



Inside Psoriatic Disease

CARDIOVASCULAR DISEASE

Contents

Abbreviations	3
More than skin deep	4
The link between psoriatic disease and CVD	6
Psoriatic disease increases the risk of CVD	7
Tools to evaluate the risk of CVD and cardiovascular events (CVE)	11
Psoriatic march and the onset of CVD	12
The added burden of hypertension	13
Biomarkers associated with CVD	15
Disease management and effect on CVD risk	18
Recommendations for reducing the risk of CVD in people with psoriatic disease	20
Recommendations for people living with psoriatic disease	21
Recommendations for health care professionals (HCPs)	22
Recommendations to policymakers	23
Conclusions	24
References	26

Abbreviations

BMI – body mass index

CCL20 – chemokine ligand 20

CRP – C-reactive protein

CV – cardiovascular

CVD – cardiovascular disease

CVE – cardiovascular event

FRS – Framingham Risk Score

GlycA – Glycoprotein acetylation

GPP – Generalized Pustular Psoriasis

HLA – human leukocyte antigen

IFN- γ – interferon-gamma

IL - interleukin

MACE – major adverse cardiovascular event

MI – myocardial infarction

FDG PET/CT - Fluorodeoxyglucose F-18 positron
emission tomography computed tomography

PCE – Pooled Cohort Equations

RSS – Reynolds Risk Score

SCORE – Systematic Coronary Risk Evaluation

TNF- α – tumor necrosis factor-alpha



More than skin deep

Psoriatic disease is an immune-mediated chronic disease commonly recognized by the presence of lesions on the skin, also called psoriasis. But this disease is more than skin deep and approximately 30% of people living with psoriatic disease also see their joints and tendons affected by it, known as psoriatic arthritis. For that reason, the term psoriatic disease was coined, and includes both psoriasis and psoriatic arthritis.

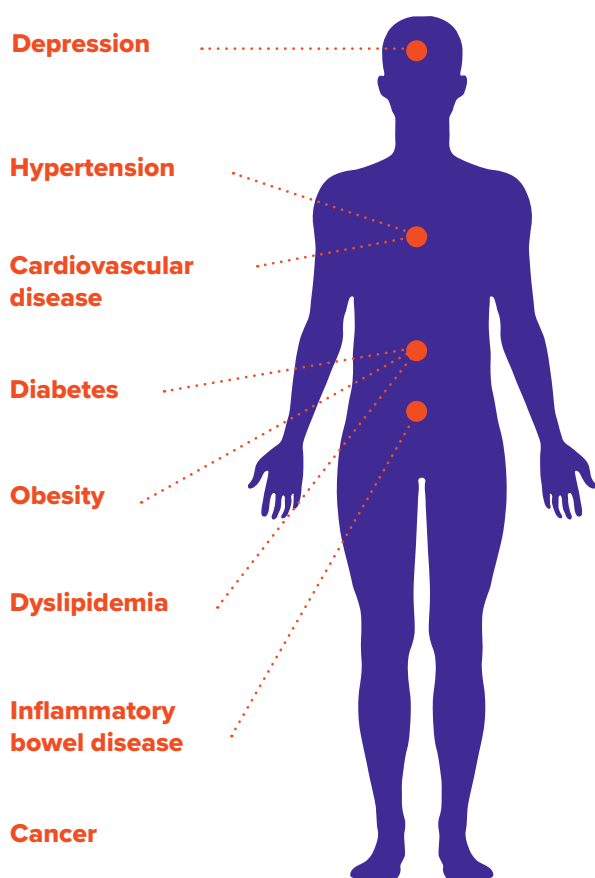
People living with psoriatic disease also have an increased risk of developing other related diseases, or comorbidities, such as mental health disorders (anxiety and depression), obesity, hypertension, dyslipidemia, diabetes, inflammatory bowel disease, metabolic syndrome and cardiovascular disease¹. Most of these diseases are interconnected and are considered risk factors for the development of the other comorbidities²⁻⁴.

What is psoriatic disease?

Psoriatic disease is a systemic condition affecting multiple body sites, predominately the skin, the joints, or both. Skin and joint symptoms are different manifestations of the same disease. They may manifest independently.

