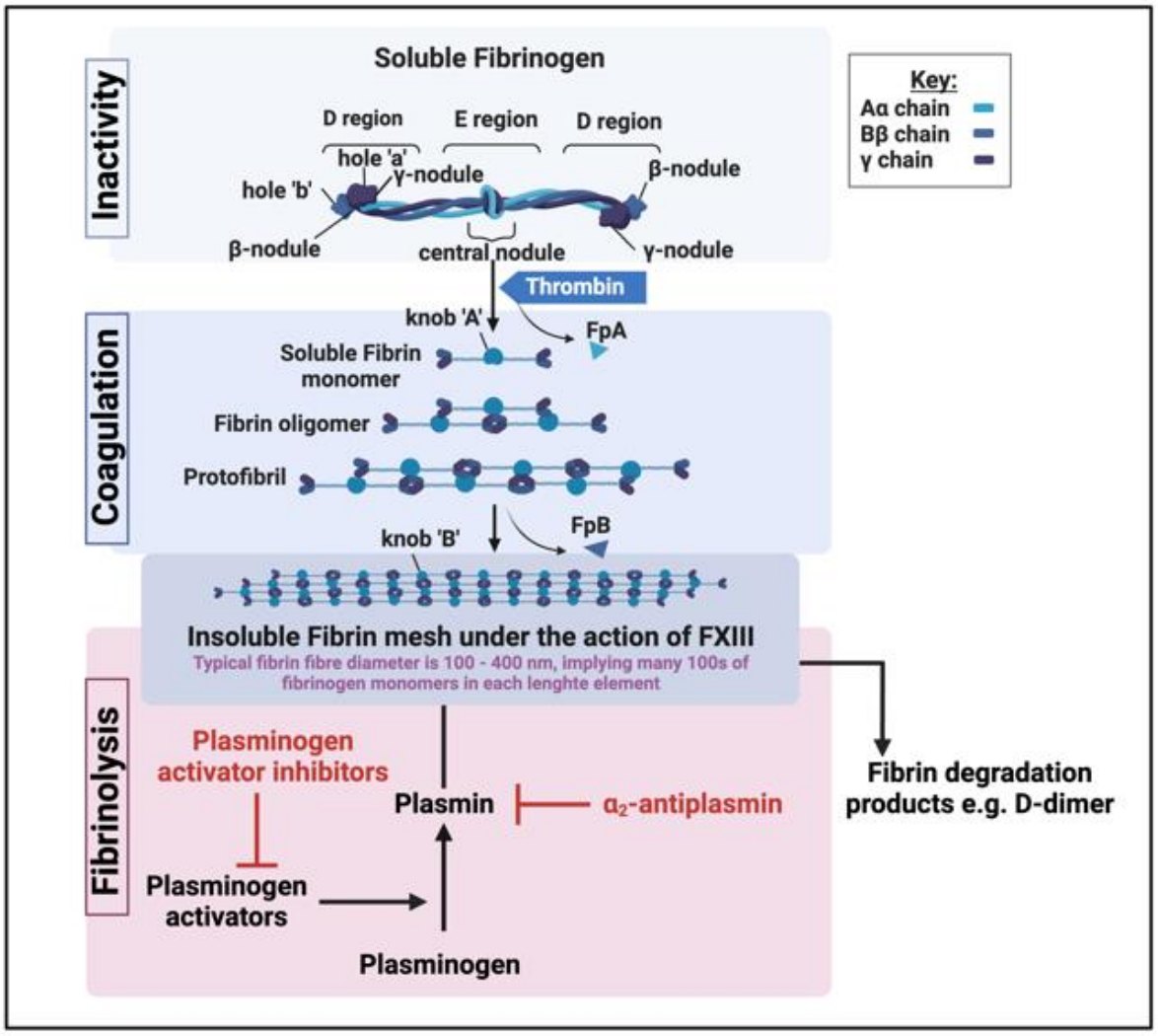

Figure 3. A high-level illustration of fibrinogen polymerisation into fibrin as a part of blood clotting.

Much of the left-hand part is redrawn from a CC-BY article at (Kell et al. 2022). Fibrinolysis can be decreased by a variety of endogeneous inhibitors, as well (see below) as when fibrin adopts an anomalous amyloid-type form. Created with BioRender.com

Early studies in the electron microscope by one of us (EP) showed that while images of the fibrin fibres of 'normal' clots looked much like nicely cooked spaghetti, those in a variety of chronic, inflammatory and other conditions looked much as if such spaghetti had been parboiled and stuck together in an unholy mess (Pretorius 2011; Pretorius et al. 2009; Pretorius et al. 2010; Pretorius et al. 2011a; Pretorius et al. 2011b; Pretorius et al. 2011c), a finding referred to at the time as 'dense matted deposits' (see Figure 4). These anomalous fibres could be induced by the presence of free iron (Kell et al. 2020a; Kell and Pretorius 2018a; Kell and Pretorius 2015; Lipinski and Pretorius 2012; Pretorius et al. 2016a; Pretorius and Kell 2014; Pretorius et al. 2013).

 doi:10.20944/preprints202401.1945.v1

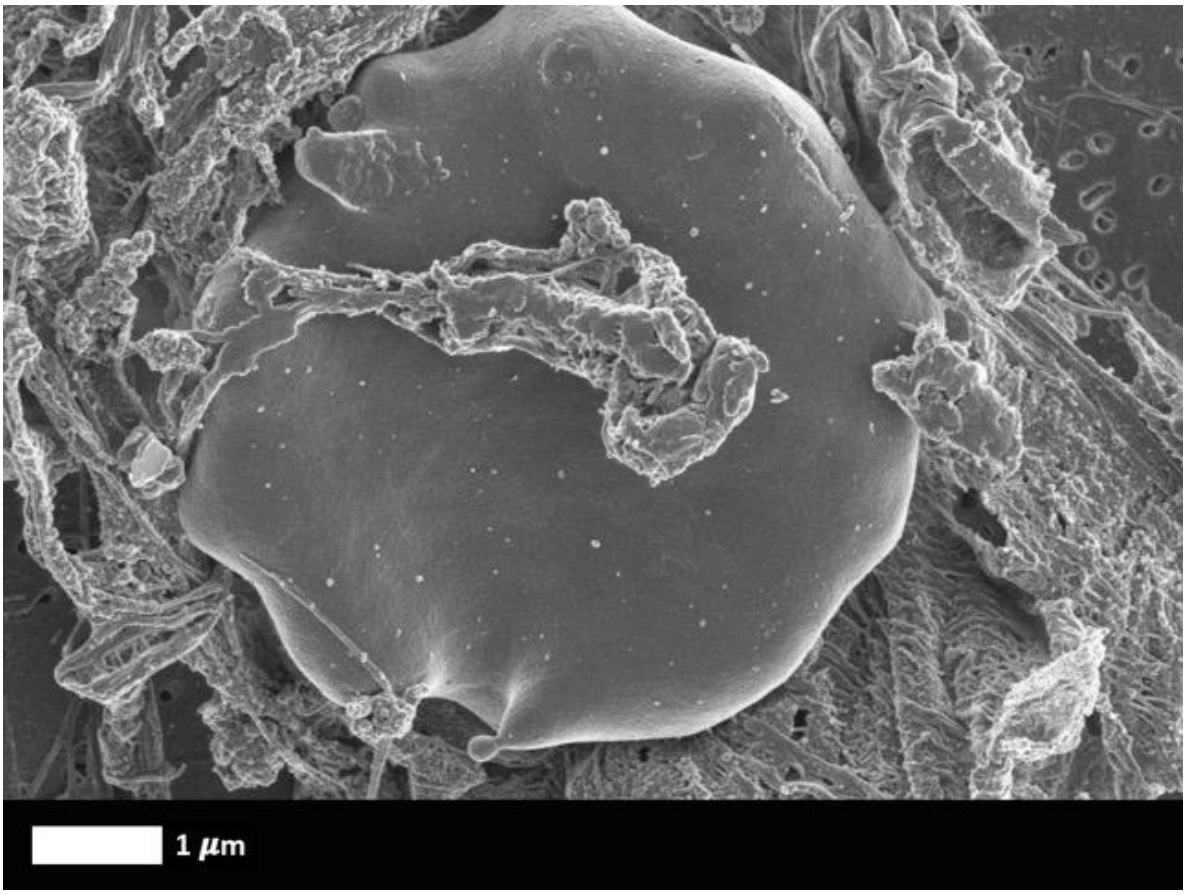

Figure 4. Scanning electron microscopy figure of dense matted deposits entrapping a red blood cell.

Healthy whole blood was exposed to ferric chloride (raw data from (Lipinski et al. 2012)).

Many proteins can fold into a stabler, beta-sheet-rich 'amyloid' form, with no change in sequence. Some of these are related to a variety of more-or-less well known diseases ('classical amyloidoses', e.g. (Crystal et al. 2003; Martinez-Naharro et al. 2018; Palladini and Merlini 2013)) in which unfolded forms of proteins such as Ab and a-synuclein are detected, but even proteins such as insulin (Fagihi and Bhattacharjee 2022) and lysozyme (Kuo et al. 2017) can adopt amyloid forms. The apotheosis of this kind of behaviour is represented by prion proteins (e.g. (Aguzzi and De Cecco 2020; Aguzzi and Lakkaraju 2016; Frontzek et al. 2022; Kell and Pretorius 2023, 2017)), that can adopt a variety of stable, amyloid-type states (without changes in primary sequence) that can even catalyse their own (con)formation. We later showed that the 'dense matted deposits' were in fact amyloid in character (Kell et al. 2022; Kell and Pretorius 2017; Kruger et al. 2022; Pretorius et al. 2018a, b; Pretorius et al. 2016c; Pretorius et al. 2017b; Pretorius et al. 2017c; Pretorius et al. 2018c; Pretorius et al. 2018d; Pretorius et al. 2022; Pretorius et al. 2020; Turner et al. 2023) as they could be stained with the well-stablished amyloid stain thioflavin T, as well as the commercial 'Amytracker' stains (de Waal et al. 2018; Pretorius et al. 2017c; Pretorius et al. 2018c). This was confirmed by correlating images from the electron and fluorescence microscopes (de Waal et al. 2018). Such diseases (discussed in more detail below) were also accompanied by significant platelet activation. Figure 5 illustrates these phenomena.

 doi:10.20944/preprints202401.1945.v1

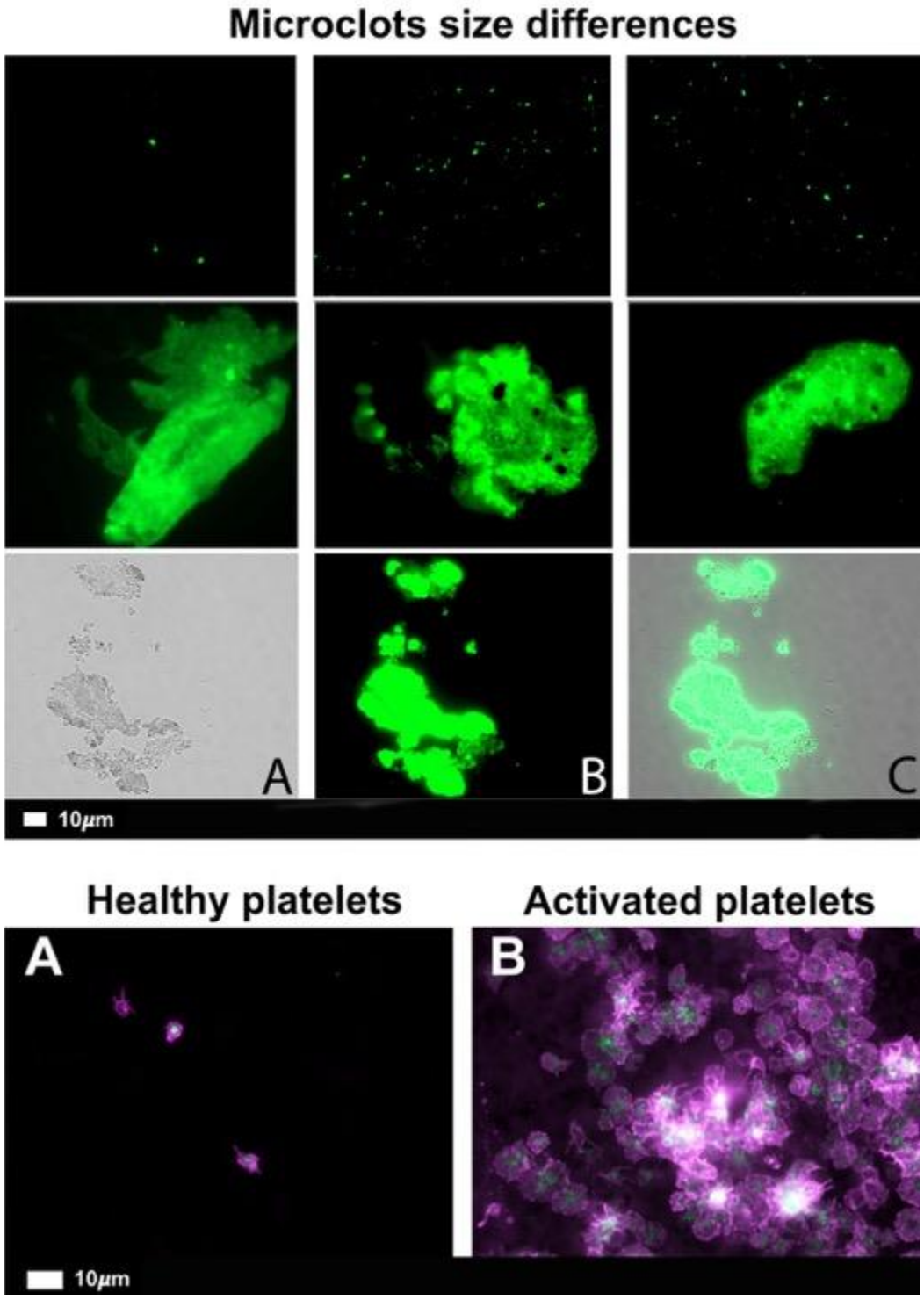

Figure 5. Microclots and platelets in healthy individuals and in individuals with Long COVID (raw data from (Lipinski et al. 2012).

A particular feature of such clots is that – like prion proteins – they are far more resistant than normal to proteolysis (in this case fibrinolysis) (Kell and Pretorius 2023, 2017), and their sizes can vary widely over the main approximate range 2-100 mm diameter. The addition of known amyloids to clotting systems can induce similar effects (Zamolodchikov and Strickland 2012). Also, like prion proteins, these amyloid forms are thermodynamically more stable than are the non-amyloid form(s) normally adopted, and the abnormal form can catalyse the transformation of the normal form into itself; consequently this can be triggered by minuscule amount of suitable substances, such as

 doi:10.20944/preprints202401.1945.v1

bacterial cell wall materials (Pretorius et al. 2016c; Pretorius et al. 2018c) or viral surface proteins (Grobbelaar et al. 2021). Noting that far more small molecules bind to proteins than was widely assumed (e.g. (Kell 2011; Li et al. 2010; Li and Snyder 2011)), it is reasonable that any number of small molecules beyond iron ions might also effect the nature of fibrinogen polymerisation, and certainly some (such as 7-b-oestradiol (Swanepoel et al. 2014; Swanepoel et al. 2016)) are known to do so. Other features known to affect the rate of fibrinolysis (Undas 2014) include fibre diameters (Carr and Alving 1995) and the presence of anti-plasmin(ogen) proteins (Bryk et al. 2020; Kruger et al. 2022; Pretorius et al. 2021). We illustrate the two types of fibrin as a cartoon in Figure 6.

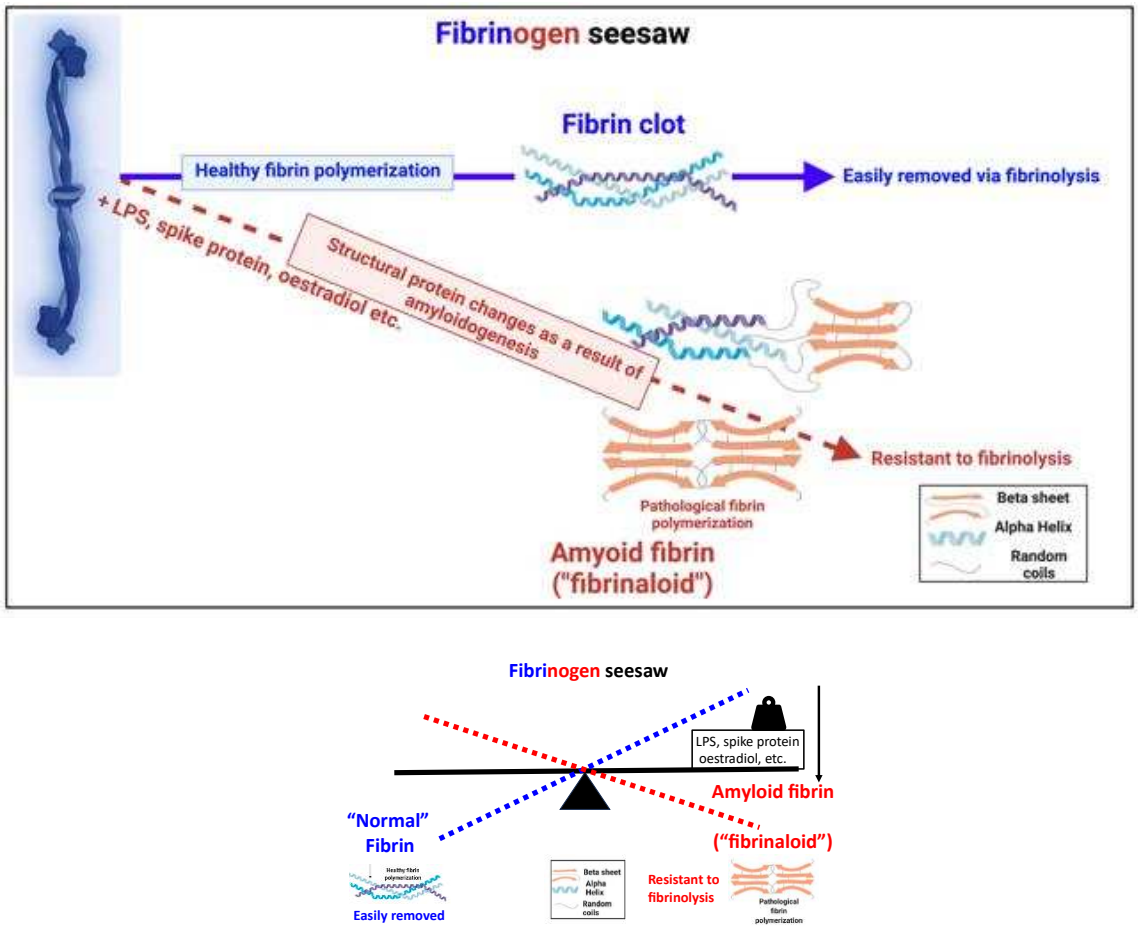

Figure 6. Cartoon illustrating the ability of fibrinogen to polymerise either to its a-helix-rich normal form or its crossed-b-sheet amyloid 'fibrinaloid' form depending on the presence of various small-molecule triggers. Glyphs taken from the CC-BY Open Access publication (Laubscher et al. 2021). Created with BioRender.com.

The typical size range of these fibrinaloid microclots can allow them to travel widely through the vasculature, essentially blocking up capillaries of a suitable diameter, inhibiting blood flow and hence O_2 transfer to tissues, and thus accounting in principle for the very wide range of symptoms in syndromes such as Long Covid, including fatigue (Kell et al. 2022), post-exertional symptom exacerbation (Kell and Pretorius 2022), and autoantibody induction (Kell and Pretorius 2023). Very recently, amyloid deposits have also been found in muscle tissues (not just plasma) of individuals with Long COVID (Appelman et al. 2024). Armed with this brief summary of fibrinaloid microclots, we now turn to risk factors for atrial fibrillation.

Risk factors for AF that are not to be seen as disease comorbidities

Many studies have examined how the prevalence of AF varies with properties such as age, gender, BMI, etc that are not *per se* normally seen as comorbidities, and we shall look at them first,

 doi:10.20944/preprints202401.1945.v1

mostly to see if they give any hints with the incidence of microclots before we move to the other factors (see e.g. (Zhang et al. 2021a), while the guidelines of Hindricks and colleagues provide a comprehensive list (Hindricks et al. 2021)). These few are summarised in table 1. The focus here is on prevalence more than outcomes, since the application of therapies is not necessarily uniform (Essien et al. 2022).

Table 1. Variation of the prevalence of AF with certain properties of individuals.

Risk factor	Comments	Selected references
Age	Normally a significant increase in AF with age	(Hindricks et al. 2021; Lowres et al. 2019; Marinigh et al. 2010; Zhang et al. 2021a)
	In some cases the opposite can be true for athletes.	(Ayinde et al. 2018; Goudis et al. 2015)
	May involve age-dependent Na^+ channel expression	(Isaac et al. 2020)
BMI	Obesity is sometimes a clear risk factor (Benjamin et al. 1998) (as for many metabolic diseases), but there are also (and more commonly) a variety of so-called 'obesity paradoxes' where the hazard ratios for acquiring or manifesting AF, and in particular suffering disease sequelae therefrom, are actually significantly greater for those with a lower BMI.	(Li et al. 2022; Liu et al. 2020; Overvad et al. 2013; Panchal et al. 2019b; Proietti and Boriani 2020; Proietti et al. 2017; Rodríguez-Reyes et al. 2021; Sandhu et al. 2016; Sandhu et al. 2018; Wanahita et al. 2008; Wang et al. 2004; Wu et al. 2023b; Zhu et al. 2016)
	Obesity may induce sleep apnoea, which is a known risk factor for AF	(Al-Falahi et al. 2017; Benjafield et al. 2019; Khan et al. 2018; Zhang et al. 2021b)
Ethnicity	More prevalent among Caucasians; not entirely clear how much is genetics, culture/lifestyle, or GxE, and as with genetics no studies really seek to deconvolve these factors	(Zhang et al. 2021a)
Familial associations/ Genetics	Mostly less significant than lifestyle factors and co-morbidities, apart from some particular and relatively uncommon ion channelopathies	(Feghaly et al. 2018);
	Monozygotic:dizygotic ratio does predict a role for genetics, so not purely cultural associations	(Christophersen et al. 2013; Christophersen et al. 2009)
	Highly polygenic, with genes involved in developmental, contractile, and electrophysiological functions. Necessarily	(Kalstø et al. 2019; Lee et al. 2023; Roselli et al. 2018; Selewa et al. 2023; Weng et al. 2017)

 doi:10.20944/preprints202401.1945.v1

	convolved with GxE association that cannot be interpreted from GWAS studies alone.	
Gender	More prevalent in males, though outcomes can be worse for females (so being female contributes to the CHA_2DS_2-VASc score (Friberg et al. 2012; Lip et al. 2010)). Less important than age for asymptomatic AF.	(Li et al. 2019; Xiong et al. 2015; Zhang et al. 2021a)

Interestingly, with the possible exception of age, none of these is especially associated with AF (independently of disease) and neither is the prevalence of microclots (for instance age and male gender do associate with acute covid but long covid is far more prevalent in women (and often not the older ones)). That is already a useful test, because if there were very strong associations with 'pure' AF but not with microclots it would be harder to argue for a major role of microclots in AF or vice versa.

Risk factors for AF based on lifestyle factors

While BMI might have been placed in this category, (i) it is an effect as much as a cause, (ii) a high BMI can cover a multitude of physiques, such that (iii) a high BMI in a professional rugby player would not necessarily be seen as significant a risk factor as it might be in an office worker. However, other lifestyle choices are more obviously under the control of individuals, e.g. alcohol consumption, and we next look at these (Table 2). Although exposure to particulate matter may not be seen as a lifestyle choice, urban *vs* rural living is one and particulate matter exposure (especially from cars) is far worse in the former, and the effects are substantial. They also show the importance of particulate irritants, a category into which fibrinaloid microclots might be considered to fall.

Table 2. Variation of the prevalence of AF with certain 'lifestyle' risk factors.

Risk factor	**Comments**	**Selected references**
Alcohol consumption	Some increase in AF risk as a function of alcohol intake; greater in men; studies mainly not controlled for BMI. Not a huge effect for moderate levels of consumption.	(Djoussé et al. 2004; Mukamal et al. 2005; Panchal et al. 2019b)
Exercise	As with BMI, the relationship is nonlinear, with moderate exercise and general cardio-respiratory fitness being beneficial but excess exercise (which could cause oxidative stress (Powers et al. 2020; Thirupathi et al. 2020), inflammation (Cerqueira et al. 2019; da Rocha et al. 2019), hypoxaemia (Durand and Raberin 2021), etc) having negative effects.	(Aizer et al. 2009; Panchal et al. 2019b; Qureshi et al. 2015)
Particulate matter exposure	New-onset AF can follow exposure to particulate matter. This can be an acute occurence Increases with known genetic risk factors	(Blaszczyk et al. 2023; Link et al. 2013; Mandaglio-Collados et al. 2023; Zhang et al. 2023) (Ma et al. 2023)

 doi:10.20944/preprints202401.1945.v1

	Meta-analyses. Particulate matter is also amyloidogenic	 (Shao et al. 2016; Wang et al. 2021; Yue et al. 2021) (Calderón-Garcidueñas et al. 2008; Iaccarino et al. 2021; Jang et al. 2018; Sahu et al. 2021)
Psychosocial Stress	As estimated by surrogates reflecting anger and hostility, can be a minor risk factor in men but not women, even after controlling for hypertension.	(Eaker et al. 2004; Panchal et al. 2019b)
Smoking	Although important to other cardiovascular diseases, for AF seemingly a marginal risk, and probably dwarfed by other risks of smoking such as lung cancer	(Panchal et al. 2019a)

Table 2 implies that within reasonable bounds these lifestyle factors have a measurable but not massive influence on the appearance of AF in the population. However, we note that they are modifiable.

Risk factors that are recognised as known disease comorbidities

Most chronic, inflammatory diseases share many properties (Kell and Pretorius 2018a), including inflammation (Kell et al. 2022), oxidative stress (Kell and Pretorius 2022), and iron dysregulation (Kell 2009; Kell 2010; Kell et al. 2020b; Kell and Pretorius 2014) (and also, as we shall see later and in Table 3, fibrinaloid microclots). This of itself might lead one to suppose that they have a broadly similar, ultimate type of cause (i.e. something labelled "Y" in Figure 1), and the evidence for this "something" points rather squarely at an infectious origin (see table 3).

Table 3. Some supposedly non-communicable diseases for which there is in fact substantial evidence of an infectious element and/or evidence of fibrinaloid microclots.

Disease or syndrome	Comments	References regarding an infectious origin	References illustrating anomalous clotting/ microclots
Alzheimer's	Many references, not least from Ruth Itzhaki focusing on HSV, imply this strongly. Other organisms have also been implicated.	(Grobler et al. 2023; Itzhaki 2018; Itzhaki et al. 2008; Itzhaki and Lathe 2018; Itzhaki et al. 2016)	(de Waal et al. 2018; Pretorius et al. 2016a; Pretorius et al. 2018a)
Diabetes, type 2	Originally asked by Gundersen in 1927. Even greater evidence for type	(Craighead 1975; Gundersen 1927; Notkins 1977; Rajsfus et	(Pretorius et al. 2011a) (de Waal et al. 2018; Pretorius et al. 2015;

 doi:10.20944/preprints202401.1945.v1

	1 (Jean-Baptiste et al. 2017), not covered here.	al. 2023; Yoon and Notkins 1983)	Pretorius et al. 2017c; Pretorius et al. 2020) (Pretorius et al. 2022; Soma and Pretorius 2015)
	Many reviews (also those with T2D are more susceptible to infections; this direction is not discussed here).	(B 2022; Nobs et al. 2023; Sohail et al. 2022)	
	Increased diabetes prevalence following COVID-19 infection	(Naveed et al. 2023)	
Multiple sclerosis	Now recognised as being caused by Epstein-Barr virus	(Rousseau and Bhaduri-McIntosh 2023; Schönrich et al. 2022; Wekerle 2022)	Not yet studied
Myalgic encephalitis/ chronic fatigue syndrome (ME/CFS)	Clear infectious origin, likely viral and most likely a herpes virus	(Nunes et al. 2023)	(Nunes et al. 2023; Nunes et al. 2022)
Parkinson's	Induction of disease progression by bacterial LPS and by viruses	(Cannon and Gruenheid 2022; Leta et al. 2022)	(de Waal et al. 2018)
	Reviews	(Caggiu et al. 2019; Limphaibool et al. 2019)	
Rheumatoid arthritis	Absolutely clear evidence for *Proteus* spp. as the infectious agent	(Ebringer 2012; Ebringer and Rashid 2014, 2009; Ebringer et al. 2010)	(Bezuidenhout et al. 2020; Kell and Pretorius 2022; Pretorius et al. 2017a; Pretorius et al. 2012)
Sleep Apnoea	Obstructive Sleep Apnoea is a strong risk factor or comorbidity of AF, also associated with obesity (Al-Falahi et al. 2017; Goudis and Ketikoglou 2017; Staerk et al. 2017; Zhang et al.	(Chiner et al. 2016; Hariyanto and Kurniawan 2021; Su et al. 2014)	Not yet studied

 doi:10.20944/preprints202401.1945.v1

	2021b) and both acute (Miller and Cappuccio 2021) and Long COVID (Mandel et al. 2023)		

Apart from multiple sclerosis and sleep apnoea, that we have not yet studied, it is striking that each of the supposedly non-communicable diseases listed in Table 3 can be seen to have an infectious origin, and we know that components of both bacteria (e.g. LPS, lipoteichoic acid) and viruses (e.g. SARS-CoV-2 spike protein) can induce the fibrinaloid microclots (see also below). However, our next task is to list some of these comorbidities on the grounds that they surely contain clues as to the origins of the syndrome of our present, prime focus, viz atrial fibrillation.

Thus Table 4 lists some of the known comorbidities of various diseases and AF. Because of the relative lack, until recently, of long-term screening, it is not normally easy to determine longitudinal trends (potentially then causal chains), but for present purposes an association is sufficient, before we move to cases in which we absolutely know that a specific infection can lead to AF. Table 4 makes clear that each of the diseases there also makes an appearance in Table 4, implying that they are related to each other, whether as effects of an earlier cause (as we consider likelier, Fig 1) or on their own causal chain in either direction, or both.

Table 4. Some diseases or comorbidities known to be associated with AF.

Disease	**Comments**	**Selected references**
Alzheimer's	AF is of course related to age, as is AD. Stroke is also related to vascular dementia. Strong comorbidities between cardiovascular disease and AD,	(Ihara and Washida 2018) (Benenati et al. 2021)
	Some indications that AF is associated with exacerbation of the onset of AD and related dementias, but not causally	(Falsetti et al. 2018; Manemann et al. 2023; Nakase et al. 2023; Pan et al. 2020; Papanastasiou et al. 2021; Proietti et al. 2020)
Diabetes, type 2	Very strong association of AF with diabetic complications, and of diabetes increasing the risk of AF	(Alijla et al. 2021; Bohne et al. 2019; Choi et al. 2023; Ding et al. 2022a; Domek et al. 2020; Kwon et al. 2023; Lorenzo-Almorós et al. 2023; Wang et al. 2019; Xiong et al. 2018)
Parkinson's	Some evidence of an association of AF with early PD, much less so if PD diagnosed later (i.e. evidence either way there is relatively weak)	(Alves et al. 2021; Cereja et al. 2023; Han et al. 2021; Hong et al. 2019)

 doi:10.20944/preprints202401.1945.v1

Rheumatoid arthritis	Small, significant association, but confounded with use of small molecule drugs Also associated with greater risk of cardiovascular disease	(Rong et al. 2023) (Kim et al. 2023) (Kerola et al. 2021; Semb et al. 2022)

Examples in which we know that infection can lead to atrial fibrillation

The conclusion from the above is that there is strong associative evidence for comorbidities of supposedly non-infectious diseases, in which fibrinaloid microclots have been demonstrated, and AF. Unfortunately, however, in most cases a causative mechanism (or a set of mechanisms or chain of causal reasoning) is not to hand.

However, infections represent a class of disease in which the temporal origin (of the infection) is usually known from early symptoms, so it is reasonable to ask the question of whether infection is known to lead to AF in populations previously known not to manifest it. Not least since the appearance of Long COVID (albeit there are many similar post-infection syndromes such as ME/CFS, Gulf War syndrome, post-Ebola syndrome, etc)), we have come to recognise that a variety of infections can cause major and sometimes debilitating symptoms for extended periods after the infection has nominally cleared. In the same way, pre-eclampsia is associated with a significantly increased risk of cardiovascular disease (Thilaganathan and Kalafat 2019; Wu et al. 2017), often for many years after the pregnancy in question.

The following facts relating infection to subsequent AF are thus highly pertinent:

- 7.6% of cases of community acquired pneumonia led to new-onset AF (Corica et al. 2023b)
- AF is a common occurrence following infection with SARS-CoV-2 (COVID-19) (Abbasi 2022; Al-Abbas et al. 2021; Bagnato et al. 2022; Bhatla et al. 2020; Duckheim and Schreieck 2021; García-Granja et al. 2021; Kanuri et al. 2023; Mouram et al. 2022; Niehues et al. 2022; Rav-Acha et al. 2021; Wu et al. 2023a)
- The Odds Ratio OR for AF 365 days after COVID-19 compared to a well-established control group was 1.83 in a large study (Berman et al. 2023).
- A previous use of DOACs is protective against AF following SARS-CoV-2 infection (Azaña Gómez et al. 2022). Note that AF increased the bleeding risk of those on anticoagulants (Rubini-Costa et al. 2022).
- There was an increased mortality from acute COVID-19 in patients with AF (Musikantow et al. 2021; Pardo Sanz et al. 2021; Zuin et al. 2021), especially older ones.
- The same applies to Long COVID (Huseynov et al. 2023) (which is not surprising giving its incidence following acute COVID). Incidence after covid and refs
- Cardiac arrhythmias also seem to be caused by COVID-19 vaccination (Pari et al. 2023) (which of course includes spike protein or RNA coding for it) and spike protein is known to cause microclots (Grobbelaar et al. 2022; Grobbelaar et al. 2021).
- New-onset AF is a common occurrence in sepsis (which of course convolves e.g. infection and inflammation), increasing as sepsis leads to severe sepsis and then septic shock, and leading to poorer outcomes (Aibar and Schulman 2021; Bashar et al. 2020; Bosch et al. 2019; Corica et al. 2022; Downes et al. 2023; Honorato et al. 2023; Induruwa et al. 2022; Klein Klouwenberg et al. 2017; Kuipers et al. 2014; Proietti and Romiti 2021; Walkey et al. 2013; Xiao et al. 2021).

 doi:10.20944/preprints202401.1945.v1

- Sepsis (we ignore subtypes (Cano-Gamez et al. 2022; van Amstel et al. 2023)) likely involves microclots (Kell and Pretorius 2018b), which can be induced experimentally in the presence of cell-surface components of infectious agents such as bacterial lipopolysaccharide (Pretorius et al. 2018a; Pretorius et al. 2016b; Pretorius et al. 2018c; Pretorius et al. 2018d) or lipoteichoic acid (Pretorius et al. 2018c), or the spike protein of SARS-CoV-2 (Grobbelaar et al. 2022; Grobbelaar et al. 2021; Pretorius and Kell 2023)
- Coagulation, in the worst case disseminated intravascular coagulation, is a frequent accompaniment of sepsis (Allen et al. 2015; Gando 2010; Iba et al. 2013; Levi 2010; Levi et al. 1997; Li and Ma 2017; Murao and Yamakawa 2019; Yu et al. 2022)
- Anticoagulants are significantly protective against the complications of sepsis when timed properly (Meziani et al. 2017; Scarlatescu et al. 2017) and especially in the presence of disseminated intravascular coagulation (Qi et al. 2023; Umemura et al. 2023; Umemura and Yamakawa 2018)

This raises the suspicion that coagulopathies may often precede AF, and before we look at this we shall rehearse a few of the potentially relevant biomarkers.

Infection and Stroke

We note that stroke and infection are often associated (Bustamante et al. 2017; Kazemi et al. 2021; Kishore et al. 2018; Shim and Wong 2016; Westendorp et al. 2018), and when co-occurring often lead to an unfavourable outcome (Vermeij et al. 2009; Westendorp et al. 2011) (implying some co-causality). Infections associated with stroke are usually called or referred to as a 'post-stroke infection' (that is following a stroke), but it is equally plausible (and in some cases demonstrable (Mélé and Turc 2018)) that the earlier stages of infection precede the stroke event that is referred to (Westendorp et al. 2011). Some of the evidence for this includes the fact that similar changes in the gut microbiome could be predictive of both stroke itself and post-stroke infection (Haak et al. 2021). However, apart from lowering urinary tract infections, prophylactic antibiotics were mostly not preventive (Kalra et al. 2015; Vermeij et al. 2018; Westendorp et al. 2021; Westendorp et al. 2015), cf. (Badve et al. 2018; Badve et al. 2019; Sluis et al. 2022); one interpretation of this is simply that the amount of bacterial cell wall product in the plasma necessary to induce microclots is absolute minuscule (Pretorius et al. 2016c; Pretorius et al. 2018c), and a tiny fraction of the total bacterial load within a person. Note, however, that certain antibiotics also increase the release of such amyloidogenic bacterial cell wall materials (Jackson and Kropp 1992; Mickiewicz et al. 2019; Opal et al. 1996; van Langevelde et al. 1998), thereby negating (or worse) the benefits of antibiosis *per se*.

One might also add here that the same co-association and likely causation, for which antibiotics are also not protective (Huang et al. 2018), is also true of Parkinson's disease (Dardiotis et al. 2018; Meng et al. 2019; Smeyne et al. 2021; Wang et al. 2020).

Some biochemical changes accompanying AF

Given the above, and a variety of biomarkers that might have something useful, it is also of interest to survey biochemical markers that might also correlate with AF. Table 5 summarises some markers that have been found to be raised in AF and that might be related to the genesis or presence of coagulopathies generally, and potentially fibrinaloid microclots.

Table 5. Some markers that are raised in AF and that have been related to the genesis or presence of fibrinaloid microclots and coagulopathies generally.

Biochemical marker	Comments	Selected references

 doi:10.20944/preprints202401.1945.v1

Ferritin	Serum ferritin is a marker of cell death (Kell and Pretorius 2014), whose accompanying release of free iron can cause microclots and may itself be induced by them or other traumas. It is significantly raised in AF	(Altieri et al. 2022; Mikkelsen et al. 2019)
Fibrinogen	Fibrinogen (including g' (Farrell 2012)) fibrinogen levels are commonly raised in inflammatory diseases (Luyendyk et al. 2019). Fibrinogen levels are higher in individuals with AF (and in those having a higher CHA_2DS_2-VASc score and likelihood of stroke), consistent with a role of microclots in the onset of AF	(Bao et al. 2023; Di Lecce et al. 2003; Li-Saw-Hee et al. 2001; Lip et al. 1996b, 1995; Mukamal et al. 2006; Rafaqat et al. 2022; Semczuk-Kaczmarek et al. 2019; Tilly et al. 2023; Weymann et al. 2017)
	Fibrin clot properties also relate to stroke likelihood/severity in AF, though no amyloid measurements were yet made	(Drabik et al. 2020; Drabik et al. 2017)
Inflammation	Occurs (by definition) in all kinds of chronic, inflammatory disease (Kell and Pretorius 2018a), but is certainly associated with AF. An accompaniment to all syndromes involving microclots.	(Korantzopoulos et al. 2018; Paquissi 2016; Rafaqat et al. 2022)
Plasminogen Activator Inhibitor-1 (PAI-1)	Significantly raised in AF, potentially reducing the rate at which fibrinaloid microclots might be removed	(Li et al. 2021; Marín et al. 1999 ; Pretorius et al. 2007)
Platelet Factor-4 and platelet activation	Platelet activation is another key feature of chronic, inflammatory diseases accompanied by microclots	(Drabik et al. 2015; Sohara et al. 1997; Yamauchi et al. 1986)
b-Thromboglobulin	Raised in AF	(Kamath et al. 2002; Lip et al. 1996a; Yamauchi et al. 1986)
Troponin (cardiac isoforms)	Probably more a metric of severity of cardiac events, but as a measure of cell death (like ferritin) may have predictive value	(Bai et al. 2018; Cortés et al. 2022; Costabel et al. 2017; Kaura et al. 2020; Lucrecia Maria et al. 2020; Sepehri Shamloo et al. 2021)

 doi:10.20944/preprints202401.1945.v1

Von Willebrand Factor	Note that it is unlikely to be a simple function, as too much or too little can be bad (Grobler et al. 2020)	(Freestone et al. 2008b; Weymann et al. 2017; Zhong et al. 2018)

Virchow's triad: coagulopathies and thrombogenic potential as predictors of AF

Although, as mentioned, AF is widely recognised as predictive of thrombus formation, our proposal is that the converse is also true (if not even more so). Is there further evidence for this? While our preferred metric is the presence of fibrinaloid microclots (measures such as D-dimer reflecting those of clot breakdown rather than clot presence (Kell et al. 2022)), these have not been done, so we need to look to more traditional measures of clotting potential, where similar suspicions have been raised (Danese et al. 2014; Ding et al. 2020; Ding et al. 2022b; Downes et al. 2023; Marín et al. 2003), and some limited longitudinal evidence brought forward (Tilly et al. 2023).