A third of people with skin manifestations of psoriatic disease (psoriasis) will develop a type of inflammatory arthritis affecting joints and tendons (psoriatic arthritis). In some people, joint symptoms develop before skin lesions.

People with psoriatic disease have an increased risk of developing other noncommunicable diseases:



More information on psoriatic disease and the link with other comorbidities such as mental health and diabetes can be found here:

Mental health

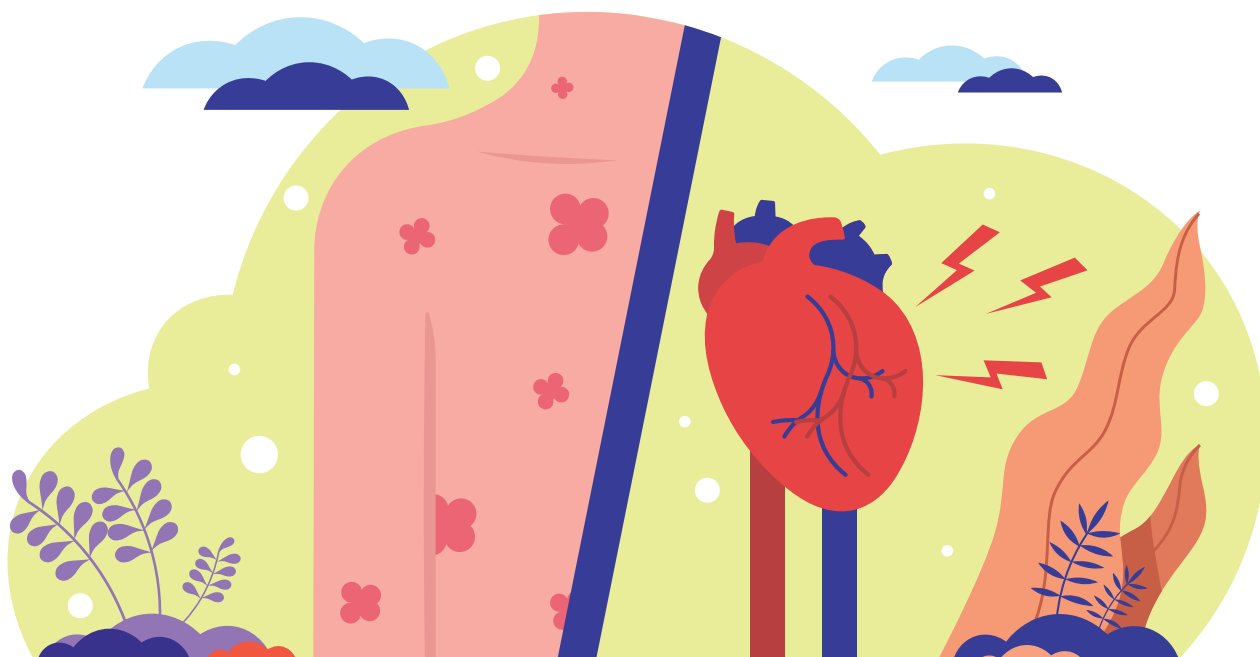


Diabetes



The association between psoriatic disease and its comorbidities is clear, and the risk of developing some of the comorbidities increases with the severity of psoriatic disease⁵. Good disease management and comorbidity surveillance are essential measures to avoid their onset and reduce the burden of disease for people living with psoriatic disease and, consequently, to the healthcare system.

It is challenging to isolate the association between psoriatic disease and any individual comorbidity. Nevertheless, in this report we will focus on the pathways suggested to directly connect psoriatic disease and cardiovascular disease (CVD).



The link between psoriatic disease and CVD

The relationship between these two diseases and the increased risk of CVD in severe forms of psoriatic disease has been extensively demonstrated. One of the main commonalities is inflammation and its downstream effects. In addition, other factors, namely risk behaviors, are associated with an increased risk for developing CVD. Such behaviors include smoking, unhealthy eating habits, and a sedentary lifestyle (low exercise). These also increase the risk for obesity, hypertension, high cholesterol and diabetes, other psoriatic disease comorbidities that, consequently, increase the CVD risk.