"Virchow's triad" reflects or consists of 'abnormal blood constituents', 'vessel wall abnormalities' (endothelialitis) and 'abnormal blood flow' (Bagot and Arya 2008), a set of coagulopathies leading to venous thrombosis, that also occur in AF (Ali et al. 2022; Arvanitis et al. 2022; Chung and Lip 2003; Darlington and McCauley 2020; Ding et al. 2020; Freestone et al. 2008a; Freestone and Lip 2008; Khan and Lip 2019; Qureshi et al. 2022; Schnabel et al. 2019; Watson et al. 2009; Yamashita 2016) and indeed are common in both acute (Ahmed et al. 2020; Carbillon et al. 2021; Conway et al. 2022; Flaumenhaft et al. 2022; Gonzalez-Gonzalez et al. 2021; Mehta et al. 2020; Wadowski et al. 2023; Zheng et al. 2020) and Long (Invernizzi et al. 2021; Jing et al. 2022; Zanini et al. 2024) COVID (which of course are also characterised by fibrinaloid microclots). Note again that the special feature of these fibrinaloid microclots which not only makes them easy to see but makes them significantly more resistant to the normal means of fibrinolysis. This again points strongly to the potential for microclots as being causative in AF and not merely a consequence. Similarly, it is easy to suppose that microclots are potentially able to aggregate into the better known microclots; it seems highly desirable to test these as to whether or not they are amyloid in character.

Clinical risk scores, e.g. CHA_2DS_2-VASc

From the point of view of risk factor analysis, the main present assessment for predicting the risk of stroke in individuals known to have AF is known as (and leads to) clinical risk scores, such as the CHA_2DS_2-VASc score (Lip et al. 2010), a backronym related to **C**ongestive Heart Failure, **H**ypertension, **A**ge (>75y) (2 points), **D**iabetes Mellitus, prior **S**troke or TIA or thromboembolism (2 points), **V**ascular disease, **A**ge (again, 65-74y) and **S**ex **c**ategory (female). The elements not marked as two points score one point, and age is either one or two points, giving a maximum score of 9. These are now in wide common use in guidelines globally (Chao et al. 2022; Writing Committee Members et al. 2024).

However, notwithstanding that strokes are clearly caused by microclots, as phrased by Qureshi *et al*. (Qureshi et al. 2022) these scores "rely mostly on clinical comorbidities, rather than thrombogenic mechanisms such as blood stasis, hypercoagulability and endothelial dysfunction—known as Virchow's triad." In view of the above arguments, it does seem very timely to revisit these, and indeed to develop new methods of assessment based on markers of thrombotic problems including biochemical markers such as those in Table 5, more physiological methods of endothelial dysfunction such as flow-mediated dilatation (Freestone et al. 2008a), and in particular fibrinaloid microclots. Given the tendency of unfolded/amyloid proteins to nucleate and increase in size (e.g. (Camino et al. 2021; Cawood et al. 2021; Chi et al. 2010; De and Klenerman 2019; Michaels et al. 2017; Michaels et al. 2023; Seuma et al. 2021; Seuma et al. 2022; Taylor et al. 2018)), it is highly plausible that microclots may serve as precursors to macroclots. Figure 7 provides a summary and overview of the kinds of evidence that we have brought together here.

 doi:10.20944/preprints202401.1945.v1

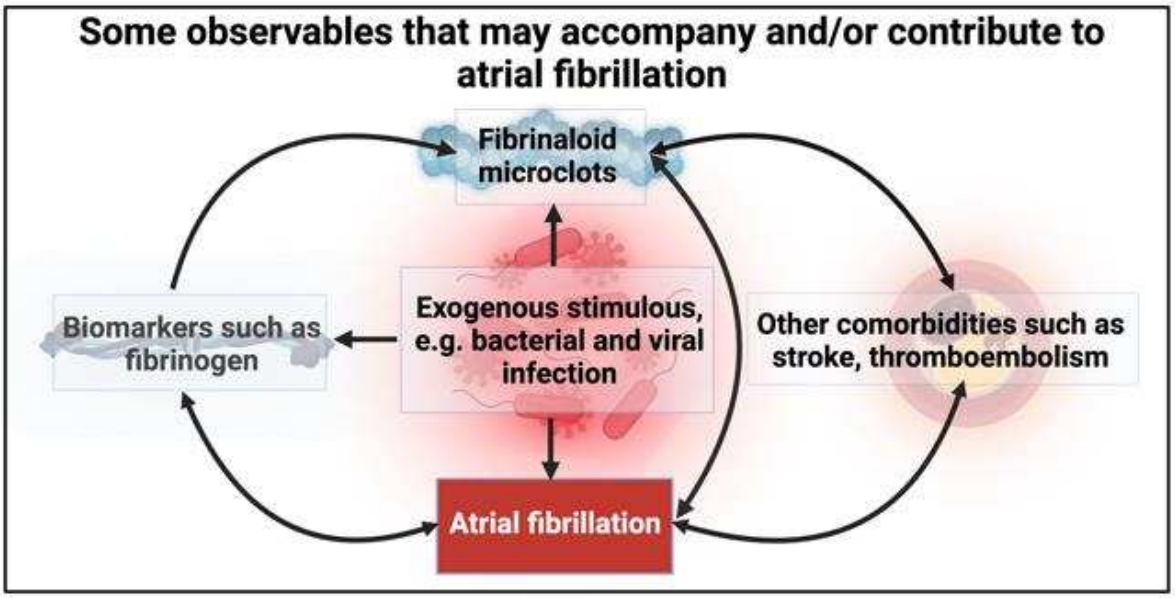

Figure 7. Some of the features on which we have focused in this review, indicating those (indicated by thick arrows) for which there is well established evidence, plus others that we consider likely but for which further evidence needs to be sought. Created with BioRender.com.

Machine learning in AF

As we move towards a post-genomic, data-driven, biology (Kell and Oliver 2004), it is increasingly recognised that hypothesis-free methods can play a valuable role in deconstructing complex phenomena. Thus, within the AF field, machine learning has been applied to the predictive risk of many inputs (Sekelj et al. 2021; Tseng and Noseworthy 2021), including more narrowly on ECGs (Rizwan et al. 2021; Siontis et al. 2020) and in COVID-19 (Lip et al. 2021). In one study, 15% of AF patients assigned to the AF cohort by the algorithm had a secondary care diagnosis with no record of AF in primary care (Pollock et al. 2020). Implementing such algorithms would be highly cost effective (Szymanski et al. 2022).

Discussion, conclusions, and a forward look

Although we have focused here on AF, we recognise that many other cardiac and (more generally) cardiovascular disorders are also accompanied by thromboses of various kinds. These include type 2 diabetes (Grant 2007; Konieczynska et al. 2014), heart failure (Karaban et al. 2024), myocarditis (Antoniak et al. 2008), peripheral arterial disease (Bennett et al. 2009), various disorders of pregnancy (Staff et al. 2016), and others that are not always (but should be) seen to be associated with vascular problems, such as Alzheimer's and Parkinson's (Roy et al. 2022). Cardiac amyloidosis (Martinez-Naharro et al. 2020; Martinez-Naharro et al. 2019) are of especial interest here. The multifaceted clinical complexity of patients with AF has led to the current overall holistic or integrated care management approach to AF care (Romiti et al. 2023; Romiti et al. 2022a), as is recommended in guidelines (Chao et al. 2022).

Learning from this collective of syndromes allows one to see common factors, at least one of which involves fibrinaloid microclots. Up to now these have not been studied as an independent risk factor for AF. This clearly needs to change.

Funding: EP: Funding was provided by NRF of South Africa (grant number 142142) and SA MRC (self-initiated research (SIR) grant), and Balvi Foundation. DBK thanks the Balvi Foundation (grant 18) and the Novo Nordisk Foundation for funding (grant NNF10CC1016517). The content and findings reported and illustrated are the sole deduction, view and responsibility of the researchers and do not reflect the official position and sentiments of the funders.

References

Abbasi J: The COVID Heart-One Year After SARS-CoV-2 Infection, Patients Have an Array of Increased Cardiovascular Risks. *JAMA* 2022; 327:1113-1114.

Aguzzi A, De Cecco E: Shifts and drifts in prion science. *Science* 2020; 370:32-34.

Aguzzi A, Lakkaraju AKK: Cell Biology of Prions and Prionoids: A Status Report. *Trends Cell Biol* 2016; 26:40-51.

Ahmed S, Zimba O, Gasparyan AY: Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. *Clin Rheumatol* 2020; 39:2529-2543.

Aibar J, Schulman S: New-Onset Atrial Fibrillation in Sepsis: A Narrative Review. *Semin Thromb Hemost* 2021; 47:18-25.

Aizer A, Gaziano JM, Cook NR, Manson JE, Buring JE, Albert CM: Relation of vigorous exercise to risk of atrial fibrillation. *Am J Cardiol* 2009; 103:1572-1577.

Al-Abbas O, Alshaikhli A, Amran HA: New-Onset Atrial Fibrillation and Multiple Systemic Emboli in a COVID-19 Patient. *Cureus* 2021; 13:e12917.

Al-Falahi Z, Williamson J, Dimitri H: Atrial Fibrillation and Sleep Apnoea: Guilt by Association? *Heart Lung Circ* 2017; 26:902-910.

Ali S, Saadat V, Co ML, Contractor T, Mandapati R, Parwani P: Permanent left atrial thrombi after multiple atrial fibrillation ablations: Acquired Virchow's triad? *HeartRhythm Case Rep* 2022; 8:715-718.

Alijla F, Buttia C, Reichlin T, Razvi S, Minder B, Wilhelm M, Muka T, Franco OH, Bano A: Association of diabetes with atrial fibrillation types: a systematic review and meta-analysis. *Cardiovasc Diabetol* 2021; 20:230.

Allen KS, Sawheny E, Kinasewitz GT: Anticoagulant modulation of inflammation in severe sepsis. *World J Crit Care Med* 2015; 4:105-115.

Allotey J, Snell KIE, Smuk M, Hooper R, Chan CL, Ahmed A, Chappell LC, von Dadelszen P, Dodds J, Green M, Kenny L, Khalil A, Khan KS, Mol BW, Myers J, Poston L, Thilaganathan B, Staff AC, Smith GCS, Ganzevoort W, Laivuori H, Odibo AO, Ramírez JA, Kingdom J, Daskalakis G, Farrar D, Baschat AA, Seed PT, Prefumo F, da Silva Costa F, Groen H, Audibert F, Masse J, Skråstad RB, Salvesen KÅ, Haavaldsen C, Nagata C, Rumbold AR, Heinonen S, Askie LM, Smits LJM, Vinter CA, Magnus PM, Eero K, Villa PM, Jenum AK, Andersen LB, Norman JE, Ohkuchi A, Eskild A, Bhattacharya S, McAuliffe FM, Galindo A, Herraiz I, Carbillon L, Klipstein-Grobusch K, Yeo S, Teede HJ, Browne JL, Moons KGM, Riley RD, Thangaratinam S: Validation and development of models using clinical, biochemical and ultrasound markers for predicting pre-eclampsia: an individual participant data meta-analysis. *Health Technol Assess* 2020; 24:72.

Alon U: *An introduction to systems biology: design principles of biological circuits*. London: Chapman and Hall/CRC, 2006.

Alshehri AM: Stroke in atrial fibrillation: Review of risk stratification and preventive therapy. *J Family Community Med* 2019; 26:92-97.

Alsheikh AJ, Wollenhaupt S, King EA, Reeb J, Ghosh S, Stolzenburg LR, Tamim S, Lazar J, Davis JW, Jacob HJ: The landscape of GWAS validation; systematic review identifying 309 validated non-coding variants across 130 human diseases. *BMC Med Genomics* 2022; 15:74.

Altieri C, Pisano C, Vincenzo L, Ferrante MS, Pellerito V, Nardi P, Bassano C, Buioni D, Greco E, Ruvolo G, Balistreri CR: Circulating Levels of Ferritin, RDW, PTLs as Predictive Biomarkers of Postoperative Atrial Fibrillation Risk after Cardiac Surgery in Extracorporeal Circulation. *Int J Mol Sci* 2022; 23:14800.

Alves M, Abrantes AM, Portugal G, Cruz MM, Reimao S, Caldeira D, Ferro JM, Ferreira JJ: Does Parkinson's Disease Increase the Risk of Atrial Fibrillation? Insights From Electrocardiogram and Risk Scores From a Case-Control Study. *Front Neurol* 2021; 12:633900.

Antoniak S, Boltzen U, Riad A, Kallwellis-Opara A, Rohde M, Dorner A, Tschope C, Noutsias M, Pauschinger M, Schultheiss HP, Rauch U: Viral myocarditis and coagulopathy: increased tissue factor expression and plasma thrombogenicity. *J Mol Cell Cardiol* 2008; 45:118-126.

Appelman B, Charlton BT, Goulding RP, Kerkhoff TJ, Breedveld EA, Noort W, Offringa C, Bloemers FW, van Weeghel M, Schomakers BV, Coelho P, Posthuma JJ, Aronica E, Wiersinga WJ, van Vugt M, Wüst RCI: Muscle abnormalities worsen after postexertional malaise in long COVID. *Nat Commun* 2024; 15:17.

Arvanitis P, Johansson AK, Frick M, Malmborg H, Gerovasileiou S, Larsson EM, Blomström-Lundqvist C: Recent-onset atrial fibrillation: a study exploring the elements of Virchow's triad after cardioversion. *J Interv Card Electrophysiol* 2022; 64:49-58.

Ayinde H, Schweizer ML, Crabb V, Ayinde A, Abugroun A, Hopson J: Age modifies the risk of atrial fibrillation among athletes: A systematic literature review and meta-analysis. *Int J Cardiol Heart Vasc* 2018; 18:25-29.

Azaña Gómez J, Pérez-Belmonte LM, Rubio-Rivas M, Bascuñana J, Quirós-López R, Martínez MLT, Hernandez EM, Roque-Rojas F, Méndez-Bailón M, Gómez-Huelgas R, SEMI-COVID-19 Group: Mortality risk factors in patients with SARS-CoV-2 infection and atrial fibrillation: Data from the SEMI-COVID-19 registry. *Med Clin (Engl Ed)* 2022; 159:457-464.

B J: Historical aspects and current understanding of the connections and implications of viruses and diabetes: A narrative review. *Clin Epidemiol Global Health* 2022; 16:101110.

Badve MS, Zhou Z, Anderson CS, Hackett ML: Effectiveness and Safety of Antibiotics for Preventing Pneumonia and Improving Outcome after Acute Stroke: Systematic Review and Meta-analysis. *J Stroke Cerebrovasc Dis* 2018; 27:3137-3147.

Badve MS, Zhou Z, van de Beek D, Anderson CS, Hackett ML: Frequency of post-stroke pneumonia: Systematic review and meta-analysis of observational studies. *Int J Stroke* 2019; 14:125-136.

Bagnato G, Imbalzano E, Aragona CO, Ioppolo C, Di Micco P, La Rosa D, Costa F, Micari A, Tomeo S, Zirilli N, Sciacqua A, D'Angelo T, Cacciola I, Bitto A, Irrera N, Russo V, Roberts WN, Gangemi S, Versace AG: New-Onset Atrial Fibrillation and Early Mortality Rate in COVID-19 Patients: Association with IL-6 Serum Levels and Respiratory Distress. *Medicina (Kaunas)* 2022; 58:530.

Bagot CN, Arya R: Virchow and his triad: a question of attribution. *Br J Haematol* 2008; 143:180-190.

Bai Y, Guo SD, Liu Y, Ma CS, Lip GYH: Relationship of troponin to incident atrial fibrillation occurrence, recurrence after radiofrequency ablation and prognosis: a systematic review, meta-analysis and meta-regression. *Biomarkers* 2018; 23:512-517.

Baker M: Genomics: The search for association. *Nature* 2010; 467:1135-1138.

Bao J, Gao Z, Hu Y, Liu W, Ye L, Wang L: Serum fibrinogen-to-albumin ratio predicts new-onset atrial fibrillation risk during hospitalization in patients with acute myocardial infarction after percutaneous coronary intervention: a retrospective study. *BMC Cardiovasc Disord* 2023; 23:432.

Bartsch E, Medcalf KE, Park AL, Ray JG, High Risk of Pre-eclampsia Identification G: Clinical risk factors for pre-eclampsia determined in early pregnancy: systematic review and meta-analysis of large cohort studies. *BMJ* 2016; 353:i1753.

Bashar SK, Hossain MB, Ding E, Walkey AJ, McManus DD, Chon KH: Atrial Fibrillation Detection During Sepsis: Study on MIMIC III ICU Data. *IEEE J Biomed Health Inform* 2020; 24:3124-3135.

Belcher HA, Guthold M, Hudson NE: What is the diameter of a fibrin fiber? *Res Pract Thromb Haemost* 2023; 7:100285.

Benenati S, Canale C, De Marzo V, Della Bona R, Rosa GM, Porto I: Atrial fibrillation and Alzheimer's disease: A conundrum. *Eur J Clin Invest* 2021; 51:e13451.

Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pepin JL, Peppard PE, Sinha S, Tufik S, Valentine K, Malhotra A: Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. *Lancet Respir Med* 2019; 7:687-698.

Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D: Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998; 98:946-952.

Benjamini Y, Hochberg Y: Controlling the False Discovery Rate - a Practical and Powerful Approach to Multiple Testing. *J Roy Stat Soc B Met* 1995; 57:289-300.

Bennett PC, Silverman SH, Gill PS, Lip GYH: Peripheral arterial disease and Virchow's triad. *Thromb Haemost* 2009; 101:1032-1040.

Berman A, Iglesias M, Khanna R, Beaulieu T: The association between COVID-19 infection and incident atrial fibrillation: results from a retrospective cohort study using a large US commercial insurance database. *Open Heart* 2023; 10.

Bezuidenhout J, Venter C, Roberts T, Tarr G, Kell D, Pretorius E: Detection of citrullinated fibrin in plasma clots of RA patients and its relation to altered structural clot properties, disease-related inflammation and prothrombotic tendency. *Front Immunol* 2020; 11:577523.

Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, Moss J, Chahal AA, Anesi G, Denduluri S, Domenico CM, Arkles J, Abella BS, Bullinga JR, Callans DJ, Dixit S, Epstein AE, Frankel DS, Garcia FC, Kumareswaram R, Nazarian S, Riley MP, Santangeli P, Schaller RD, Supple GE, Lin D, Marchlinski F, Deo R: COVID-19 and cardiac arrhythmias. *Heart Rhythm* 2020; 17:1439-1444.

Bilano VL, Ota E, Ganchimeg T, Mori R, Souza JP: Risk factors of pre-eclampsia/eclampsia and its adverse outcomes in low- and middle-income countries: a WHO secondary analysis. *PLoS One* 2014; 9:e91198.

Blaszczyk RT, Gorlo A, Dukacz M, Konopka A, Glowniak A: Association between exposure to air pollution and incidence of atrial fibrillation. *Ann Agric Environ Med* 2023; 30:15-21.

Bohne LJ, Johnson D, Rose RA, Wilton SB, Gillis AM: The Association Between Diabetes Mellitus and Atrial Fibrillation: Clinical and Mechanistic Insights. *Front Physiol* 2019; 10:135.

Bommasani R, Hudson DA, Adeli E, Altman R, Arora S, Arx Sv, Bernstein MS, Bohg J, Bosselut A, Brunskill E, Brynjolfsson E, Buch S, Card D, Castellon R, Chatterji N, Chen A, Creel K, Davis JQ, Demszky D, Donahue C, Doumbouya M, Durmus E, Ermon S, Etchemendy J, Ethayarajh K, Fei-Fei L, Finn C, Gale T, Gillespie L, Goel K, Goodman N, Grossman S, Guha N, Hashimoto T, Henderson P, Hewitt J, Ho DE, Hong J, Hsu K, Huang J, Icard T, Jain S, Jurafsky D, Kalluri P, Karamcheti S, Keeling G, Khani F, Khattab O, Kohd PW, Krass M, Krishna R, Kuditipudi R, Kumar A, Ladhak F, Lee M, Lee T, Leskovec J, Levent I, Li XL, Li X, Ma T, Malik A, Manning CD, Mirchandani S, Mitchell E, Munyikwa Z, Nair S, Narayan A, Narayanan D, Newman B, Nie A, Niebles JC, Nilforoshan H, Nyarko J, Ogut G, Orr L, Papadimitriou I, Park JS, Piech C, Portelance E, Potts C, Raghunathan A, Reich R, Ren H, Rong F, Roohani Y, Ruiz C, Ryan J, Ré C, Sadigh D, Sagawa S, Santhanam K, Shih A, Srinivasan K, Tamkin A, Taori R, Thomas AW, Tramèr F, Wang RE, Wang

W, Wu B, Wu J, Wu Y, Xie S, Yasunaga M, You J, Zaharia M, Zhang M, Zhang T, Zhang X, Zhang Y, Zheng L, Zhou K, Liang P: On the Opportunities and Risks of Foundation Models. *arXiv* 2021:2108.07258.