In this report we will discuss in more detail the mechanisms behind the onset of CVD in people with psoriatic disease. The cascade of events starting with skin inflammation and how it results in CVD is also known as *psoriatic march*⁶.

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One of the main commonalities is inflammation and its downstream effects.

PSORIATIC DISEASE INCREASES THE RISK OF CVD

The link between psoriatic disease and CVD has been studied for many years. It has become clear that psoriatic disease is associated with myocardial infarction, stroke, and cardiovascular-related death, also defined as **MACE**, or major adverse cardiovascular events.

The term **cardiovascular disease includes different conditions:**



Heart disease
heart and blood vessel disease, often associated with atherosclerosis

Heart attack
blockage of blood flow to the heart by a blood clot, also known as myocardial infarction

Heart failure
when the heart is still beating but is not pumping blood as well as it should

Stroke
blockage of blood flow to the brain, usually from a blood clot

Arrhythmia
when the heart pumps at a slower, faster, or irregular rhythm

American Heart Association
[heart.org](https://www.heart.org)

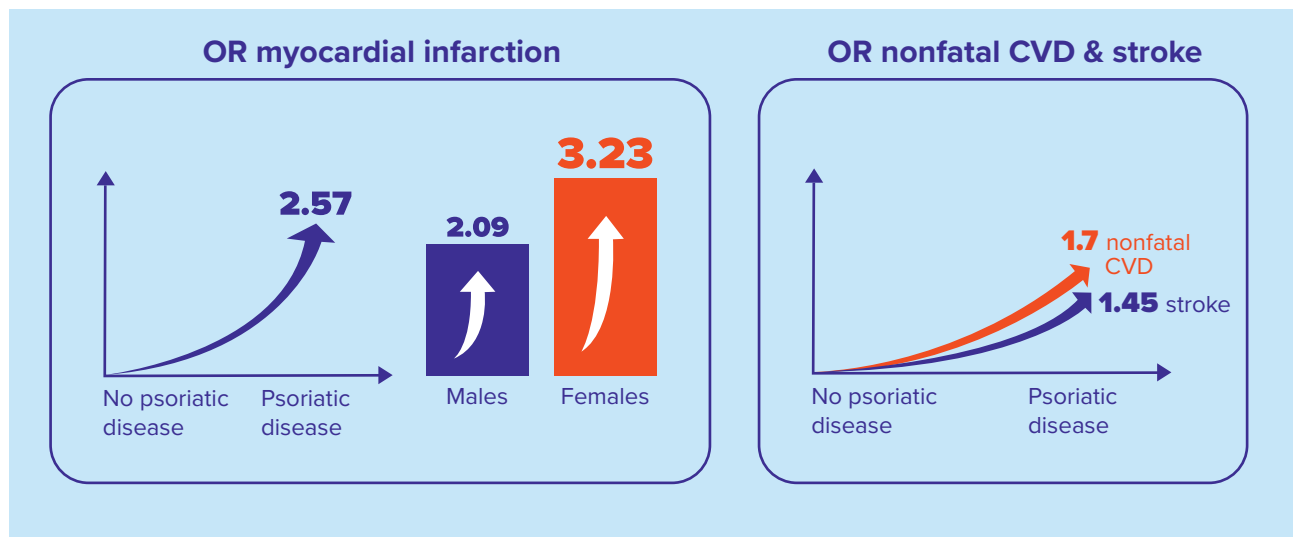
Several studies show an increased incidence of CVD in people with psoriatic disease when compared to people without psoriatic disease (controls). In these studies, risk is usually presented as an **odds ratio (OR)**, or hazard ratio (see box on next side). Research has shown a higher risk for myocardial infarction, angina, nonfatal CVD, stroke and other MACE in people with psoriatic disease compared to controls⁷⁻¹¹. One large study conducted in Germany, for example, showed that people with psoriatic disease experience myocardial infarction on average 5 years earlier than people without the disease¹². Moreover, people with psoriatic arthritis are reported to be at an even higher risk for CVD when compared to controls and, in some cohorts, compared with people with psoriasis. In these studies the OR was as high as 3.57^{10,13-15}.