Bosch NA, Cohen DM, Walkey AJ: Risk Factors for New-Onset Atrial Fibrillation in Patients With Sepsis: A Systematic Review and Meta-Analysis. *Crit Care Med* 2019; 47:280-287.

Broadhurst D, Kell DB: Statistical strategies for avoiding false discoveries in metabolomics and related experiments. *Metabolomics* 2006; 2:171-196.

Bryk AH, Natorska J, Zabczyk M, Zettl K, Wiśniewski JR, Undas A: Plasma fibrin clot proteomics in patients with acute pulmonary embolism: Association with clot properties. *J Proteomics* 2020; 229:103946.

Bustamante A, Garcia-Berrocoso T, Penalba A, Giralt D, Simats A, Muchada M, Zapata E, Rubiera M, Montaner J: Sepsis biomarkers reprofiling to predict stroke-associated infections. *J Neuroimmunol* 2017; 312:19-23.

Buzan T: *How to mind map*. London: Thorsons, 2002.

Caggiu E, Arru G, Hosseini S, Niegowska M, Sechi G, Zarbo IR, Sechi LA: Inflammation, Infectious Triggers, and Parkinson's Disease. *Front Neurol* 2019; 10.

Calderón-Garcidueñas L, Solt AC, Henriquez-Roldán C, Torres-Jardon R, Nuse B, Herritt L, Villarreal-Calderón R, Osnaya N, Stone I, Garcia R, Brooks DM, González-Maciel A, Reynoso-Robles R, Delgado-Chávez R, Reed W: Long-term air pollution exposure is associated with neuroinflammation, an altered innate immune response, disruption of the blood-brain barrier, ultrafine particulate deposition, and accumulation of amyloid beta-42 and alpha-synuclein in children and young adults. *Toxicol Pathol* 2008; 36:289-310.

Camacho EM, Lip GYH: Estimating the impact of implementing an integrated care management approach with Atrial fibrillation Better Care (ABC) pathway for patients with atrial fibrillation in England from 2020-2040. *European Heart Journal - Quality of Care and Clinical Outcomes* 2023.

Camino JD, Gracia P, Cremades N: The role of water in the primary nucleation of protein amyloid aggregation. *Biophys Chem* 2021; 269:106520.

Cannon T, Gruenheid S: Microbes and Parkinson's disease: from associations to mechanisms. *Trends Microbiol* 2022; 30:749-760.

Cano-Gamez E, Burnham KL, Goh C, Allcock A, Malick ZH, Overend L, Kwok A, Smith DA, Peters-Sengers H, Antcliffe D, GAinS Investigators, McKechnie S, Scicluna BP, van der Poll T, Gordon AC, Hinds CJ, Davenport EE, Knight JC, Webster N, Galley H, Taylor J, Hall S, Addison J, Roughton S, Tennant H, Guleri A, Waddington N, Arawwawala D, Durcan J, Short A, Swan K, Williams S, Smolen S, Mitchell-Inwang C, Gordon T, Errington E, Templeton M, Venatesh P, Ward G, McCauley M, Baudouin S, Higham C, Soar J, Grier S, Hall E, Brett S, Kitson D, Wilson R, Mountford L, Moreno J, Hall P, Hewlett J, McKechnie S, Garrard C, Millo J, Young D, Hutton P, Parsons P, Smiths A, Faras-Arraya R, Soar J, Raymode P, Thompson J, Bowrey S, Kazembe S, Rich N, Andreou P, Hales D, Roberts E, Fletcher S, Rosbergen M, Glister G, Cuesta JM, Bion J, Millar J, Perry EJ, Willis H, Mitchell N, Ruel S, Carrera R, Wilde J, Nilson A, Lees S, Kapila A, Jacques N, Atkinson J, Brown A, Prowse H, Krige A, Bland M, Bullock L, Harrison D, Mills G, Humphreys J, Armitage K, Laha S, Baldwin J, Walsh A, Doherty N, Drage S, Ortiz-Ruiz de Gordoa L, Lowes S, Higham C, Walsh H, Calder V, Swan C, Payne H, Higgins D, Andrews S, Mappleback S, Hind C, Garrard C, Watson D, McLees E, Purdy A, Stotz M, Ochelli-Okpue A, Bonner S, Whitehead I, Hugil K, Goodridge V, Cawthor L, Kuper M, Pahary S, Bellingan G, Marshall R, Montgomery H, Ryu JH, Bercades G, Boluda S, Bentley A, McCalman K, Jefferies F, Knight J, Davenport E, Burnham K, Maugeri N, Radhakrishnan J, Mi Y, Allcock A, Goh C: An immune dysfunction score for stratification of patients with acute infection based on whole-blood gene expression. *Sci Transl Med* 2022; 14:eabq4433.

Carbillon L, Fermaut M, Benbara A, Boujenah J: COVID-19, Virchow's triad and thromboembolic risk in obese pregnant women. *Clin Cardiol* 2021; 44:593-594.

Carr ME, Jr., Alving BM: Effect of fibrin structure on plasmin-mediated dissolution of plasma clots. *Blood Coag Fibrinol* 1995; 6:567-573.

Cawood EE, Karamanos TK, Wilson AJ, Radford SE: Visualizing and trapping transient oligomers in amyloid assembly pathways. *Biophys Chem* 2021; 268:106505.

Cereja F, Alves M, Ferreira JJ, Caldeira D: Atrial fibrillation risk on Parkinson's disease - a systematic review and meta-analysis. *J Thromb Thrombolysis* 2023; 55:747-750.

Cerqueira E, Marinho DA, Neiva HP, Lourenco O: Inflammatory Effects of High and Moderate Intensity Exercise-A Systematic Review. *Front Physiol* 2019; 10:1550.

Chao TF, Joung B, Takahashi Y, Lim TW, Choi EK, Chan YH, Guo Y, Sriratanasathavorn C, Oh S, Okumura K, Lip GYH: 2021 Focused Update Consensus Guidelines of the Asia Pacific Heart Rhythm Society on Stroke Prevention in Atrial Fibrillation: Executive Summary. *Thromb Haemost* 2022; 122:20-47.

Chi EY, Frey SL, Winans A, Lam KL, Kjaer K, Majewski J, Lee KY: Amyloid-beta fibrillogenesis seeded by interface-induced peptide misfolding and self-assembly. *Biophys J* 2010; 98:2299-2308.

Chiner E, Llombart M, Valls J, Pastor E, Sancho-Chust JN, Andreu AL, Sanchez-de-la-Torre M, Barbe F: Association between Obstructive Sleep Apnea and Community-Acquired Pneumonia. *PLoS One* 2016; 11:e0152749.

Choi J, Lee SR, Choi EK, Lee H, Han M, Ahn HJ, Kwon S, Lee SW, Han KD, Oh S, Lip GYH: Accumulated hypertension burden on atrial fibrillation risk in diabetes mellitus: a nationwide population study. *Cardiovasc Diabetol* 2023; 22:12.

Christophersen IE, Budtz-Jorgensen E, Olesen MS, Haunso S, Christensen K, Svendsen JH: Familial atrial fibrillation predicts increased risk of mortality: a study in Danish twins. *Circ Arrhythm Electrophysiol* 2013; 6:10-15.

Christophersen IE, Ravn LS, Budtz-Jørgensen E, Skytthe A, Haunsø S, Svendsen JH, Christensen K: Familial aggregation of atrial fibrillation: a study in Danish twins. *Circ Arrhythm Electrophysiol* 2009; 2:378-383.

Chugh SS, Havmoeller R, Narayanan K, Singh D, Rienstra M, Benjamin EJ, Gillum RF, Kim YH, McAnulty JH, Jr., Zheng ZJ, Forouzanfar MH, Naghavi M, Mensah GA, Ezzati M, Murray CJ: Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation* 2014; 129:837-847.

Chung I, Lip GYH: Virchow's triad revisited: blood constituents. *Pathophysiol Haemost Thromb* 2003; 33:449-454.

Collet JP, Park D, Lesty C, Soria J, Soria C, Montalescot G, Weisel JW: Influence of fibrin network conformation and fibrin fiber diameter on fibrinolysis speed: dynamic and structural approaches by confocal microscopy. *Arterioscler Thromb Vasc Biol* 2000; 20:1354-1361.

Conway EM, Mackman N, Warren RQ, Wolberg AS, Mosnier LO, Campbell RA, Gralinski LE, Rondina MT, van de Veerdonk FL, Hoffmeister KM, Griffin JH, Nugent D, Moon K, Morrissey JH: Understanding COVID-19-associated coagulopathy. *Nat Rev Immunol* 2022; 22:639-649.

Corica B, Bonini N, Imberti JF, Romiti GF, Vitolo M, Attanasio L, Basili S, Freedman B, Potpara TS, Boriani G, Lip GYH, Proietti M: Yield of diagnosis and risk of stroke with screening strategies for atrial fibrillation: a comprehensive review of current evidence. *Eur Heart J Open* 2023a; 3:oead031.

Corica B, Romiti GF, Basili S, Proietti M: Prevalence of New-Onset Atrial Fibrillation and Associated Outcomes in Patients with Sepsis: A Systematic Review and Meta-Analysis. *J Pers Med* 2022; 12:547.

Corica B, Tartaglia F, Oliva A, Raparelli V, Cangemi R, Basili S, Lip GYH, Proietti M, Romiti GF: Prevalence of new-onset atrial fibrillation in hospitalized patients with community-acquired pneumonia: a systematic review and meta-analysis. *Intern Emerg Med* 2023b; 18:127-135.

Cortés, M., Arbucci R, Lambardi F, Furmento J, Muñoz F, Viruel M, Alexander B, Baranchuk A, Costabel JP: High-Sensitivity Troponin T For The Risk Assessment Of Patients With Acute Atrial Fibrillation. *Curr Probl Cardiol* 2022; 47:101079.

Costabel JP, Burgos LM, Trivi M: The Significance Of Troponin Elevation In Atrial Fibrillation. *J Atr Fibrillation* 2017; 9:1530.

Craighead JE: The role of viruses in the pathogenesis of pancreatic disease and diabetes mellitus. *Prog Med Virol* 1975; 19:161-214.

Crystal AS, Giasson BI, Crowe A, Kung MP, Zhuang ZP, Trojanowski JQ, Lee VM: A comparison of amyloid fibrillogenesis using the novel fluorescent compound K114. *J Neurochem* 2003; 86:1359-1368.

da Rocha AL, Pinto AP, Kohama EB, Pauli JR, de Moura LP, Cintra DE, Ropelle ER, da Silva ASR: The proinflammatory effects of chronic excessive exercise. *Cytokine* 2019; 119:57-61.

Dai H, Zhang Q, Much AA, Maor E, Segev A, Beinart R, Adawi S, Lu Y, Bragazzi NL, Wu J: Global, regional, and national prevalence, incidence, mortality, and risk factors for atrial fibrillation, 1990-2017: results from the Global Burden of Disease Study 2017. *Eur Heart J Qual Care Clin Outcomes* 2021; 7:574-582.

Danese E, Montagnana M, Cervellin G, Lippi G: Hypercoagulability, D-dimer and atrial fibrillation: an overview of biological and clinical evidence. *Ann Med* 2014; 46:364-371.

Dardiotis E, Tsouris Z, Mentis AA, Siokas V, Michalopoulou A, Sokratous M, Dastamani M, Bogdanos DP, Deretzi G, Kountouras J: *H. pylori* and Parkinson's disease: Meta-analyses including clinical severity. *Clin Neurol Neurosurg* 2018; 175:16-24.

Darlington A, McCauley MD: Atrial Cardiomyopathy: An Unexplored Limb of Virchow's Triad for AF Stroke Prophylaxis. *Front Cardiovasc Med* 2020; 7:11.

De S, Klenerman D: Imaging individual protein aggregates to follow aggregation and determine the role of aggregates in neurodegenerative disease. *Biochim Biophys Acta Proteins Proteom* 2019; 1867:870-878.

de Waal GM, Engelbrecht L, Davis T, de Villiers WJS, Kell DB, Pretorius E: Correlative Light-Electron Microscopy detects lipopolysaccharide and its association with fibrin fibres in Parkinson's Disease, Alzheimer's Disease and Type 2 Diabetes Mellitus. *Scientific reports* 2018; 8:16798.

Di Lecce VN, Loffredo L, Fimognari FL, Cangemi R, Violi F: Fibrinogen as predictor of ischemic stroke in patients with non-valvular atrial fibrillation. *J Thromb Haemost* 2003; 1:2453-2455.

Ding WY, Gupta D, Lip GYH: Atrial fibrillation and the prothrombotic state: revisiting Virchow's triad in 2020. *Heart* 2020; 106:1463-1468.

Ding WY, Kotalczyk A, Boriani G, Marin F, Blomström-Lundqvist C, Potpara TS, Fauchier L, Lip GYH, ESC-EHRA EORP-AF Long-Term General Registry Investigators: Impact of diabetes on the management and outcomes in atrial fibrillation: an analysis from the ESC-EHRA EORP-AF Long-Term General Registry. *Eur J Intern Med* 2022a; 103:41-49.

Ding WY, Protty MB, Davies IG, Lip GYH: Relationship between lipoproteins, thrombosis, and atrial fibrillation. *Cardiovasc Res* 2022b; 118:716-731.

Djoussé L, Levy D, Benjamin EJ, Blease SJ, Russ A, Larson MG, Massaro JM, D'Agostino RB, Wolf PA, Ellison RC: Long-term alcohol consumption and the risk of atrial fibrillation in the Framingham Study. *Am J Cardiol* 2004; 93:710-713.

Domek M, Li YG, Gumprecht J, Asaad N, Rashed W, Alsheikh-Ali A, Nabrdalik K, Gumprecht J, Zubaid M, Lip GYH: One-year all-cause mortality risk among atrial fibrillation patients in Middle East with and without diabetes: The Gulf SAFE registry. *Int J Cardiol* 2020; 302:47-52.

Downes M, Welters ID, Johnston BW: Study protocol: A systematic review and meta-analysis regarding the influence of coagulopathy and immune activation on new onset atrial fibrillation in patients with sepsis. *PLoS One* 2023; 18:e0290963.

Drabik L, Konieczynska M, Undas A: Clot Lysis Time Predicts Stroke During Anticoagulant Therapy in Patients with Atrial Fibrillation. *Can J Cardiol* 2020; 36:119-126.

Drabik L, Wolkow P, Undas A: Denser plasma clot formation and impaired fibrinolysis in paroxysmal and persistent atrial fibrillation while on sinus rhythm: association with thrombin generation, endothelial injury and platelet activation. *Thromb Res* 2015; 136:408-414.

Drabik L, Wolkow P, Undas A: Fibrin Clot Permeability as a Predictor of Stroke and Bleeding in Anticoagulated Patients With Atrial Fibrillation. *Stroke* 2017; 48:2716-2722.

Duckheim M, Schreieck J: COVID-19 and Cardiac Arrhythmias. *Hamostaseologie* 2021; 41:372-378.

Durand F, Raberin A: Exercise-Induced Hypoxemia in Endurance Athletes: Consequences for Altitude Exposure. *Front Sports Act Living* 2021; 3:663674.

Eaker ED, Sullivan LM, Kelly-Hayes M, D'Agostino RB, Sr., Benjamin EJ: Anger and hostility predict the development of atrial fibrillation in men in the Framingham Offspring Study. *Circulation* 2004; 109:1267-1271.

Ebringer A: *Rheumatoid arthritis and Proteus*. London: Springer, 2012.

Ebringer A, Rashid T: Rheumatoid arthritis is caused by a *Proteus* urinary tract infection. *APMIS* 2014; 122:363-368.

Ebringer A, Rashid T: Rheumatoid arthritis is caused by *Proteus*: the molecular mimicry theory and Karl Popper. *Front Biosci (Elite Ed)* 2009; 1:577-586.

Ebringer A, Rashid T, Wilson C: Rheumatoid arthritis, Proteus, anti-CCP antibodies and Karl Popper. *Autoimmun Rev* 2010; 9:216-223.

Elawad T, Scott G, Bone JN, Elwell H, Lopez CE, Filippi V, Green M, Khalil A, Kinshella MW, Mistry HD, Pickerill K, Shanmugam R, Singer J, Townsend R, Tsigas EZ, Vidler M, Volvert ML, von Dadelszen P, Magee LA, Network P: Risk factors for pre-eclampsia in clinical practice guidelines: Comparison with the evidence. *BJOG* 2024; 131:46-62.

Emdin CA, Wong CX, Hsiao AJ, Altman DG, Peters SAE, Woodward M, Odutayo AA: Atrial fibrillation as risk factor for cardiovascular disease and death in women compared with men: systematic review and meta-analysis of cohort studies. *BMJ* 2016; 532:h7013.

Essien UR, Chiswell K, Kaltenbach LA, Wang TY, Fonarow GC, Thomas KL, Turakhia MP, Benjamin EJ, Rodriguez F, Fang MC, Magnani JW, Yancy CW, Piccini JP, Sr.: Association of Race and Ethnicity With Oral Anticoagulation and Associated Outcomes in Patients With Atrial Fibrillation: Findings From the Get With The Guidelines-Atrial Fibrillation Registry. *JAMA Cardiol* 2022; 7:1207-1217.

Fagihi MHA, Bhattacharjee S: Amyloid Fibrillation of Insulin: Amelioration Strategies and Implications for Translation. *ACS Pharmacol Transl Sci* 2022; 5:1050-1061.

Falsetti L, Viticchi G, Buratti L, Grigioni F, Capucci A, Silvestrini M: Interactions between Atrial Fibrillation, Cardiovascular Risk Factors, and ApoE Genotype in Promoting Cognitive Decline in Patients with Alzheimer's Disease: A Prospective Cohort Study. *J Alzheimers Dis* 2018; 62:713-725.

Farrell DH: gamma' Fibrinogen as a novel marker of thrombotic disease. *Clin Chem Lab Med* 2012; 50:1903-1909.

Feghaly J, Zakka P, London B, MacRae CA, Refaat MM: Genetics of Atrial Fibrillation. *J Am Heart Assoc* 2018; 7:e009884.

Ferri S, Kojima K, Sode K: Review of glucose oxidases and glucose dehydrogenases: a bird's eye view of glucose sensing enzymes. *J Diabetes Sci Technol* 2011; 5:1068-1076.

Flaumenhaft R, Enjyoji K, Schmaier AA: Vasculopathy in COVID-19. *Blood* 2022; 140:222-235.

Freestone B, Chong AY, Nuttall S, Lip GY: Impaired flow mediated dilatation as evidence of endothelial dysfunction in chronic atrial fibrillation: relationship to plasma von Willebrand factor and soluble E-selectin levels. *Thromb Res* 2008a; 122:85-90.

Freestone B, Gustafsson F, Chong AY, Corell P, Kistorp C, Hildebrandt P, Lip GYH: Influence of atrial fibrillation on plasma von willebrand factor, soluble E-selectin, and N-terminal pro B-type natriuretic peptide levels in systolic heart failure. *Chest* 2008b; 133:1203-1208.

Freestone B, Lip GYH: The endothelium and atrial fibrillation. The prothrombotic state revisited. *Hamostaseologie* 2008; 28:207-212.

Friberg L, Rosenqvist M, Lip GYH: Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation: the Swedish Atrial Fibrillation cohort study. *Eur Heart J* 2012; 33:1500-1510.

Frontzek K, Bardelli M, Senatore A, Henzi A, Reimann RR, Bedir S, Marino M, Hussain R, Jurt S, Meisl G, Pedotti M, Mazzola F, Siligardi G, Zerbe O, Losa M, Knowles T, Lakkaraju A, Zhu C, Schwarz P, Hornemann S, Holt MG, Simonelli L, Varani L, Aguzzi A: A conformational switch controlling the toxicity of the prion protein. *Nat Struct Mol Biol* 2022; 29:831-840.

Gando S: Microvascular thrombosis and multiple organ dysfunction syndrome. *Crit Care Med* 2010; 38:S35-S42.

García-Granja PE, Veras C, Aparisi Á, Amat-Santos IJ, Catalá P, Marcos M, Cabezón G, Candela J, Gil JF, Uribarri A, Revilla A, Carrasco M, Gómez I, San Román JA: Atrial fibrillation in patients with SARS-CoV-2 infection. *Med Clin (Engl Ed)* 2021; 157:58-63.

Giannakou K, Evangelou E, Papatheodorou SI: Genetic and non-genetic risk factors for pre-eclampsia: umbrella review of systematic reviews and meta-analyses of observational studies. *Ultrasound Obstet Gynecol* 2018; 51:720-730.

Gillis J, Pavlidis P: "Guilt by association" is the exception rather than the rule in gene networks. *PLoS Comput Biol* 2012; 8:e1002444.

Gonzalez-Gonzalez FJ, Ziccardi MR, McCauley MD: Virchow's Triad and the Role of Thrombosis in COVID-Related Stroke. *Front Physiol* 2021; 12:769254.

Goudis CA, Ketikoglou DG: Obstructive sleep and atrial fibrillation: Pathophysiological mechanisms and therapeutic implications. *Int J Cardiol* 2017; 230:293-300.