In this report the information presented is mostly focused on common forms of psoriatic disease, because these are subjected to most scientific studies. Even though there is a lack of research on rare subtypes of psoriasis, an increase in CVD is still detected. Wu et al showed an increased risk and prevalence of CVD in people living with erythrodermic psoriasis when compared with healthy controls in China¹⁶. A study on people living with generalized pustular psoriasis (GPP) in France showed a correlation between admission to an intensive care unit and myocardial infarction history (OR 4.29)¹⁷. In cases of fatal GPP, the OR of myocardial infarction was even higher (5.1) than for people with GPP not admitted to intensive care¹⁷. These studies show that all types of psoriatic disease deserve attention and people living with rare types of psoriatic disease should also be routinely checked for comorbidities.



Odds ratio (OR)

Odds ratio measures the likelihood or strength of the association between two events. An OR of 1.5 means that there is a 50% higher risk for an event to occur and, conversely, an OR of 0.8 means that the risk is 20% lower.



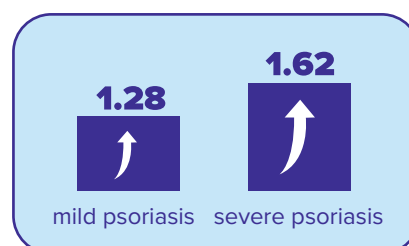
Even though it is challenging to calculate risk for individual variables, **several factors seem to independently impact the risk for CVD in psoriatic disease:**



Psoriatic disease severity:

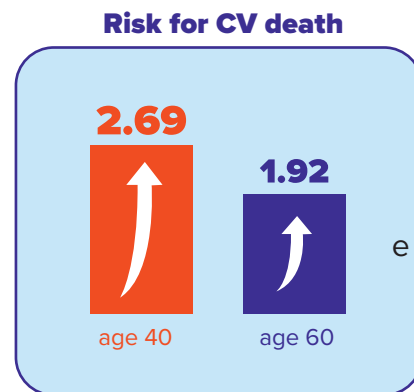
several reports have demonstrated that milder presentations of psoriatic disease are associated with a lower risk for CVD when compared to severe psoriatic disease^{18,19}.

Risk for MACE



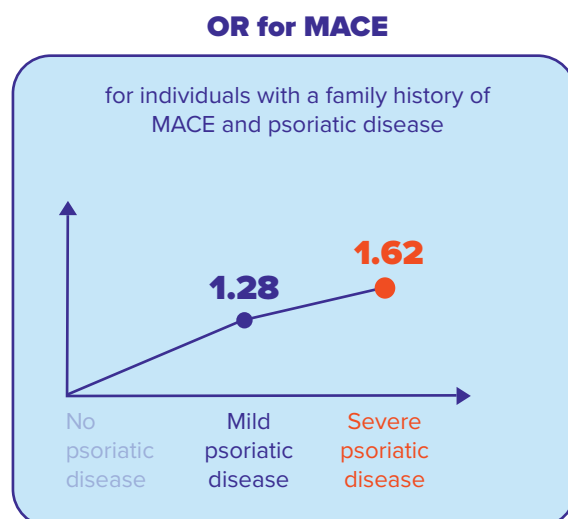


Age of the person with psoriatic disease: research has shown that younger people have an increased risk for CVD. When comparing people in the same age group with and without psoriatic disease, the risk for MI for 30-year-olds is 3.10 and 1.36 for 60-year-olds with severe psoriatic disease²⁰⁻²². Even though this may be a puzzling finding, it is plausible that younger people are generally under less surveillance and have less access to medication that reduces the risk for CVD. Conversely, old people are more likely to be on medication to control blood pressure and CVD onset, such as statins. Another plausible reason for the lower risk for 60-year-olds may be that fewer people with psoriatic disease and a high risk of MI survive to old age.



Duration of disease: several studies suggest a positive correlation between the duration of disease and CVD risk. A study from Egeberg et al showed a 1% added risk per additional year of psoriatic disease duration²³.

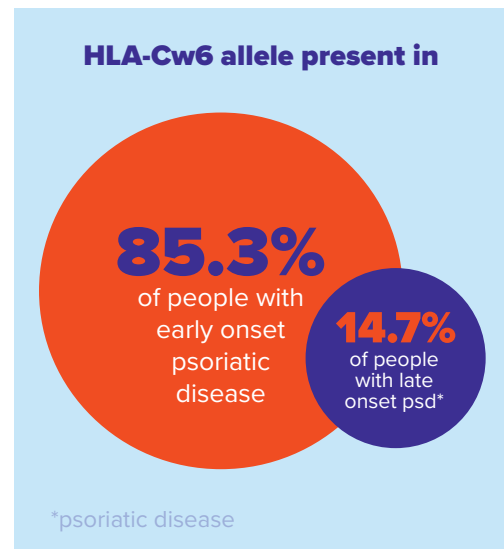
Family history: it is well established that a family history of psoriatic disease increases the likelihood for an individual to develop the disease. Interestingly, a study showed that, among young people with psoriatic



disease (average age 26.6 years), a family history of MACE increases their own risk for these events. The risk is higher for severe psoriatic disease. Conversely, no added risk to young individuals with no family history of MACE was found¹⁸. The findings show that obtaining information from family history of CVD from people with psoriatic disease by healthcare professionals (HCP) can help evaluate CVD risk and plan for appropriate monitoring.



Genetic factors: Several genes or chromosomal regions have been associated with an increased predisposition for the development of psoriatic disease and CVD. One of the main associations between genetics and disease is HLA-Cw6 (human leukocyte antigen) allele or variant²⁴. Studies showed that HLA-Cw6 was present in most people with early onset psoriatic disease than in people with late-onset disease²⁴, and at a higher prevalence in people with psoriatic disease than people without it²⁵.



HLA-Cw6 is associated with the immune system²⁶ and with an increased risk for CVD²⁷, showing that this allele confers a double burden for psoriatic and CVD. Another allele, HLA-Cw1, more prevalent in Asian populations, has also been associated with psoriatic disease and dyslipidemia, another comorbidity associated with increased CVD risk²⁸. Genetic variations in IL-23 have also been linked to an increased risk for the development of psoriatic disease and premature coronary artery disease^{29,30}.

With the technical advances and the reduction of costs associated with genome investigations it has been possible to understand in more depth how genes impact the onset and progression of disease. This knowledge has the potential to uncover disease mechanisms, if and how genes affect disease severity, and how individuals respond to treatment. With that, it is possible to move closer to personalized treatment, with the potential for increasing efficacy and reducing side effects.



Finding factors associated with disease is of utmost significance, as it can help to better evaluate risk and plan for appropriate disease prevention and management.

Finding factors associated with disease is of utmost significance, as it can help to better evaluate risk and plan for appropriate disease prevention and management. Guidelines for HCPs considering all risk factors can also have a profound impact on reducing the burden of CVD in people with psoriatic disease.

TOOLS TO EVALUATE THE RISK OF CVD AND CARDIOVASCULAR EVENTS (CVE)

Several methods have been developed to accurately estimate someone's risk of developing CVD or experiencing a cardiovascular event (CVE). Such risk scores include: QRISK-3³¹; Systematic Coronary Risk Evaluation or SCORE³²; CUORE^{33,34}; Pooled Cohort Equations or PCE³⁵; Reynolds Risk Score or RSS^{36,37}, and Framingham Risk Score or FRS^{38,39}.

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The development of tools to rapidly evaluate the risk of CVD is of high importance and applicability. These tools should be used to complement other tests used to stratify and monitor risk.

Even though there are differences between what parameters are used to calculate the different scores, these tools generally consider the person's age, gender, ethnicity, total cholesterol, high-density lipoprotein cholesterol, blood pressure, diabetes and smoking status on the risk assessment. Interestingly, CVD risk prediction tools perform differently depending on the population they are tested on. As an example, the FRS, established with population data from Framingham, Massachusetts, is more accurate to predict the risk for CVD in populations from

the USA, Australia or New Zealand than European populations⁴⁰. Conversely, SCORE was developed from cohorts from 12 European countries, performs generally better in European populations³². Other studies validated the FRS to calculate the CVD risk in Malaysia^{41,42}, even though the revised PCR score is the most useful in predicting risk in Asian populations⁴². On the contrary, SCORE and SCORE2 perform poorly, overestimating the risk for CVD in Asian populations⁴³.