Goudis CA, Ntalas IV, Ketikoglou DG: Atrial Fibrillation in Athletes. *Cardiol Rev* 2015; 23:247-251.

Grant PJ: Diabetes mellitus as a prothrombotic condition. *J Intern Med* 2007; 262:157-172.

Grobbelaar LM, Kruger A, Venter C, Burger EM, Laubscher GJ, Maponga TG, Kotze MJ, Kwaan HC, Miller JB, Fulkerson D, Huff W, Chang E, Wiarda G, Bunch CM, Walsh MM, Raza S, Zamlut M, Moore HB, Moore EE, Neal MD, Kell DB, Pretorius E: Relative hypercoagulopathy of the SARS-CoV-2 Beta and Delta variants when compared to the less severe Omicron variants is related to TEG parameters, the extent of fibrin amyloid microclots, and the severity of clinical illness. *Semin Thromb Haemost* 2022; 48:858-868.

Grobbelaar LM, Venter C, Vlok M, Ngoepe M, Laubscher GJ, Lourens PJ, Steenkamp J, Kell DB, Pretorius E: SARS-CoV-2 spike protein S1 induces fibrin(ogen) resistant to fibrinolysis: implications for microclot formation in COVID-19. *Biosci Rep* 2021; 41:BSR20210611.

Grobler C, Maphumulo SC, Grobbelaar LM, Bredenkamp` J, Laubscher J, Lourens PJ, Steenkamp J, Kell DB, Pretorius E: COVID-19: The Rollercoaster of Fibrin(ogen), D-dimer, von Willebrand Factor, P-selectin and Their Interactions with Endothelial Cells, Platelets and Erythrocytes. *Int J Mol Sci* 2020; 21:5168.

Grobler C, van Tongeren M, Gettemans J, Kell D, Pretorius E: Alzheimer-type dementia: a systems view provides a unifying explanation of its development. *J Alz Dis* 2023; 91:43-70.

Gundersen E: Is Diabetes of Infectious Origin? . *J Infect Dis* 1927; 41:197-202.

Gunning M, Pavlidis P: "Guilt by association" is not competitive with genetic association for identifying autism risk genes. *Scientific reports* 2021; 11:15950.

Guthold M, Liu W, Stephens B, Lord ST, Hantgan RR, Erie DA, Taylor RM, Jr., Superfine R: Visualization and mechanical manipulations of individual fibrin fibers suggest that fiber cross section has fractal dimension 1.3. *Biophys J* 2004; 87:4226-4236.

Haak BW, Westendorp WF, van Engelen TSR, Brands X, Brouwer MC, Vermeij JD, Hugenholtz F, Verhoeven A, Derks RJ, Giera M, Nederkoorn PJ, de Vos WM, van de Beek D, Wiersinga WJ: Disruptions of Anaerobic Gut Bacteria Are Associated with Stroke and Post-stroke Infection: a Prospective Case-Control Study. *Transl Stroke Res* 2021; 12:581-592.

Han S, Moon I, Choi EK, Han KD, Cho HC, Lee SY, Yang S, Kwon S, Choi YJ, Lee HJ, Lee E, Lee SR, Oh S: Increased atrial fibrillation risk in Parkinson's disease: A nationwide population-based study. *Ann Clin Transl Neurol* 2021; 8:238-246.

Hariyanto TI, Kurniawan A: Obstructive sleep apnea (OSA) and outcomes from coronavirus disease 2019 (COVID-19) pneumonia: a systematic review and meta-analysis. *Sleep Med* 2021; 82:47-53.

Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Dan GA, Dilaveris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL, Group ESCSD: 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; 42:373-498.

Hong CT, Chan L, Wu D, Chen WT, Chien LN: Association Between Parkinson's Disease and Atrial Fibrillation: A Population-Based Study. *Front Neurol* 2019; 10:22.

Honorato MO, Sousa Filho JT, Honorato Junior LFB, Watanabe N, Goulart GM, Prado RRD: Atrial Fibrillation and Sepsis in Elderly Patients and Their Associaton with In-Hospital Mortality. *Arq Bras Cardiol* 2023; 120:e20220295.

Huang HK, Wang JH, Lei WY, Chen CL, Chang CY, Liou LS: *Helicobacter pylori* infection is associated with an increased risk of Parkinson's disease: A population-based retrospective cohort study. *Parkinsonism Relat Disord* 2018; 47:26-31.

Hull D, Pettifer SR, Kell DB: Defrosting the digital library: bibliographic tools for the next generation web. *PLoS Comput Biol* 2008; 4:e1000204. doi:1000210.1001371/journal.pcbi.1000204.

Huseynov A, Akin I, Duerschmied D, Scharf RE: Cardiac Arrhythmias in Post-COVID Syndrome: Prevalence, Pathology, Diagnosis, and Treatment. *Viruses* 2023; 15.

Iaccarino L, La Joie R, Lesman-Segev OH, Lee E, Hanna L, Allen IE, Hillner BE, Siegel BA, Whitmer RA, Carrillo MC, Gatsonis C, Rabinovici GD: Association Between Ambient Air Pollution and Amyloid Positron Emission Tomography Positivity in Older Adults With Cognitive Impairment. *JAMA Neurol* 2021; 78:197-207.

Iba T, Nagaoka I, Boulat M: The anticoagulant therapy for sepsis-associated disseminated intravascular coagulation. *Thromb Res* 2013; 131:383-389.

Ihara M, Washida K: Linking Atrial Fibrillation with Alzheimer's Disease: Epidemiological, Pathological, and Mechanistic Evidence. *J Alzheimers Dis* 2018; 62:61-72.

Induruwa I, Hennebry E, Hennebry J, Thakur M, Warburton EA, Khadjooi K: Sepsis-driven atrial fibrillation and ischaemic stroke. Is there enough evidence to recommend anticoagulation? *Eur J Intern Med* 2022; 98:32-36.

Invernizzi A, Schiuma M, Parrulli S, Torre A, Zicarelli F, Colombo V, Marini S, Villella E, Bertoni A, Antinori S, Rizzardini G, Galli M, Meroni L, Giacomelli A, Staurenghi G: Retinal vessels modifications in acute and post-COVID-19. *Scientific reports* 2021; 11:19373.

Isaac E, Cooper SM, Jones SA, Loubani M: Do age-associated changes of voltage-gated sodium channel isoforms expressed in the mammalian heart predispose the elderly to atrial fibrillation? *World J Cardiol* 2020; 12:123-135.

Itzhaki RF: Corroboration of a Major Role for Herpes Simplex Virus Type 1 in Alzheimer's Disease. *Front Aging Neurosci* 2018; 10:324.

Itzhaki RF, Cosby SL, Wozniak MA: Herpes simplex virus type 1 and Alzheimer's disease: the autophagy connection. *J Neurovirol* 2008; 14:1-4.

Itzhaki RF, Lathe R: Herpes Viruses and Senile Dementia: First Population Evidence for a Causal Link. *J Alzheimers Dis* 2018; 64:363-366.

Itzhaki RF, Lathe R, Balin BJ, Ball MJ, Braak H, Bearer EL, Bullido MJ, Carter C, Clerici M, Cosby SL, Del Tredici K, Field H, Fulop T, Grassi C, Griffin WST, Haas J, Hudson AP, Kamer A, Kell DB, Licastro F, Letenneur L, Lövheim H, Mancuso R, Miklossy J, Otth C, Palamara AT, Perry G, Preston C, Pretorius E, Strandberg T, Tabet N, Taylor-Robinson SD, Whittum-Hudson JA: Microbes and Alzheimer's Disease. *J Alzheimers Dis* 2016; 51:979-984.

Jackson JJ, Kropp H: beta-Lactam antibiotic-induced release of free endotoxin: in vitro comparison of penicillin-binding protein (PBP) 2-specific imipenem and PBP 3-specific ceftazidime. *J Infect Dis* 1992; 165:1033-1041.

Jang S, Kim EW, Zhang Y, Lee J, Cho SY, Ha J, Kim H, Kim E: Particulate matter increases beta-amyloid and activated glial cells in hippocampal tissues of transgenic Alzheimer's mouse: Involvement of PARP-1. *Biochem Biophys Res Commun* 2018; 500:333-338.

Jean-Baptiste VSE, Xia CQ, Clare-Salzler MJ, Horwitz MS: Type 1 Diabetes and Type 1 Interferonopathies: Localization of a Type 1 Common Thread of Virus Infection in the Pancreas. *EBioMedicine* 2017; 22:10-17.

Jing H, Wu X, Xiang M, Liu L, Novakovic VA, Shi J: Pathophysiological mechanisms of thrombosis in acute and long COVID-19. *Front Immunol* 2022; 13:992384.

Joseph PG, Healey JS, Raina P, Connolly SJ, Ibrahim Q, Gupta R, Avezum A, Dans AL, Lopez-Jaramillo P, Yeates K, Teo K, Douma R, Bahonar A, Chifamba J, Lanas F, Dagenais GR, Lear SA, Kumar R, Kengne AP, Keskinler M, Mohan V, Mony P, Alhabib KF, Huisman H, Iype T, Zatonska K, Ismail R, Kazmi K, Rosengren A, Rahman O, Yusufali A, Wei L, Orlandini A, Islam S, Rangarajan S, Yusuf S, Investigators P: Global variations in the prevalence, treatment, and impact of atrial fibrillation in a multi-national cohort of 153 152 middle-aged individuals. *Cardiovasc Res* 2021; 117:1523-1531.

Kalarus Z, Mairesse GH, Sokal A, Boriani G, Sredniawa B, Casado-Arroyo R, Wachter R, Frommeyer G, Traykov V, Dagres N, Lip GYH, Boersma L, Peichl P, Dobrev D, Bulava A, Blomstrom-Lundqvist C, de Groot NMS, Schnabel R, Heinzel F, Van Gelder IC, Carbuccichio C, Shah D, Eckardt L: Searching for atrial fibrillation: looking harder, looking longer, and in increasingly sophisticated ways. An EHRA position paper. *Europace* 2023; 25:185-198.

Kalra L, Irshad S, Hodsoll J, Simpson M, Gulliford M, Smithard D, Patel A, Rebollo-Mesa I, Investigators S-I: Prophylactic antibiotics after acute stroke for reducing pneumonia in patients with dysphagia (STROKE-

INF): a prospective, cluster-randomised, open-label, masked endpoint, controlled clinical trial. *Lancet* 2015; 386:1835-1844.

Kalstø SM, Siland JE, Rienstra M, Christophersen IE: Atrial Fibrillation Genetics Update: Toward Clinical Implementation. *Front Cardiovasc Med* 2019; 6:127.

Kamath S, Blann AD, Chin BS, Lanza F, Aleil B, Cazenave JP, Lip GYH: A study of platelet activation in atrial fibrillation and the effects of antithrombotic therapy. *Eur Heart J* 2002; 23:1788-1795.

Kannel WB, Abbott RD, Savage DD, McNamara PM: Coronary heart disease and atrial fibrillation: the Framingham Study. *Am Heart J* 1983; 106:389-396.

Kanuri SH, Jayesh Sirrkay P, Ulucay AS: COVID-19 HEART unveiling as atrial fibrillation: pathophysiology, management and future directions for research. *Egypt Heart J* 2023; 75:36.

Karaban K, Slupik D, Reda A, Gajewska M, Rolek B, Borovac JA, Papakonstantinou PE, Bongiovanni D, Ehrlinder H, Parker WAE, Siniarski A, Gasecka A: Coagulation Disorders and Thrombotic Complications in Heart Failure With Preserved Ejection Fraction. *Curr Probl Cardiol* 2024; 49:102127.

Kaura A, Arnold AD, Panoulas V, Glampson B, Davies J, Mulla A, Woods K, Omigie J, Shah AD, Channon KM, Weber JN, Thursz MR, Elliott P, Hemingway H, Williams B, Asselbergs FW, O'Sullivan M, Lord GM, Melikian N, Lefroy DC, Francis DP, Shah AM, Kharbanda R, Perera D, Patel RS, Mayet J: Prognostic significance of troponin level in 3121 patients presenting with atrial fibrillation (The NIHR Health Informatics Collaborative TROP-AF study). *J Am Heart Assoc* 2020; 9:e013684.

Kazemi S, Pourgholaminejad A, Saberi A: Stroke Associated with SARS-CoV-2 Infection and its Pathogenesis: A Systematic Review. *Basic Clin Neurosci* 2021; 12:569-586.

Kell DB: Iron behaving badly: inappropriate iron chelation as a major contributor to the aetiology of vascular and other progressive inflammatory and degenerative diseases. *BMC Med Genom* 2009; 2:2

Kell DB: Metabolites do social networking. *Nat Chem Biol* 2011; 7:7-8.

Kell DB: Towards a unifying, systems biology understanding of large-scale cellular death and destruction caused by poorly liganded iron: Parkinson's, Huntington's, Alzheimer's, prions, bactericides, chemical toxicology and others as examples. *Arch Toxicol* 2010; 577:825-889. .

Kell DB, Heyden EL, Pretorius E: The biology of lactoferrin, an iron-binding protein that can help defend against viruses and bacteria *Frontiers Immunol* 2020a; 11:1221.

Kell DB, Heyden EL, Pretorius E: The biology of lactoferrin, an iron-binding protein that defends against viruses and bacteria. *OSF Preprints* 2020b:https://osf.io/fxudj/.

Kell DB, Kenny LC: A dormant microbial component in the development of pre-eclampsia. *Front Med Obs Gynecol* 2016; 3:60.

Kell DB, Knowles JD: The role of modeling in systems biology. In Szallasi Z, Stelling J, Periwal V (eds.): *System modeling in cellular biology: from concepts to nuts and bolts*. Cambridge: MIT Press, 2006:3-18.

Kell DB, Laubscher GJ, Pretorius E: A central role for amyloid fibrin microclots in long COVID/PASC: origins and therapeutic implications. *Biochem J* 2022; 479:537-559.

Kell DB, Oliver SG: Here is the evidence, now what is the hypothesis? The complementary roles of inductive and hypothesis-driven science in the post-genomic era. *Bioessays* 2004; 26:99-105.

Kell DB, Pretorius E: Are fibrinaloid microclots a cause of autoimmunity in Long Covid and other post-infection diseases? *Biochem J* 2023; 480:1217-1240.

Kell DB, Pretorius E: No effects without causes. The Iron Dysregulation and Dormant Microbes hypothesis for chronic, inflammatory diseases. *Biol Rev* 2018a; 93:1518-1557.

Kell DB, Pretorius E: The potential role of ischaemia-reperfusion injury in chronic, relapsing diseases such as rheumatoid arthritis, long COVID and ME/CFS: evidence, mechanisms, and therapeutic implications. *Biochem J* 2022; 479:1653-1708.

Kell DB, Pretorius E: Proteins behaving badly. Substoichiometric molecular control and amplification of the initiation and nature of amyloid fibril formation: lessons from and for blood clotting. *Progr Biophys Mol Biol* 2017; 123:16-41.

Kell DB, Pretorius E: Serum ferritin is an important disease marker, and is mainly a leakage product from damaged cells. *Metallomics* 2014; 6:748-773.

Kell DB, Pretorius E: The simultaneous occurrence of both hypercoagulability and hypofibrinolysis in blood and serum during systemic inflammation, and the roles of iron and fibrin(ogen). *Integr Biol* 2015; 7:24-52.

Kell DB, Pretorius E: To what extent are the terminal stages of sepsis, septic shock, SIRS, and multiple organ dysfunction syndrome actually driven by a toxic prion/amyloid form of fibrin? *Semin Thromb Hemost* 2018b; 44:224-238.

Kenny LC, Kell DB: Immunological tolerance, pregnancy and pre-eclampsia: the roles of semen microbes and the father. *Front Med Obs Gynecol* 2018; 4:239.

Kerola AM, Rollefstad S, Semb AG: Atherosclerotic Cardiovascular Disease in Rheumatoid Arthritis: Impact of Inflammation and Antirheumatic Treatment. *Eur Cardiol* 2021; 16:e18.

Khan AA, Lip GYH: The prothrombotic state in atrial fibrillation: pathophysiological and management implications. *Cardiovasc Res* 2019; 115:31-45.

Khan SU, Duran CA, Rahman H, Lekkala M, Saleem MA, Kaluski E: A meta-analysis of continuous positive airway pressure therapy in prevention of cardiovascular events in patients with obstructive sleep apnoea. *Eur Heart J* 2018; 39:2291-2297.

Kim HW, Han M, Jung I, Ahn SS: New-onset atrial fibrillation in seropositive rheumatoid arthritis: association with disease-modifying anti-rheumatic drugs treatment. *Rheumatology (Oxford)* 2023.

Kishore AK, Vail A, Jeans AR, Chamorro A, Di Napoli M, Kalra L, Langhorne P, Roffe C, Westendorp W, Nederkoorn PJ, Garau J, van de Beek D, Montaner J, Woodhead M, Meisel A, Smith CJ, Pneumonia in Stroke Consensus G: Microbiological Etiologies of Pneumonia Complicating Stroke: A Systematic Review. *Stroke* 2018; 49:1602-1609.

Klein Klouwenberg PMC, Frencken JF, Kuipers S, Ong DSY, Peelen LM, van Vught LA, Schultz MJ, van der Poll T, Bonten MJ, Cremer OL, MARS Consortium: Incidence, Predictors, and Outcomes of New-Onset Atrial Fibrillation in Critically Ill Patients with Sepsis. A Cohort Study. *Am J Respir Crit Care Med* 2017; 195:205-211.

Klipp E, Herwig R, Kowald A, Wierling C, Lehrach H: *Systems biology in practice: concepts, implementation and clinical application*. Berlin: Wiley/VCH, 2005.

Kollman JM, Pandi L, Sawaya MR, Riley M, Doolittle RF: Crystal Structure of Human Fibrinogen. *Biochemistry* 2009; 48:3877-3886.

Konieczynska M, Fil K, Bazanek M, Undas A: Prolonged duration of type 2 diabetes is associated with increased thrombin generation, prothrombotic fibrin clot phenotype and impaired fibrinolysis. *Thromb Haemost* 2014; 111:685-693.

Korantzopoulos P, Letsas KP, Tse G, Fragakis N, Goudis CA, Liu T: Inflammation and atrial fibrillation: A comprehensive review. *J Arrhythm* 2018; 34:394-401.

Kruger A, Vlok M, Turner S, Venter C, Laubscher GJ, Kell DB, Pretorius E: Proteomics of fibrin amyloid microclots in Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) shows many entrapped pro-inflammatory molecules that may also contribute to a failed fibrinolytic system. *Cardiovasc Diabetol* 2022; 21:190.

Kuipers S, Klein Klouwenberg PMC, Cremer OL: Incidence, risk factors and outcomes of new-onset atrial fibrillation in patients with sepsis: a systematic review. *Crit Care* 2014; 18:688.

Kuo CT, Chen YL, Hsu WT, How SC, Cheng YH, Hsueh SS, Liu HS, Lin TH, Wu JW, Wang SS: Investigating the effects of erythrosine B on amyloid fibril formation derived from lysozyme. *Int J Biol Macromol* 2017; 98:159-168.

Kwon S, Lee SR, Choi EK, Ahn HJ, Lee SW, Jung JH, Han KD, Oh S, Lip GYH: Association Between Atrial Fibrillation and Diabetes-Related Complications: A Nationwide Cohort Study. *Diabetes Care* 2023; 46:2240-2248.

Lappalainen T, Scott AJ, Brandt M, Hall IM: Genomic Analysis in the Age of Human Genome Sequencing. *Cell* 2019; 177:70-84.

Laubscher GJ, Lourens PJ, Venter C, Kell DB, Pretorius E: TEG®, Microclot and Platelet Mapping for Guiding Early Management of Severe COVID-19 Coagulopathy. *J Clin Med* 2021; 10:5381.

Lee DSM, Damrauer SM, Levin MG: Genetics of atrial fibrillation. *Curr Opin Cardiol* 2023; 38:162-168.

Lee K, Brayboy L, Tripathi A: Pre-eclampsia: a Scoping Review of Risk Factors and Suggestions for Future Research Direction. *Regen Eng Transl Med* 2022; 8:394-406.

Leta V, Urso D, Batzu L, Lau YH, Mathew D, Boura I, Raeder V, Falup-Pecurariu C, van Wamelen D, Ray Chaudhuri K: Viruses, parkinsonism and Parkinson's disease: the past, present and future. *J Neural Transm (Vienna)* 2022; 129:1119-1132.

Levi M: The coagulant response in sepsis and inflammation. *Hamostaseologie* 2010; 30:10-12, 14-16.

Levi M, van der Poll T, ten Cate H, van Deventer SJ: The cytokine-mediated imbalance between coagulant and anticoagulant mechanisms in sepsis and endotoxaemia. *Eur J Clin Invest* 1997; 27:3-9.

Li-Saw-Hee FL, Blann AD, Gurney D, Lip GY: Plasma von Willebrand factor, fibrinogen and soluble P-selectin levels in paroxysmal, persistent and permanent atrial fibrillation. Effects of cardioversion and return of left atrial function. *Eur Heart J* 2001; 22:1741-1747.