Despite CVD risk scores being initially developed using data from populations without chronic diseases, their validity in other cohorts, such as people with psoriatic disease, have been tested and compared. Not surprisingly, the different scores mentioned above are able to predict the risk for CVD in psoriatic disease populations with different accuracies⁴⁴⁻⁴⁸. A drop in accuracy is also observed when these tools are applied to cohorts of people with psoriatic arthritis⁴⁹. To improve the accuracy of risk calculation in individuals with rheumatic diseases, including psoriatic arthritis, the European League Against Rheumatism (EULAR) recommended risk scores to be multiplied by 1.5. This recommendation resulted in an overall improvement in accuracy for some populations⁵⁰ but not others⁴⁸.

The development of tools to rapidly evaluate the risk of CVD is of high importance and applicability. There are, however, several factors that limit the accuracy of the results, especially when applied to a specific subset of the population with diseases that may, on their own, be risk factors for the onset of CVD. Therefore, these tools should be used to complement other tests used to stratify and monitor risk.

PSORIATIC MARCH AND THE ONSET OF CVD

According to the concept of *psoriatic march* summarised by Boehncke et al⁶, systemic inflammation is suggested to be the factor that links psoriatic disease and atherosclerosis, a key hallmark on the onset of CVD.

Psoriatic disease is an immune mediated inflammatory disease. Research has found that molecules, such as cytokines, and cells involved in inflammation in psoriatic disease are also involved in the development of CVD. This link shows a direct association between the two diseases, and people living with psoriatic disease need to be aware of the increased risk of developing CVD or experiencing a cardiovascular event (MACE).

Despite the lack of definitive understanding on what the triggers and mechanisms involved in the onset of psoriatic disease are, in this report we will mention the known pathways that link the two diseases⁵¹⁻⁵⁹.

It all seems to start with a trigger that activates the immune system in the skin and initiates the onset of psoriatic disease. This environment becomes rich in pro-inflammatory cytokines such as IL-17, IL-23, IFN, TNF- α and many others. The presence in high levels of these cytokines in turn promotes the proliferation of keratinocyte (skin cells), resulting in thickening and scaling of the skin, and the expansion and differentiation of T cells secreting TNF- α and IFN- γ .

The initially local inflammation that starts in the skin in individuals with severe psoriatic disease can expand systemically. This expansion can affect several organs in the body, including the joints (associated with the development of psoriatic arthritis) or the endothelium (the inner lining of the blood vessels). The changes in endothelial function and integrity triggered by inflammation constitute the early steps in the process of plaque formation, resulting in atherosclerosis. Atherosclerosis plaques are made of neutrophils, macrophages, T-cells and platelets, pro-inflammatory molecules, extracellular matrix, lipids such as cholesterol and low-density lipoprotein (LDL). With the understanding of the cellular mechanisms associated with systemic inflammation, it was possible to uncover specific molecules that are linked to an increased risk for the development of CVD. These molecules that can be found in the blood, facilitating the monitoring of inflammation and, consequently, CVD risk stratification. These are described below in the Biomarkers associated with CVD section.

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Atherosclerosis in the blood vessels is linked to an increase in the thickness of the carotid intima-media layers, arterial stiffness, and coronary artery calcification, impairing vessel function^{55,60-65}.

The presence of pro-inflammatory cytokines in the body, such as IL-17, triggered by the psoriatic lesions and their microenvironment, creates a perfect storm for the development of atherosclerosis that increases the risk for CVD. Interestingly, GPP is characterized by a different pro-inflammatory profile than psoriasis, but people living with GPP seem to also be at a high risk for MACE. Despite the lack of studies in GPP in the possible association between the two diseases, this finding may not be entirely surprising. Research has showed that IL-36, one of the most important cytokines in GPP, is able to induce IL-17 and IL-23 expression, linked to increase CVD risk⁶⁶⁻⁶⁸.

Moreover, psoriatic disease is also associated with ventricular hypertrophy (enlargement of the muscle making it more difficult to pump blood), diastolic dysfunction (when the cardiac muscle does not relax, affecting blood pumping), or reduced ejection fraction (how much blood is pumped out of the heart with each heartbeat)^{69,70}. These changes can be assessed by echocardiographic imaging, a simple and non-invasive technique that uses ultrasound to visualize the heart and blood vessels. Monitoring the heart structure and cardiac function should be used as a routine preventive assessment of risk for CVD in people living with psoriatic disease. This is particularly relevant for those with severe symptoms, as they are more susceptible to experiencing a CVE.

THE ADDED BURDEN OF HYPERTENSION

Hypertension is a major cause of premature death worldwide. According to the World Health Organization (WHO), it is estimated that 1.28 billion adults (aged 30-79) have hypertension and around 46% of adults with hypertension do not know they have it. Moreover, only 1 in 5 adults with high blood pressure have it under control.

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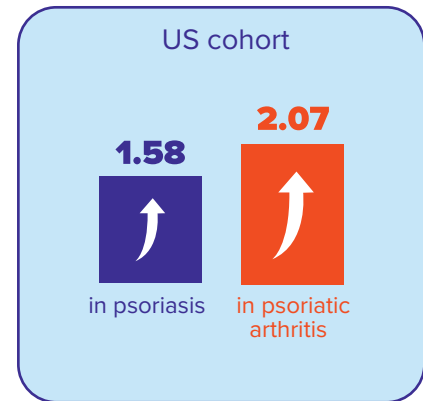
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The widely prevalent hypertension is not only a comorbidity with direct effect on increasing the CVD risk, but research has shown that psoriatic disease in itself has a role in the onset of hypertension⁷¹⁻⁷³. This shows that people with psoriatic disease have an increased risk for CVD and an added burden to keep this risk low.

To date, a large proportion of studies on hypertension have focused on the prevalence of this comorbidity in psoriatic disease. These studies report that people with mild and severe psoriasis have between 30 and 50% higher risk for hypertension, respectively, when compared to people without the disease. Moreover, the prevalence of hypertension correlates with the duration of the disease⁷⁴ and people with joint symptoms of psoriatic disease, psoriatic arthritis, have more than double the risk for developing hypertension^{71,75}.

Not only do people with psoriatic disease have an increased likelihood of hypertension, but the disease is also an added burden that hinders the maintenance of normal blood pressure⁷³. A study by Armstrong et al showed that people with psoriatic disease are more likely to be on multiple anti-hypertensive therapies than people with high blood pressure and no psoriatic disease⁷⁶. The findings clearly show that people with psoriatic disease require a higher number of anti-hypertensive medications to be able to control their blood pressure.

Risk for hypertension



Psoriasis patients with hypertension were:

5x
more likely
to be on a monotherapy antihypertensive regimen

9,5x
more likely
to be on dual antihypertensive therapy

16,5x
more likely
to be on triple anti-hypertensive regimen

19,9x
more likely
to be on quadruple therapy or centrally acting agent

A few studies have investigated the mechanisms that link psoriatic disease and hypertension. There seems to be an association between key factors important for both diseases. Hypertension-associated factors are expressed at high levels in people with psoriatic disease, often associated with disease severity, suggesting a correlation between the two. IL-17, one of the pro-inflammatory cytokines involved with the onset of psoriatic disease, has also been associated with Angiotensin II-induced hypertension⁷⁷. Renin, a protein part of the renin-angiotensin system, is found to be elevated in lesional skin of people with psoriatic disease⁷⁸, supporting the link between the two diseases. The expression of the vasoconstrictor Endothelin-1 by the endothelium and keratinocytes, important for the regulation of blood pressure, is also higher in people with psoriatic disease^{79,80}. Moreover, the increase in Endothelin-1 correlates with the severity of psoriatic disease⁷⁹. These findings show a traceable signature for the onset of hypertension in psoriatic disease, that consequently increases the risk for CVD. Monitoring inflammation, Endothelin-1 expression and blood pressure in people with psoriatic disease are available and important avenues to evaluate risk and prevent both hypertension and CVD progression.

BIOMARKERS ASSOCIATED WITH CVD

Biomarkers are molecules that can and are used to diagnose, monitor, and stratify disease risk and outcomes. These biomarkers can be found, for example, in the blood, easily accessible for analysis. Because of the deeper understanding of the disease mechanisms of psoriatic disease, key molecules associated with disease onset, progression or severity have been identified. These biomarkers can be used for early disease detection, including evaluating the risk for the onset of comorbidities.