Li Q, Lai Y, Gao X, Li X, Deng CY, Guo H, Zhao J, Yang H, Xu Y, Wu S, Xue Y, Rao F: Involvement of plasminogen activator inhibitor-1 and its related molecules in atrial fibrosis in patients with atrial fibrillation. *PeerJ* 2021; 9:e11488.

Li W, Sigley J, Pieters M, Helms CC, Nagaswami C, Weisel JW, Guthold M: Fibrin Fiber Stiffness Is Strongly Affected by Fiber Diameter, but Not by Fibrinogen Glycation. *Biophys J* 2016; 110:1400-1410.

Li X, Gianoulis TA, Yip KY, Gerstein M, Snyder M: Extensive *in vivo* metabolite-protein interactions revealed by large-scale systematic analyses. *Cell* 2010; 143:639-650.

Li X, Ma X: The role of heparin in sepsis: much more than just an anticoagulant. *Br J Haematol* 2017; 179:389-398.

Li X, Snyder M: Metabolites as global regulators: a new view of protein regulation: systematic investigation of metabolite-protein interactions may help bridge the gap between genome-wide association studies and small molecule screening studies. *Bioessays* 2011; 33:485-489.

Li YG, Miyazawa K, Wolff A, Zubaid M, Alsheikh-Ali AA, Sulaiman K, Lip GYH: One-year risks of stroke and mortality in patients with atrial fibrillation from different clinical settings: The Gulf SAFE registry and Darlington AF registry. *Int J Cardiol* 2019; 274:158-162.

Li YG, Xie PX, Alsheikh-Ali AA, AlMahmeed W, Sulaiman K, Asaad N, Liu SW, Zubaid M, Lip GYH: The "obesity paradox" in patients with atrial fibrillation: Insights from the Gulf SAFE registry. *Front Cardiovasc Med* 2022; 9:1032633.

Limphaibool N, Iwanowski P, Holstad MJV, Kobylarek D, Kozubski W: Infectious Etiologies of Parkinsonism: Pathomechanisms and Clinical Implications. *Front Neurol* 2019; 10:652.

Link MS, Luttmann-Gibson H, Schwartz J, Mittleman MA, Wessler B, Gold DR, Dockery DW, Laden F: Acute exposure to air pollution triggers atrial fibrillation. *J Am Coll Cardiol* 2013; 62:816-825.

Lip GYH, Genaidy A, Tran G, Marroquin P, Estes C: Incident atrial fibrillation and its risk prediction in patients developing COVID-19: A machine learning based algorithm approach. *Eur J Intern Med* 2021; 91:53-58.

Lip GYH, Genaidy A, Tran G, Marroquin P, Estes C, Sloop S: Improving Stroke Risk Prediction in the General Population: A Comparative Assessment of Common Clinical Rules, a New Multimorbid Index, and Machine-Learning-Based Algorithms. *Thromb Haemost* 2022a; 122:142-150.

Lip GYH, Lane DA, Lenarczyk R, Boriani G, Doehner W, Benjamin LA, Fisher M, Lowe D, Sacco RL, Schnabel R, Watkins C, Ntaios G, Potpara T: Integrated care for optimizing the management of stroke and associated heart disease: a position paper of the European Society of Cardiology Council on Stroke. *Eur Heart J* 2022b; 43:2442-2460.

Lip GYH, Lenarczyk R, Pastori D, Ntaios G, Doehner W, Schnabel RB: Poststroke Cardiovascular Management: Current Concepts, Integrated Care, and Future Developments. *Curr Probl Cardiol* 2023; 48:101738.

Lip GYH, Lip PL, Zarifis J, Watson RDS, Bareford D, Lowe GDO, Beevers DG: Fibrin D-dimer and beta-thromboglobulin as markers of thrombogenesis and platelet activation in atrial fibrillation. Effects of introducing ultra-low-dose warfarin and aspirin. *Circulation* 1996a; 94:425-431.

Lip GYH, Lowe GD, Rumley A, Dunn FG: Fibrinogen and fibrin D-dimer levels in paroxysmal atrial fibrillation: evidence for intermediate elevated levels of intravascular thrombogenesis. *Am Heart J* 1996b; 131:724-730.

Lip GYH, Lowe GD, Rumley A, Dunn FG: Increased markers of thrombogenesis in chronic atrial fibrillation: effects of warfarin treatment. *Br Heart J* 1995; 73:527-533.

Lip GYH, Nieuwlaat R, Pisters R, Lane DA, Crijns HJGM: Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. *Chest* 2010; 137:263-272.

Lipinski B, Pretorius E: Novel pathway of iron-induced blood coagulation: implications for diabetes mellitus and its complications. *Pol Arch Med Wewn* 2012; 122:115-122.

Lipinski B, Pretorius E, Oberholzer HM, van der Spuy WJ: Interaction of fibrin with red blood cells: the role of iron. *Ultrastruct Pathol* 2012; 36:79-84.

Liu X, Guo L, Xiao K, Zhu W, Liu M, Wan R, Hong K: The obesity paradox for outcomes in atrial fibrillation: Evidence from an exposure-effect analysis of prospective studies. *Obes Rev* 2020; 21:e12970.

Lorenzo-Almorós A, Casado Cerrada J, Álvarez-Sala Walther LA, Méndez Bailón M, Lorenzo González Ó: Atrial Fibrillation and Diabetes Mellitus: Dangerous Liaisons or Innocent Bystanders? *J Clin Med* 2023; 12.

Lowres N, Olivier J, Chao TF, Chen SA, Chen Y, Diederichsen A, Fitzmaurice DA, Gomez-Doblas JJ, Harbison J, Healey JS, Hobbs FDR, Kaasenbrood F, Keen W, Lee VW, Lindholt JS, Lip GYH, Mairesse GH, Mant J, Martin JW, Martin-Rioboó E, McManus DD, Muniz J, Munzel T, Nakamya J, Neubeck L, Orchard JJ, Pérula de Torres LÁ, Proietti M, Quinn FR, Roalfe AK, Sandhu RK, Schnabel RB, Smyth B, Soni A, Tieleman R, Wang J, Wild PS, Yan BP, Freedman B: Estimated stroke risk, yield, and number needed to screen for atrial fibrillation detected through single time screening: a multicountry patient-level meta-analysis of 141,220 screened individuals. *PLoS medicine* 2019; 16:e1002903.

Lucrecia Maria B, Marcelo T, Andreina GR, Juan Pablo C: Prognostic Value of Troponin in Patients with Atrial Fibrillation Admitted to an Emergency Department: Review and Meta-Analysis. *J Atr Fibrillation* 2020; 13:2346.

Luyendyk JP, Schoenecker JG, Flick MJ: The multifaceted role of fibrinogen in tissue injury and inflammation. *Blood* 2019; 133:511-520.

Ma Y, Su B, Li D, Cui F, Tang L, Wang J, Tian Y, Zheng X: Air pollution, genetic susceptibility, and the risk of atrial fibrillation: A large prospective cohort study. *Proc Natl Acad Sci U S A* 2023; 120:e2302708120.

Machano MM, Joho AA: Prevalence and risk factors associated with severe pre-eclampsia among postpartum women in Zanzibar: a cross-sectional study. *BMC Public Health* 2020; 20:1347.

Mandaglio-Collados D, López-Gálvez R, Ruiz-Alcaraz AJ, López-García C, Roldán V, Lip GYH, Marín F, Rivera-Caravaca JM: Impact of particulate matter on the incidence of atrial fibrillation and the risk of adverse clinical outcomes: A review. *Sci Total Environ* 2023; 880:163352.

Mandel HL, Colleen G, Abedian S, Ammar N, Charles Bailey L, Bennett TD, Daniel Brannock M, Brosnahan SB, Chen Y, Chute CG, Divers J, Evans MD, Haendel M, Hall MA, Hirabayashi K, Hornig M, Katz SD, Krieger AC, Loomba J, Lorman V, Mazzotti DR, McMurry J, Moffitt RA, Pajor NM, Pfaff E, Radwell J, Razzaghi H,

Redline S, Seibert E, Sekar A, Sharma S, Thaweethai T, Weiner MG, Jae Yoo Y, Zhou A, Thorpe LE: Risk of post-acute sequelae of SARS-CoV-2 infection associated with pre-coronavirus disease obstructive sleep apnea diagnoses: an electronic health record-based analysis from the RECOVER initiative. *Sleep* 2023; 46.

Manemann SM, Chamberlain AM, Bielinski SJ, Jiang R, Weston SA, Roger VL: Predicting Alzheimer's Disease and Related Dementias in Heart Failure and Atrial Fibrillation. *Am J Med* 2023; 136:302-307.

Marín F, Roldan V, Lip GYH: Fibrinolytic function and atrial fibrillation. *Thromb Res* 2003; 109:233-240.

Marín F, Roldan V, Monmeneu JV, Bodí V, Fernández C, Garía de Burgos F, Marco P, Sogorb F: Prothrombotic state and elevated levels of plasminogen activator inhibitor-1 in mitral stenosis with and without atrial fibrillation. *Am J Cardiol* 1999; 84:862-864, A869.

Marini C, De Santis F, Sacco S, Russo T, Olivieri L, Totaro R, Carolei A: Contribution of atrial fibrillation to incidence and outcome of ischemic stroke: results from a population-based study. *Stroke* 2005; 36:1115-1119.

Marinigh R, Lip GY, Fiotti N, Giansante C, Lane DA: Age as a risk factor for stroke in atrial fibrillation patients: implications for thromboprophylaxis. *J Am Coll Cardiol* 2010; 56:827-837.

Martinez-Naharro A, Baksi AJ, Hawkins PN, Fontana M: Diagnostic imaging of cardiac amyloidosis. *Nat Rev Cardiol* 2020; 17:413-426.

Martinez-Naharro A, Gonzalez-Lopez E, Corovic A, Mirelis JG, Baksi AJ, Moon JC, Garcia-Pavia P, Gillmore JD, Hawkins PN, Fontana M: High Prevalence of Intracardiac Thrombi in Cardiac Amyloidosis. *J Am Coll Cardiol* 2019; 73:1733-1734.

Martinez-Naharro A, Hawkins PN, Fontana M: Cardiac amyloidosis. *Clin Med (Lond)* 2018; 18:s30-s35.

Mehta JL, Calcaterra G, Bassareo PP: COVID-19, thromboembolic risk, and Virchow's triad: Lesson from the past. *Clin Cardiol* 2020; 43:1362-1367.

Mélé N, Turc G: Stroke Associated With Recent *Mycoplasma pneumoniae* Infection: A Systematic Review of Clinical Features and Presumed Pathophysiological Mechanisms. *Front Neurol* 2018; 9:1109.

Meng L, Shen L, Ji HF: Impact of infection on risk of Parkinson's disease: a quantitative assessment of case-control and cohort studies. *J Neurovirol* 2019; 25:221-228.

Meziani F, Gando S, Vincent JL: Should all patients with sepsis receive anticoagulation? Yes. *Intensive Care Med* 2017; 43:452-454.

Michaels TCT, Liu LX, Meisl G, Knowles TPJ: Physical principles of filamentous protein self-assembly kinetics. *J Phys Condens Matter* 2017; 29:153002.

Michaels TCT, Qian D, Šarić A, Vendruscolo M, Linse S, Knowles TPJ: Amyloid formation as a protein phase transition. *Nature Rev Phys* 2023; 5:379-397.

Mickiewicz KM, Kawai Y, Drage L, Gomes MC, Davison F, Pickard R, Hall J, Mostowy S, Aldridge PD, Errington J: Possible role of L-form switching in recurrent urinary tract infection. *Nat Commun* 2019; 10:4379.

Mikkelsen LF, Nordestgaard BG, Schnohr P, Ellervik C: Increased Ferritin Concentration and Risk of Atrial Fibrillation and Heart Failure in Men and Women: Three Studies of the Danish General Population Including 35799 Individuals. *Clin Chem* 2019; 65:180-188.

Miller MA, Cappuccio FP: A systematic review of COVID-19 and obstructive sleep apnoea. *Sleep Med Rev* 2021; 55:101382.

Mouram S, Pannone L, Gauthey A, Sorgente A, Vergara P, Bisignani A, Monaco C, Mojica J, Al Housari M, Miraglia V, Del Monte A, Paparella G, Ramak R, Overeinder I, Bala G, Almorad A, Stroker E, Sieira J, Brugada P, La Meir M, Chierchia GB, de Asmundis C: Incidence and Predictors of Cardiac Arrhythmias in Patients With COVID-19. *Front Cardiovasc Med* 2022; 9:908177.

Mukamal KJ, Tolstrup JS, Friberg J, Gronbaek M, Jensen G: Fibrinogen and albumin levels and risk of atrial fibrillation in men and women (the Copenhagen City Heart Study). *Am J Cardiol* 2006; 98:75-81.

Mukamal KJ, Tolstrup JS, Friberg J, Jensen G, Gronbaek M: Alcohol consumption and risk of atrial fibrillation in men and women: the Copenhagen City Heart Study. *Circulation* 2005; 112:1736-1742.

Murao S, Yamakawa K: A Systematic Summary of Systematic Reviews on Anticoagulant Therapy in Sepsis. *J Clin Med* 2019; 8:1869.

Musikantow DR, Turagam MK, Sartori S, Chu E, Kawamura I, Shivamurthy P, Bokhari M, Oates C, Zhang C, Pumill C, Malick W, Hashemi H, Ruiz-Maya T, Hadley MB, Gandhi J, Sperling D, Whang W, Koruth JS, Langan MN, Sofi A, Gomes A, Harcum S, Cammack S, Ellsworth B, Dukkipati SR, Bassily-Marcus A, Kohli-Seth R, Goldman ME, Halperin JL, Fuster V, Reddy VY: Atrial Fibrillation in Patients Hospitalized With COVID-19: Incidence, Predictors, Outcomes, and Comparison to Influenza. *JACC Clin Electrophysiol* 2021; 7:1120-1130.

Nakase T, Tatewaki Y, Thyreau B, Odagiri H, Tomita N, Yamamoto S, Takano Y, Muranaka M, Taki Y: Impact of atrial fibrillation on the cognitive decline in Alzheimer's disease. *Alzheimers Res Ther* 2023; 15:15.

Naveed Z, Velasquez Garcia HA, Wong S, Wilton J, McKee G, Mahmood B, Binka M, Rasali D, Janjua NZ: Association of COVID-19 Infection With Incident Diabetes. *JAMA Netw Open* 2023; 6:e238866.

Niehues P, Wegner FK, Wolfes J, Willy K, Ellermann C, Vollenberg R, Reinecke H, Rosenow F, Lepper J, Sackarnd J, Eckardt L: Incidence and predictors of cardiac arrhythmias in patients with COVID-19 induced ARDS. *J Cardiol* 2022; 80:298-302.

Nobs SP, Kolodziejczyk AA, Adler L, Horesh N, Botscharnikow C, Herzog E, Mohapatra G, Hejndorf S, Hodgetts RJ, Spivak I, Schorr L, Fluhr L, Kviatcovsky D, Zacharia A, Njuki S, Barasch D, Stettner N, Dori-Bachash M, Harmelin A, Brandis A, Mehlman T, Erez A, He Y, Ferrini S, Puschhof J, Shapiro H, Kopf M, Moussaieff A, Abdeen SK, Elinav E: Lung dendritic-cell metabolism underlies susceptibility to viral infection in diabetes. *Nature* 2023; 624:645-652.

Notkins AL: Virus-induced diabetes mellitus. *Arch Virol* 1977; 54:1-17.

Nunes JM, Kell DB, Pretorius E: Cardiovascular and haematological pathology in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS): a role for Viruses. *Blood Rev* 2023; 60:101075.

Nunes JM, Kruger A, Proal A, Kell DB, Pretorius E: The Occurrence of Hyperactivated Platelets and Fibrinaloid Microclots in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). *Pharmaceuticals (Basel)* 2022; 15:931.

Odutayo A, Wong CX, Hsiao AJ, Hopewell S, Altman DG, Emdin CA: Atrial fibrillation and risks of cardiovascular disease, renal disease, and death: systematic review and meta-analysis. *BMJ* 2016; 354:i4482.

Okafor C, Byrnes J, Stewart S, Scuffham P, Afoakwah C: Cost Effectiveness of Strategies to Manage Atrial Fibrillation in Middle- and High-Income Countries: A Systematic Review. *Pharmacoeconomics* 2023; 41:913-943.

Oliver SG: Guilt-by-association goes global. *Nature* 2000; 403:601-603.

Opal SM, Horn DL, Palardy JE, Parejo N, Jhung J, Bhattacharjee A, Young LD: The *in vivo* significance of antibiotic-induced endotoxin release in experimental Gram-negative sepsis. *J Endotox Res* 1996; 3:245-252.

Overvad TF, Rasmussen LH, Skjøth F, Overvad K, Lip GYH, Larsen TB: Body mass index and adverse events in patients with incident atrial fibrillation. *Am J Med* 2013; 126:640 e649-617.

Ozdemir H, Sagris D, Lip GYH, Abdul-Rahim AH: Stroke in Atrial Fibrillation and Other Atrial Dysrhythmias. *Curr Cardiol Rep* 2023; 25:357-369.

Palladini G, Merlini G: Systemic amyloidoses: what an internist should know. *Eur J Intern Med* 2013; 24:729-739.

Palsson BØ: *Systems biology: properties of reconstructed networks*. Cambridge: Cambridge University Press, 2006.

Pan Y, Wang Y, Wang Y: Investigation of Causal Effect of Atrial Fibrillation on Alzheimer Disease: A Mendelian Randomization Study. *J Am Heart Assoc* 2020; 9:e014889.

Panchal G, Mahmood M, Lip GYH: Revisiting the risks of incident atrial fibrillation: a narrative review. Part 1. *Kardiol Pol* 2019a; 77:430-436.

Panchal G, Mahmood M, Lip GYH: Revisiting the risks of incident atrial fibrillation: a narrative review. Part 2. *Kardiol Pol* 2019b; 77:515-524.

Papanastasiou CA, Theochari CA, Zareifopoulos N, Arfaras-Melainis A, Giannakoulas G, Karamitsos TD, Palaiodimos L, Ntaios G, Avgerinos KI, Kapogiannis D, Kokkinidis DG: Atrial Fibrillation Is Associated with Cognitive Impairment, All-Cause Dementia, Vascular Dementia, and Alzheimer's Disease: a Systematic Review and Meta-Analysis. *J Gen Intern Med* 2021; 36:3122-3135.

Paquissi FC: The Predictive Role of Inflammatory Biomarkers in Atrial Fibrillation as Seen through Neutrophil-Lymphocyte Ratio Mirror. *J Biomark* 2016; 2016:8160393.

Pardo Sanz A, Salido Tahoces L, Ortega Pérez R, González Ferrer E, Sánchez Recalde Á, Zamorano Gómez JL: New-onset atrial fibrillation during COVID-19 infection predicts poor prognosis. *Cardiol J* 2021; 28:34-40.

Pari B, Babbili A, Kattubadi A, Thakre A, Thotamgari S, Gopinathannair R, Olshansky B, Dominic P: COVID-19 Vaccination and Cardiac Arrhythmias: A Review. *Curr Cardiol Rep* 2023; 25:925-940.

Petsko GA: Guilt by association. *Genome Biol* 2009; 10:104.

Pollock KG, Sekelj S, Johnston E, Sandler B, Hill NR, Ng FS, Khan S, Nassar A, Farooqui U: Application of a machine learning algorithm for detection of atrial fibrillation in secondary care. *Int J Cardiol Heart Vasc* 2020; 31:100674.

Powers SK, Deminice R, Ozdemir M, Yoshihara T, Bomkamp MP, Hyatt H: Exercise-induced oxidative stress: Friend or foe? *J Sport Health Sci* 2020; 9:415-425.

Pretorius E: The use of a desktop scanning electron microscope as a diagnostic tool in studying fibrin networks of thrombo-embolic ischemic stroke. *Ultrastruct Pathol* 2011; 35:245-250.

Pretorius E, Akeredolu O-O, Soma P, Kell DB: Major involvement of bacterial components in rheumatoid arthritis and its accompanying oxidative stress, systemic inflammation and hypercoagulability. *Exp Biol Med* 2017a; 242:355-373.

Pretorius E, Bester J, Kell DB: A bacterial component to Alzheimer-type dementia seen via a systems biology approach that links iron dysregulation and inflammagen shedding to disease *J Alzheimers Dis* 2016a; 53:1237-1256.

Pretorius E, Bester J, Page MJ, Kell DB: The potential of LPS-binding protein to reverse amyloid formation in plasma fibrin of individuals with Alzheimer-type dementia. *Frontiers Aging Neurosci* 2018a; 10:257.

Pretorius E, Bester J, Page MJ, Kell DB: Reversal of amyloid formation in the plasma fibrin of individuals with Alzheimer-type dementia using LPS-binding protein *J Alzheimers Dis* 2018b.

Pretorius E, Bester J, Vermeulen N, Alummoottil S, Soma P, Buys AV, Kell DB: Poorly controlled type 2 diabetes is accompanied by significant morphological and ultrastructural changes in both erythrocytes and in thrombin-generated fibrin: implications for diagnostics. *Cardiovasc Diabetol* 2015; 13:30.

Pretorius E, Bronkhorst P, Briedenhann S, Smit E, Franz RC: Comparisons of the fibrin networks during pregnancy, nonpregnancy and pregnancy during dysfibrinogenaemia using the scanning electron microscope. *Blood Coag Fibrinol* 2009; 20:12-16.

Pretorius E, Kell DB: Diagnostic morphology: biophysical indicators for iron-driven inflammatory diseases. *Integrative Biol* 2014; 6:486-510.

Pretorius E, Kell DB: A perspective on how microscopy imaging of fibrinaloid microclots and platelet pathology may be applied in clinical investigations. *Semin Thromb Haemost* 2023:DOI: 10.1055/s-0043-1774796.

Pretorius E, Mbotwe S, Bester J, Robinson C, Kell DB: Acute induction of anomalous blood clotting by highly substoichiometric levels of bacterial lipopolysaccharide (LPS). bioRxiv version. *bioRxiv* 2016b:2016-053538v053531.

Pretorius E, Mbotwe S, Bester J, Robinson CJ, Kell DB: Acute induction of anomalous and amyloidogenic blood clotting by molecular amplification of highly substoichiometric levels of bacterial lipopolysaccharide. *J R Soc Interface* 2016c; 123:20160539.

Pretorius E, Mbotwe S, Kell DB: Lipopolysaccharide-binding protein (LBP) reverses the amyloid state of fibrin seen in plasma of type 2 diabetics with cardiovascular comorbidities. *Scientific reports* 2017b; 7:9680.

Pretorius E, Oberholzer HM, van der Spuy WJ, Meiring JH: The changed ultrastructure of fibrin networks during use of oral contraception and hormone replacement. *J Thromb Thrombolysis* 2010; 30:502-506.

Pretorius E, Oberholzer HM, van der Spuy WJ, Swanepoel AC, Soma P: Qualitative scanning electron microscopy analysis of fibrin networks and platelet abnormalities in diabetes. *Blood Coagul Fibrinol* 2011a; 22:463-467.

Pretorius E, Oberholzer HM, van der Spuy WJ, Swanepoel AC, Soma P: Scanning electron microscopy of fibrin networks in rheumatoid arthritis: a qualitative analysis. *Rheumatol Int* 2012; 32:1611-1615.

Pretorius E, Page MJ, Engelbrecht L, Ellis GC, Kell DB: Substantial fibrin amyloidogenesis in type 2 diabetes assessed using amyloid-selective fluorescent stains. *Cardiovasc Diabetol* 2017c; 16:141.

Pretorius E, Page MJ, Hendricks L, Nkosi NB, Benson SR, Kell DB: Both lipopolysaccharide and lipoteichoic acids potently induce anomalous fibrin amyloid formation: assessment with novel Amytracker™ stains. *J R Soc Interface* 2018c; 15:20170941.

Pretorius E, Page MJ, Mbotwe S, Kell DB: Lipopolysaccharide-binding protein (LBP) can reverse the amyloid state of fibrin seen or induced in Parkinson's disease. *PlosOne* 2018d; 13:e0192121.

Pretorius E, Steyn H, Engelbrecht M, Swanepoel AC, Oberholzer HM: Differences in fibrin fiber diameters in healthy individuals and thromboembolic ischemic stroke patients. *Blood Coagul Fibrinolysis* 2011b; 22:696-700.

Pretorius E, Swanepoel AC, Oberholzer HM, van der Spuy WJ, Duim W, Wessels PF: A descriptive investigation of the ultrastructure of fibrin networks in thrombo-embolic ischemic stroke. *J Thromb Thrombolysis* 2011c; 31:507-513.

Pretorius E, Venter C, Laubscher GJ, Kotze MJ, Oladejo S, Watson LR, Rajaratnam K, Watson BW, Kell DB: Prevalence of symptoms, comorbidities, fibrin amyloid microclots and platelet pathology in individuals with Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) *Cardiovasc Diabetol* 2022; 21:148.

Pretorius E, Venter C, Laubscher GJ, Lourens PJ, Steenkamp J, Kell DB: Prevalence of readily detected amyloid blood clots in 'unclotted' Type 2 Diabetes Mellitus and COVID-19 plasma: A preliminary report. *Cardiovasc Diabetol* 2020; 19:193.

Pretorius E, Vermeulen N, Bester J, Lipinski B, Kell DB: A novel method for assessing the role of iron and its functional chelation in fibrin fibril formation: the use of scanning electron microscopy. *Toxicol Mech Methods* 2013; 23:352-359.

Pretorius E, Vlok M, Venter C, Bezuidenhout JA, Laubscher GJ, Steenkamp J, Kell DB: Persistent clotting protein pathology in Long COVID/ Post-Acute Sequelae of COVID-19 (PASC) is accompanied by increased levels of antiplasmin. *Cardiovasc Diabetol* 2021; 20:172.

Pretorius M, Donahue BS, Yu C, Greelish JP, Roden DM, Brown NJ: Plasminogen activator inhibitor-1 as a predictor of postoperative atrial fibrillation after cardiopulmonary bypass. *Circulation* 2007; 116:I1-7.

Proietti M, Boriani G: Obesity Paradox in Atrial Fibrillation: Implications for Outcomes and Relationship with Oral Anticoagulant Drugs. *Am J Cardiovasc Drugs* 2020; 20:125-137.

Proietti M, Guiducci E, Cheli P, Lip GY: Is There an Obesity Paradox for Outcomes in Atrial Fibrillation? A Systematic Review and Meta-Analysis of Non-Vitamin K Antagonist Oral Anticoagulant Trials. *Stroke* 2017; 48:857-866.

Proietti M, Romiti GF: Management of Ventricular Heart Rate in Atrial Fibrillation Patients With Sepsis. *Chest* 2021; 159:1315-1316.

Proietti R, AlTurki A, Vio R, Licchelli L, Rivezzi F, Marafi M, Russo V, Potpara TS, Kalman JM, de Villers-Sidani E, Bunch TJ: The association between atrial fibrillation and Alzheimer's disease: fact or fallacy? A systematic review and meta-analysis. *J Cardiovasc Med (Hagerstown)* 2020; 21:106-112.

Qi W, Liu J, Li A: Effect of Anticoagulant Versus Non-Anticoagulant Therapy on Mortality of Sepsis-Induced Disseminated Intravascular Coagulation: A Systematic Review and Meta-Analysis. *Clin Appl Thromb Hemost* 2023; 29:10760296231157766.

Qureshi A, Lip GYH, Nordsletten DA, Williams SE, Aslanidi O, de Vecchi A: Imaging and biophysical modelling of thrombogenic mechanisms in atrial fibrillation and stroke. *Front Cardiovasc Med* 2022; 9:1074562.

Qureshi WT, Alirhayim Z, Blaha MJ, Juraschek SP, Keteyian SJ, Brawner CA, Al-Mallah MH: Cardiorespiratory Fitness and Risk of Incident Atrial Fibrillation: Results From the Henry Ford Exercise Testing (FIT) Project. *Circulation* 2015; 131:1827-1834.

Rafaqat S, Afzal S, Khurshid H, Safdar S, Rafaqat S, Rafaqat S: The Role of Major Inflammatory Biomarkers in the Pathogenesis of Atrial Fibrillation. *J Innov Card Rhythm Manag* 2022; 13:5265-5277.

Rajsfus BF, Mohana-Borges R, Allonso D: Diabetogenic viruses: linking viruses to diabetes mellitus. *Heliyon* 2023; 9:e15021.

Rav-Acha M, Orlev A, Itzhaki I, Zimmerman SF, Fteiha B, Bohm D, Kurd R, Samuel TY, Asher E, Helviz Y, Glikson M, Michowitz Y: Cardiac arrhythmias amongst hospitalised Coronavirus 2019 (COVID-19) patients: Prevalence, characterisation, and clinical algorithm to classify arrhythmic risk. *Int J Clin Pract* 2021; 75:e13788.

Rizwan A, Zoha A, Mabrouk IB, Sabbour HM, Al-Sumaiti AS, Alomainy A, Imran MA, Abbasi QH: A Review on the State of the Art in Atrial Fibrillation Detection Enabled by Machine Learning. *IEEE Rev Biomed Eng* 2021; 14:219-239.

Rodríguez-Reyes H, Lara-Vaca S, Ochoa-Guzmán A, Chiquete E, Registro Mexicano de Fibrilación Auricular Study Group: Obesity Paradox and 12 Month Outcome in Patients with Atrial Fibrillation. *Arch Med Res* 2021; 52:233-239.

Romiti GF, Guo Y, Corica B, Proietti M, Zhang H, Lip GYH, mAF-App II trial investigators: Mobile Health-Technology-Integrated Care for Atrial Fibrillation: A Win Ratio Analysis from the mAFA-II Randomized Clinical Trial. *Thromb Haemost* 2023; 123:1042-1048.

Romiti GF, Pastori D, Rivera-Caravaca JM, Ding WY, Gue YX, Menichelli D, Gumprecht J, Koziel M, Yang PS, Guo Y, Lip GYH, Proietti M: Adherence to the 'Atrial Fibrillation Better Care' Pathway in Patients with Atrial Fibrillation: Impact on Clinical Outcomes-A Systematic Review and Meta-Analysis of 285,000 Patients. *Thromb Haemost* 2022a; 122:406-414.

Romiti GF, Proietti M, Bonini N, Ding WY, Boriani G, Huisman MV, Lip GYH, Investigators G-A: Clinical Complexity Domains, Anticoagulation, and Outcomes in Patients with Atrial Fibrillation: A Report from the GLORIA-AF Registry Phase II and III. *Thromb Haemost* 2022b; 122:2030-2041.

Rong JC, Chen XD, Jin NK, Hong J: Exploring the causal association of rheumatoid arthritis with atrial fibrillation: a Mendelian randomization study. *Clin Rheumatol* 2023.

Roselli C, Chaffin MD, Weng LC, Aeschbacher S, Ahlberg G, Albert CM, Almgren P, Alonso A, Anderson CD, Aragam KG, Arking DE, Barnard J, Bartz TM, Benjamin EJ, Bihlmeyer NA, Bis JC, Bloom HL, Boerwinkle E, Bottinger EB, Brody JA, Calkins H, Campbell A, Cappola TP, Carlquist J, Chasman DI, Chen LY, Chen YI, Choi EK, Choi SH, Christophersen IE, Chung MK, Cole JW, Conen D, Cook J, Crijns HJ, Cutler MJ, Damrauer SM, Daniels BR, Darbar D, Delgado G, Denny JC, Dichgans M, Dörr M, Dudink EA, Dudley SC, Esa N, Esko T, Eskola M, Fatkin D, Felix SB, Ford I, Franco OH, Geelhoed B, Grewal RP, Gudnason V, Guo X, Gupta N, Gustafsson S, Gutmann R, Hamsten A, Harris TB, Hayward C, Heckbert SR, Hernesniemi J, Hocking LJ, Hofman A, Horimoto A, Huang J, Huang PL, Huffman J, Ingelsson E, Ipek EG, Ito K, Jimenez-Conde J, Johnson R, Jukema JW, Kääb S, Kahonen M, Kamatani Y, Kane JP, Kastrati A, Kathiresan S, Katschnig-Winter P, Kavousi M, Kessler T, Kietselaer BL, Kirchhof P, Kleber ME, Knight S, Krieger JE, Kubo M, Launer LJ, Laurikka J, Lehtimaki T, Leineweber K, Lemaitre RN, Li M, Lim HE, Lin HJ, Lin H, Lind L, Lindgren CM, Lokki ML, London B, Loos RJF, Low SK, Lu Y, Lyytikainen LP, Macfarlane PW, Magnusson PK, Mahajan A, Malik R, Mansur AJ, Marcus GM, Margolin L, Margulies KB, Marz W, McManus DD, Melander O, Mohanty S, Montgomery JA, Morley MP, Morris AP, Muller-Nurasyid M, Natale A, Nazarian S, Neumann B, Newton-Cheh C, Niemeijer MN, Nikus K, Nilsson P, Noordam R, Oellers H, Olesen MS, Orho-Melander M, Padmanabhan S, Pak HN, Pare G, Pedersen NL, Pera J, Pereira A, Porteous D, Psaty BM, Pulit SL, Pullinger CR, Rader DJ, Refsgaard L, Ribases M, Ridker PM, Rienstra M, Risch L, Roden DM, Rosand J, Rosenberg MA, Rost N, Rotter JI, Saba S, Sandhu RK, Schnabel RB, Schramm K, Schunkert H, Schurman C, Scott SA, Seppala I, Shaffer C, Shah S, Shalaby AA, Shim J, Shoemaker MB, Siland JE, Sinisalo J, Sinner MF, Slowik A, Smith AV, Smith BH, Smith JG, Smith JD, Smith NL, Soliman EZ, Sotoodehnia N, Stricker BH, Sun A, Sun H, Svendsen JH, Tanaka T, Tanriverdi K, Taylor KD, Teder-Laving M, Teumer A, Theriault S, Trompet S, Tucker NR, Tveit A, Uitterlinden AG, Van Der Harst P, Van Gelder IC, Van Wagoner DR, Verweij N, Vlachopoulou E, Völker U, Wang B, Weeke PE, Weijs B, Weiss R, Weiss S, Wells QS, Wiggins KL, Wong JA, Woo D, Worrall BB, Yang PS, Yao J, Yoneda ZT,

Zeller T, Zeng L, Lubitz SA, Lunetta KL, Ellinor PT: Multi-ethnic genome-wide association study for atrial fibrillation. *Nat Genet* 2018; 50:1225-1233.

Rousseau BA, Bhaduri-McIntosh S: Inflammation and Epstein-Barr Virus at the Crossroads of Multiple Sclerosis and Post-Acute Sequelae of COVID-19 Infection. *Viruses* 2023; 15:949.

Roy M, Nath AK, Pal I, Dey SG: Second Sphere Interactions in Amyloidogenic Diseases. *Chem Rev* 2022; 122:12132-12206.

Rubini-Costa R, Bermúdez-Jiménez F, Rivera-López R, Sola-García E, Nagib-Raya H, Moreno-Escobar E, López-Zúñiga MÁ, Briones-Través A, Sanz-Herrera F, Sequí-Sabater JM, Romero-Cabrera JL, Maíllo-Seco J, Fernández-Vázquez F, Rivadeneira-Ruiz M, López-Valero L, Gómez-Navarro C, Aparicio-Gómez JA, López MÁ, Tercedor L, Molina-Jiménez M, Macías-Ruiz R, Jiménez-Jáimez J: Prevalence of bleeding secondary to anticoagulation and mortality in patients with atrial fibrillation admitted with SARS-CoV-2 infection. *Med Clin (Barc)* 2022; 158:569-575.

Ruddox V, Sandven I, Munkhaugen J, Skattebu J, Edvardsen T, Otterstad JE: Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: A systematic review and meta-analysis. *Eur J Prev Cardiol* 2017; 24:1555-1566.

Sahu B, Mackos AR, Floden AM, Wold LE, Combs CK: Particulate Matter Exposure Exacerbates Amyloid-beta Plaque Deposition and Gliosis in APP/PS1 Mice. *J Alzheimers Dis* 2021; 80:761-774.

Sandhu RK, Ezekowitz J, Andersson U, Alexander JH, Granger CB, Halvorsen S, Hanna M, Hijazi Z, Jansky P, Lopes RD, Wallentin L: The 'obesity paradox' in atrial fibrillation: observations from the ARISTOTLE (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation) trial. *Eur Heart J* 2016; 37:2869-2878.

Sandhu RK, Ezekowitz JA, Hijazi Z, Westerbergh J, Aulin J, Alexander JH, Granger CB, Halvorsen S, Hanna MS, Lopes RD, Siegbahn A, Wallentin L: Obesity paradox on outcome in atrial fibrillation maintained even considering the prognostic influence of biomarkers: insights from the ARISTOTLE trial. *Open Heart* 2018; 5:e000908.

Scarlatescu E, Tomescu D, Arama SS: Anticoagulant Therapy in Sepsis. The Importance of Timing. *J Crit Care Med (Targu Mures)* 2017; 3:63-69.

Schnabel RB, Haeusler KG, Healey JS, Freedman B, Boriani G, Brachmann J, Brandes A, Bustamante A, Casadei B, Crijns H, Doehner W, Engstrom G, Fauchier L, Friberg L, Gladstone DJ, Glotzer TV, Goto S, Hankey GJ, Harbison JA, Hobbs FDR, Johnson LSB, Kamel H, Kirchhof P, Korompoki E, Krieger DW, Lip GYH, Lochen ML, Mairesse GH, Montaner J, Neubeck L, Ntaios G, Piccini JP, Potpara TS, Quinn TJ, Reiffel JA, Ribeiro ALP, Rienstra M, Rosenqvist M, Themistoclakis S, Sinner MF, Svendsen JH, Van Gelder IC, Wachter R, Wijeratne T, Yan B: Searching for Atrial Fibrillation Poststroke: A White Paper of the AF-SCREEN International Collaboration. *Circulation* 2019; 140:1834-1850.

Schönrich G, Abdelaziz MO, Raftery MJ: Epstein-Barr virus, interleukin-10 and multiple sclerosis: A ménage à trois. *Front Immunol* 2022; 13:1028972.

Sekelj S, Sandler B, Johnston E, Pollock KG, Hill NR, Gordon J, Tsang C, Khan S, Ng FS, Farooqui U: Detecting undiagnosed atrial fibrillation in UK primary care: Validation of a machine learning prediction algorithm in a retrospective cohort study. *Eur J Prev Cardiol* 2021; 28:598-605.

Selewa A, Luo K, Wasney M, Smith L, Sun X, Tang C, Eckart H, Moskowitz IP, Basu A, He X, Pott S: Single-cell genomics improves the discovery of risk variants and genes of atrial fibrillation. *Nat Commun* 2023; 14:4999.

Semb AG, Rollefstad S, Sexton J, Ikdahl E, Crowson CS, van Riel P, Kitas G, Graham I, Kerola AM, Surf-RA: Oral anticoagulant treatment in rheumatoid arthritis patients with atrial fibrillation results of an international audit. *Int J Cardiol Heart Vasc* 2022; 42:101117.

Semczuk-Kaczmarek K, Platek AE, Rys A, Adamowicz J, Legosz P, Kotkowski M, Dudzik-Plocica A, Gorko D, Szymanski FM, Filipiak KJ: CHA2DS2-VASc score and fibrinogen concentration in patients with atrial fibrillation. *Adv Clin Exp Med* 2019; 28:1451-1457.

Sepehri Shamloo A, Arya A, Darma A, Nedios S, Doring M, Bollmann A, Dagres N, Hindricks G: Atrial fibrillation: is there a role for cardiac troponin? *Diagnosis (Berl)* 2021; 8:295-303.

Seuma M, Faure AJ, Badia M, Lehner B, Bolognesi B: The genetic landscape for amyloid beta fibril nucleation accurately discriminates familial Alzheimer's disease mutations. *Elife* 2021; 10:e63364.

Seuma M, Lehner B, Bolognesi B: An atlas of amyloid aggregation: the impact of substitutions, insertions, deletions and truncations on amyloid beta fibril nucleation. *Nat Commun* 2022; 13:7084.

Shao Q, Liu T, Korantzopoulos P, Zhang Z, Zhao J, Li G: Association between air pollution and development of atrial fibrillation: A meta-analysis of observational studies. *Heart Lung* 2016; 45:557-562.

Shim R, Wong CHY: Ischemia, Immunosuppression and Infection--Tackling the Predicaments of Post-Stroke Complications. *Int J Mol Sci* 2016; 17:64.

Siontis KC, Yao X, Pirruccello JP, Philippakis AA, Noseworthy PA: How Will Machine Learning Inform the Clinical Care of Atrial Fibrillation? *Circ Res* 2020; 127:155-169.

Sluis WM, Westendorp WF, van de Beek D, Nederkoorn PJ, van der Worp HB: Preventive ceftriaxone in patients at high risk of stroke-associated pneumonia. A post-hoc analysis of the PASS trial. *PLoS One* 2022; 17:e0279700.

Smeyne RJ, Noyce AJ, Byrne M, Savica R, Marras C: Infection and Risk of Parkinson's Disease. *J Parkinsons Dis* 2021; 11:31-43.

Sohail MU, Mashood F, Oberbach A, Chennakkandathil S, Schmidt F: The role of pathogens in diabetes pathogenesis and the potential of immunoproteomics as a diagnostic and prognostic tool. *Front Microbiol* 2022; 13:1042362.

Sohara H, Amitani S, Kurose M, Miyahara K: Atrial fibrillation activates platelets and coagulation in a time-dependent manner: a study in patients with paroxysmal atrial fibrillation. *J Am Coll Cardiol* 1997; 29:106-112.

Soma P, Pretorius E: Interplay between ultrastructural findings and atherothrombotic complications in type 2 diabetes mellitus. *Cardiovasc Diabetol* 2015; 14:96.

Son MK, Lim NK, Kim HW, Park HY: Risk of ischemic stroke after atrial fibrillation diagnosis: A national sample cohort. *PLoS One* 2017; 12:e0179687.

Sposato LA, Cipriano LE, Saposnik G, Ruiz Vargas E, Riccio PM, Hachinski V: Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. *Lancet Neurol* 2015; 14:377-387.

Staerk L, Sherer JA, Ko D, Benjamin EJ, Helm RH: Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes. *Circ Res* 2017; 120:1501-1517.

Staff AC, Redman CW, Williams D, Leeson P, Moe K, Thilaganathan B, Magnus P, Steegers EA, Tsigas EZ, Ness RB, Myatt L, Poston L, Roberts JM, Global Pregnancy Collaboration: Pregnancy and Long-Term Maternal Cardiovascular Health: Progress Through Harmonization of Research Cohorts and Biobanks. *Hypertension* 2016; 67:251-260.

Su VY, Liu CJ, Wang HK, Wu LA, Chang SC, Perng DW, Su WJ, Chen YM, Lin EY, Chen TJ, Chou KT: Sleep apnea and risk of pneumonia: a nationwide population-based study. *CMAJ* 2014; 186:415-421.

Sun T, Ye M, Lei F, Qin JJ, Liu YM, Chen Z, Chen MM, Yang C, Zhang P, Ji YX, Zhang XJ, She ZG, Cai J, Jin ZX, Li H: Prevalence and trend of atrial fibrillation and its associated risk factors among the population from nationwide health check-up centers in China, 2012-2017. *Front Cardiovasc Med* 2023; 10:1151575.

Swanepoel AC, Lindeque BG, Swart PJ, Abdool Z, Pretorius E: Estrogen causes ultrastructural changes of fibrin networks during the menstrual cycle: a qualitative investigation. *Microsc Res Tech* 2014; 77:594-601.

Swanepoel AC, Visagie A, de Lange Z, Emmerson O, Nielsen VG, Pretorius E: The clinical relevance of altered fibrinogen packaging in the presence of 17beta-estradiol and progesterone. *Thromb Res* 2016; 146:23-34.

Szymanski T, Ashton R, Sekelj S, Petrungaro B, Pollock KG, Sandler B, Lister S, Hill NR, Farooqui U: Budget impact analysis of a machine learning algorithm to predict high risk of atrial fibrillation among primary care patients. *Europace* 2022; 24:1240-1247.

Taylor CG, Meisl G, Horrocks MH, Zetterberg H, Knowles TPJ, Klenerman D: Extrinsic Amyloid-Binding Dyes for Detection of Individual Protein Aggregates in Solution. *Analytical chemistry* 2018; 90:10385-10393.

Thagard P (ed.): *The cognitive science of science: explanation, discovery, and conceptual change*. Cambridge, MA: MIT Press, 2012.

Thagard P: Coherence, truth, and the development of scientific knowledge. *Philosophy of Science* 2007; 74:28-47.

Thagard P: *How scientists explain disease*. Princeton, NJ: Princeton University Press, 1999.

Thakur M, Alsinbili A, Chattopadhyay R, Warburton EA, Khadjooi K, Induruwa I: Identifying the optimal time period for detection of atrial fibrillation after ischaemic stroke and TIA: An updated systematic review and meta-analysis of randomized control trials. *Int J Stroke* 2023:17474930231215277.

Thilaganathan B, Kalafat E: Cardiovascular System in Preeclampsia and Beyond. *Hypertension* 2019; 73:522-531.

Thirupathi A, Pinho RA, Ugbolue UC, He Y, Meng Y, Gu Y: Effect of Running Exercise on Oxidative Stress Biomarkers: A Systematic Review. *Front Physiol* 2020; 11:610112.

Tian W, Zhang LV, Tasan M, Gibbons FD, King OD, Park J, Wunderlich Z, Cherry JM, Roth FP: Combining guilt-by-association and guilt-by-profiling to predict *Saccharomyces cerevisiae* gene function. *Genome Biol* 2008; 9 Suppl 1:S7.

Tilly MJ, Geurts S, Pezzullo AM, Bramer WM, de Groot NMS, Kavousi M, de Maat MPM: The association of coagulation and atrial fibrillation: a systematic review and meta-analysis. *Europace* 2023; 25:28-39.

Todros T, Vasario E, Cardaropoli S: Preeclampsia as an infectious disease. *Exp Rev Obs Gynecol* 2007; 2:735-741.

Todros T, Verdiglione P, Oggè G, Paladini D, Vergani P, Cardaropoli S: Low incidence of hypertensive disorders of pregnancy in women treated with spiramycin for toxoplasma infection. *Br J Clin Pharmacol* 2006; 61:336-340.

Treewaree S, Lip GYH, Krittayaphong R: Non-vitamin K Antagonist Oral Anticoagulant, Warfarin, and ABC Pathway Adherence on Hierarchical Outcomes: Win Ratio Analysis of the COOL-AF Registry. *Thromb Haemost* 2024; 124:69-79.

Tsao CW, Aday AW, Almarzooq ZI, Anderson CAM, Arora P, Avery CL, Baker-Smith CM, Beaton AZ, Boehme AK, Buxton AE, Commodore-Mensah Y, Elkind MSV, Evenson KR, Eze-Nliam C, Fugar S, Generoso G, Heard DG, Hiremath S, Ho JE, Kalani R, Kazi DS, Ko D, Levine DA, Liu J, Ma J, Magnani JW, Michos ED, Mussolino ME, Navaneethan SD, Parikh NI, Poudel R, Rezk-Hanna M, Roth GA, Shah NS, St-Onge MP, Thacker EL, Virani SS, Voeks JH, Wang NY, Wong ND, Wong SS, Yaffe K, Martin SS, American Heart Association Council on E, Prevention Statistics C, Stroke Statistics S: Heart Disease and Stroke Statistics-2023 Update: A Report From the American Heart Association. *Circulation* 2023; 147:e93-e621.

Tseng AS, Noseworthy PA: Prediction of Atrial Fibrillation Using Machine Learning: A Review. *Front Physiol* 2021; 12:752317.

Turner S, Laubscher GJ, Khan MA, Kell DB, Pretorius E: Accelerating discovery: A novel flow cytometric method for detecting fibrin(ogen) amyloid microclots using long COVID as a model *Heliyon* 2023; 9:e19605.

Umemura Y, Nishida T, Yamakawa K, Ogura H, Oda J, Fujimi S: Anticoagulant therapies against sepsis-induced disseminated intravascular coagulation. *Acute Med Surg* 2023; 10:e884.

Umemura Y, Yamakawa K: Optimal patient selection for anticoagulant therapy in sepsis: an evidence-based proposal from Japan. *J Thromb Haemost* 2018; 16:462-464.

Undas A: Fibrin clot properties and their modulation in thrombotic disorders. *Thromb Haemost* 2014; 112:32-42.

van Amstel RBE, Kennedy JN, Scicluna BP, Bos LDJ, Peters-Sengers H, Butler JM, Cano-Gamez E, Knight JC, Vlaar APJ, Cremer OL, Angus DC, van der Poll T, Seymour CW, van Vught LA, Consortium M: Uncovering heterogeneity in sepsis: a comparative analysis of subphenotypes. *Intensive Care Med* 2023; 49:1360-1369.

van den Oord EJ: Controlling false discoveries in genetic studies. *Am J Med Genet B Neuropsychiatr Genet* 2008; 147B:637-644.

van Langevelde P, Kwappenberg KM, Groeneveld PH, Mattie H, van Dissel JT: Antibiotic-induced lipopolysaccharide (LPS) release from *Salmonella typhi*: delay between killing by ceftazidime and imipenem and release of LPS. *Antimicrob Agents Chemother* 1998; 42:739-743.

Vaswani A, Shazeer N, Parmar N, Uszkoreit J, Jones L, Gomez AN, Kaiser L, Polosukhin I: Attention Is All You Need. *arXiv* 2017:1706.03762.

Vermeij FH, Scholte op Reimer WJ, de Man P, van Oostenbrugge RJ, Franke CL, de Jong G, de Kort PL, Dippel DW, Netherlands Stroke Survey I: Stroke-associated infection is an independent risk factor for poor outcome after acute ischemic stroke: data from the Netherlands Stroke Survey. *Cerebrovasc Dis* 2009; 27:465-471.

Vermeij JD, Westendorp WF, Dippel DWJ, van de Beek D, Nederkoorn PJ: Antibiotic therapy for preventing infections in people with acute stroke. *Cochrane Database Syst Rev* 2018; 1:CD008530.

Voy BH, Scharff JA, Perkins AD, Saxton AM, Borate B, Chesler EJ, Branstetter LK, Langston MA: Extracting gene networks for low-dose radiation using graph theoretical algorithms. *PLoS Comput Biol* 2006; 2:e89.

Wadowski PP, Panzer B, Jozkowicz A, Kopp CW, Gremmel T, Panzer S, Koppensteiner R: Microvascular Thrombosis as a Critical Factor in Severe COVID-19. *Int J Mol Sci* 2023; 24:2492.

Walkey AJ, Greiner MA, Heckbert SR, Jensen PN, Piccini JP, Sinner MF, Curtis LH, Benjamin EJ: Atrial fibrillation among Medicare beneficiaries hospitalized with sepsis: incidence and risk factors. *Am Heart J* 2013; 165:949-955 e943.

Wanahita N, Messerli FH, Bangalore S, Gami AS, Somers VK, Steinberg JS: Atrial fibrillation and obesity--results of a meta-analysis. *Am Heart J* 2008; 155:310-315.

Wang A, Green JB, Halperin JL, Piccini JP, Sr.: Atrial Fibrillation and Diabetes Mellitus: JACC Review Topic of the Week. *J Am Coll Cardiol* 2019; 74:1107-1115.

Wang F, Ahat X, Liang Q, Ma Y, Sun M, Lin L, Li T, Duan J, Sun Z: The relationship between exposure to PM(2.5) and atrial fibrillation in older adults: A systematic review and meta-analysis. *Sci Total Environ* 2021; 784:147106.

Wang H, Liu X, Tan C, Zhou W, Jiang J, Peng W, Zhou X, Mo L, Chen L: Bacterial, viral, and fungal infection-related risk of Parkinson's disease: Meta-analysis of cohort and case-control studies. *Brain Behav* 2020; 10:e01549.

Wang TJ, Parise H, Levy D, D'Agostino RB, Sr., Wolf PA, Vasan RS, Benjamin EJ: Obesity and the risk of new-onset atrial fibrillation. *JAMA* 2004; 292:2471-2477.

Watson T, Shantsila E, Lip GYH: Mechanisms of thrombogenesis in atrial fibrillation: Virchow's triad revisited. *Lancet* 2009; 373:155-166.

Weisel JW: Fibrinogen and fibrin. *Adv Protein Chem* 2005; 70:247-299.

Weisel JW, Litvinov RI: Fibrin Formation, Structure and Properties. *Subcell Biochem* 2017; 82:405-456.

Wekerle H: Epstein-Barr virus sparks brain autoimmunity in multiple sclerosis. *Nature* 2022; 603:230-232.

Weng LC, Choi SH, Klarin D, Smith JG, Loh PR, Chaffin M, Roselli C, Hulme OL, Lunetta KL, Dupuis J, Benjamin EJ, Newton-Cheh C, Kathiresan S, Ellinor PT, Lubitz SA: Heritability of Atrial Fibrillation. *Circ Cardiovasc Genet* 2017; 10.

Westendorp WF, Nederkoorn PJ, Vermeij JD, Dijkgraaf MG, van de Beek D: Post-stroke infection: a systematic review and meta-analysis. *BMC Neurol* 2011; 11:110.

Westendorp WF, Vermeij JD, Hilkens NA, Brouwer MC, Algra A, van der Worp HB, Dippel DWJ, van de Beek D, Nederkoorn PJ, PASS-Investigators: Development and internal validation of a prediction rule for post-stroke infection and post-stroke pneumonia in acute stroke patients. *Eur Stroke J* 2018; 3:136-144.

Westendorp WF, Vermeij JD, Smith CJ, Kishore AK, Hodsoll J, Kalra L, Meisel A, Chamorro A, Chang JJ, Rezaei Y, Amiri-Nikpour MR, DeFalco FA, Switzer JA, Blacker DJ, Dijkgraaf MG, Nederkoorn PJ, van de Beek D: Preventive antibiotic therapy in acute stroke patients: A systematic review and meta-analysis of individual patient data of randomized controlled trials. *Eur Stroke J* 2021; 6:385-394.

Westendorp WF, Vermeij JD, Zock E, Hooijenga IJ, Kruyt ND, Bosboom HJLW, Kwa VI, Weisfelt M, Remmers MJM, ten Houten R, Tobien Schreuder AHCM, Vermeer SE, van Dijk EJ, Dippel DW, Dijkgraaf MGW, Spanjaard L, Vermeulen M, van der Poll T, Prins JM, Vermeij FH, Roos YB, Kleyweg RP, Kerkhoff H, Brouwer MC, Zwinderman AH, van de Beek D, Nederkoorn PJ, PASS investigators: The Preventive Antibiotics in Stroke Study (PASS): a pragmatic randomised open-label masked endpoint clinical trial. *Lancet* 2015; 385:1519-1526.

Weymann A, Sabashnikov A, Ali-Hasan-Al-Saegh S, Popov AF, Jalil Mirhosseini S, Baker WL, Lotfaliani M, Liu T, Dehghan H, Yavuz S, de Oliveira Sa MP, Jang JS, Zeriouh M, Meng L, D'Ascenzo F, Deshmukh AJ, Biondi-Zoccai G, Dohmen PM, Calkins H, Surgery C, Cardiology-Group (IMSRC-Group): Predictive Role of Coagulation, Fibrinolytic, and Endothelial Markers in Patients with Atrial Fibrillation, Stroke, and Thromboembolism: A Meta-Analysis, Meta-Regression, and Systematic Review. *Med Sci Monit Basic Res* 2017; 23:97-140.

Wolf PA, Abbott RD, Kannel WB: Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; 22:983-988.

Writing Committee Members, Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, Eckhardt LL, Goldberger ZD, Gopinathannair R, Gorenek B, Hess PL, Hlatky M, Hogan G, Ibeh C, Indik JH, Kido K, Kusumoto F, Link MS, Linta KT, Marcus GM, McCarthy PM, Patel N, Patton KK, Perez MV, Piccini JP, Russo AM, Sanders P, Streur MM, Thomas KL, Times S, Tisdale JE, Valente AM, Van Wagoner DR: 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *J Am Coll Cardiol* 2024; 83:109-279.

Wu L, Jiang Z, Meulendijks ER, Baylan U, Waas ISE, Bugiani M, Tuinman PR, Fronczek J, Heunks LMA, de Groot JR, van Rossum AC, Niessen HWM, Krijnen PAJ: Atrial inflammation and microvascular thrombogenicity are increased in deceased COVID-19 patients. *Cardiovasc Pathol* 2023a; 64:107524.

Wu P, Haththotuwa R, Kwok CS, Babu A, Kotronias RA, Rushton C, Zaman A, Fryer AA, Kadam U, Chew-Graham CA, Mamas MA: Preeclampsia and Future Cardiovascular Health: A Systematic Review and Meta-Analysis. *Circ Cardiovasc Qual Outcomes* 2017; 10.

Wu S, Huang N, Chen X, Jiang S, Zhang W, Hu W, Su J, Dai H, Gu P, Huang X, Du X, Li R, Zheng Q, Lin X, Zhang Y, Zou L, Liu Y, Zhang M, Liu X, Zhu Z, Sun J, Hong S, She W, Zhang J: Association between Body Mass Index and Clinical Outcomes in Patients with Non-valvular Atrial Fibrillation Receiving Direct Oral Anticoagulants: A New Piece of Evidence on the Obesity Paradox from China. *Cardiovasc Drugs Ther* 2023b; 37:715-727.

Xiao FP, Chen MY, Wang L, He H, Jia ZQ, Kuai L, Zhou HB, Liu M, Hong M: Outcomes of new-onset atrial fibrillation in patients with sepsis: A systematic review and meta-analysis of 225,841 patients. *Am J Emerg Med* 2021; 42:23-30.

Xiong Q, Proietti M, Senoo K, Lip GYH: Asymptomatic versus symptomatic atrial fibrillation: A systematic review of age/gender differences and cardiovascular outcomes. *Int J Cardiol* 2015; 191:172-177.

Xiong Z, Liu T, Tse G, Gong M, Gladding PA, Smaill BH, Stiles MK, Gillis AM, Zhao J: A Machine Learning Aided Systematic Review and Meta-Analysis of the Relative Risk of Atrial Fibrillation in Patients With Diabetes Mellitus. *Front Physiol* 2018; 9:835.

Xue Y, Yang N, Gu X, Wang Y, Zhang H, Jia K: Risk Prediction Model of Early-Onset Preeclampsia Based on Risk Factors and Routine Laboratory Indicators. *Life (Basel)* 2023; 13:1648.

Yamashita T: Virchow triad and beyond in atrial fibrillation. *Heart Rhythm* 2016; 13:2377-2378.

Yamauchi K, Furui H, Taniguchi N, Sotobata I: Plasma beta-thromboglobulin and platelet factor 4 concentrations in patients with atrial fibrillation. *Jpn Heart J* 1986; 27:481-487.

Yang XM, Rao ZZ, Gu HQ, Zhao XQ, Wang CJ, Liu LP, Liu C, Wang YL, Li ZX, Xiao RP, Wang YJ: Atrial Fibrillation Known Before or Detected After Stroke Share Similar Risk of Ischemic Stroke Recurrence and Death. *Stroke* 2019; 50:1124-1129.

Yoon JW, Notkins AL: Virus-induced diabetes in mice. *Metabolism* 1983; 32:37-40.

Yu S, Ma X, Li X: Phenotype-oriented anticoagulant therapy for sepsis: still a work in progress. *Int J Hematol* 2022; 116:48-54.

Yue C, Yang F, Li F, Chen Y: Association between air pollutants and atrial fibrillation in general population: A systematic review and meta-analysis. *Ecotoxicol Environ Saf* 2021; 208:111508.

Zamolodchikov D, Strickland S: Abeta delays fibrin clot lysis by altering fibrin structure and attenuating plasminogen binding to fibrin. *Blood* 2012; 119:3342-3351.

Zanini G, Selleri V, Roncati L, Coppi F, Nasi M, Farinetti A, Manenti A, Pinti M, Mattioli AV: Vascular "Long COVID": A New Vessel Disease? *Angiology* 2024; 75:8-14.

Zhang J, Chen G, Xia H, Wang X, Wang C, Cai M, Gao Y, Lip GYH, Lin H: Associations of Life's Essential 8 and fine particulate matter pollution with the incidence of atrial fibrillation. *J Hazard Mater* 2023; 459:132114.

Zhang J, Johnsen SP, Guo Y, Lip GYH: Epidemiology of Atrial Fibrillation: Geographic/Ecological Risk Factors, Age, Sex, Genetics. *Card Electrophysiol Clin* 2021a; 13:1-23.

Zhang L, Ye K, Xiaokereti J, Ma M, Guo Y, Zhou X, Tang B: Histopathological substrate of the atrial myocardium in the progression of obstructive sleep apnoea-related atrial fibrillation. *Sleep Breath* 2021b; 25:807-818.

Zheng H, Stergiopoulos K, Wang L, Chen L, Cao J: COVID-19 Presenting as Major Thromboembolic Events: Virchow's Triad Revisited and Clinical Considerations of Therapeutic Anticoagulation. *Cureus* 2020; 12:e10137.

Zheng Y, Li S, Liu X, Lip GYH, Guo L, Zhu W: Effect of Oral Anticoagulants in Atrial Fibrillation Patients with Polypharmacy: A Meta-analysis. *Thromb Haemost* 2023.

Zhong C, Xin M, He L, Sun G, Shen F: Prognostic value of von Willebrand factor in patients with atrial fibrillation: A meta-analysis. *Medicine (Baltimore)* 2018; 97:e11269.

Zhu W, Wan R, Liu F, Hu J, Huang L, Li J, Hong K: Relation of Body Mass Index With Adverse Outcomes Among Patients With Atrial Fibrillation: A Meta-Analysis and Systematic Review. *J Am Heart Assoc* 2016; 5.

Zuin M, Rigatelli G, Bilato C, Zanon F, Zuliani G, Roncon L: Pre-existing atrial fibrillation is associated with increased mortality in COVID-19 Patients. *J Interv Card Electrophysiol* 2021; 62:231-238.

Zulkifly H, Lip GYH, Lane DA: Epidemiology of atrial fibrillation. *Int J Clin Pract* 2018; 72:e13070.