Several biomarkers have been associated with CVD. Some have already been mentioned above, such as the pro-inflammatory cytokines involved in the onset and progression of psoriatic disease and CVD TNF- α , IL-17. Other important biomarkers are listed below.

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CRP

C-reactive protein, or CRP, is a protein synthesized by hepatocytes (liver cells) as a response to inflammation triggers, for example cytokines such as IL-6^{81,82}. Studies have shown that CRP is a key mediator of atherosclerosis, an essential step for the onset of CVD. Given its function, CRP is one of the main markers of cardiovascular risk. For that reason, CRP and IL-6 are good biomarkers of inflammation and CVD risk stratification^{82,83}. In fact, CRP is one of the first markers used to predict CVD risk⁸⁴, and used as a parameter for some of the risk scores mentioned above. In psoriatic disease, in alignment with the findings mentioned above, CRP is found at significantly higher levels compared to controls, as high as 10x more^{75,85}.

GlycA

GlycA is a signal that detects mobile glycan residues on plasma glycoproteins. Briefly, GlycA is a marker for inflammation and associated with atherosclerosis. The signal is detected using FDG PET/CT tomography, an advanced imaging technique routinely used to detect cancer, inflammation and heart and brain activity and function. Research has shown a positive and significant correlation between GlycA and CVD and CVE^{86,87}. Importantly, people with psoriatic disease also have significantly increased GlycA compared to controls, associated with disease severity and increased risk of CVD⁸⁸. Even though FDG PET/CT tomography may be unavailable for many, the findings support the monitoring of CVD risk in psoriatic disease by quantification of GlycA.

CCL20

Other molecules that can be used as biomarkers are CCL20 (chemokine ligand 20) and homocysteine. CCL20 (chemokine ligand 20) is a proinflammatory cytokine detected in the blood and associated with vascular endothelial inflammation⁸⁹. Homocysteine is an amino acid that, when in high concentration in the blood, is associated with an increased risk for CVD⁹⁰⁻⁹². Analysis of CCL20 and homocysteine in people with psoriatic disease showed higher levels of these molecules when compared to controls^{89,93}.

Neutrophils

Neutrophils are cells from the innate immune system, the first line of defense and part of the initial phase of inflammation. One of the neutrophils' main roles is to detect and degrade pathogens. Neutrophils are found at higher concentration at the psoriatic plaques and neutrophil markers are also increased in the blood of people with psoriatic disease^{94,95}. The increase in neutrophil blood markers is also seen in vascular inflammation, showing a correlation between psoriatic disease and systemic inflammation. Neutrophils are one of the main sources of IL-17⁵⁶, one of the most important cytokines associated with systemic inflammation in psoriatic disease. Moreover, neutrophils have also been linked to CVD, namely acute coronary events⁹⁶. These and other findings suggest that neutrophil markers and neutrophil-to-lymphocyte ratio can be used as tools to predict systemic inflammation and atherosclerosis in people with psoriatic disease⁹⁷⁻¹⁰⁰.

As mentioned throughout this section, the analysis and quantification of several molecules, most of them in the blood stream, can be used to assess the inflammation and risk for CVD in people with psoriatic disease. Importantly, biomarkers can sometimes be detected before the symptoms arise, which can have valuable implications in preventive care. Implementing routine checks of some of these molecules together with good psoriatic disease management would be beneficial to early detection and intervention to prevent the onset of CVD.

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Disease management and effect on CVD risk

Depending on the severity of the psoriatic disease, different treatment options can be followed. The first-tier treatment that can be considered is to follow a healthy lifestyle, that includes eating healthily, exercising, and avoiding some behaviors that can make the disease worse, such as smoking or drinking excessively. In addition to this, active treatment options, following health care advice, are available. These can range from phototherapy, topical non-steroid or steroid treatments (containing molecules with anti-inflammatory action), systemic therapies (orals or injectables such as DMARDs - disease modifying anti-rheumatic drugs - and biologics, depending on the mode of action and therapeutic target).

When adequate treatment is given, it can improve not only the symptoms associated with psoriatic disease but also those of the associated comorbidities. This secondary effect is seen particularly with systemic non-light-based therapies. As an example, phototherapy does not seem to have a significant impact on reducing the risk of CVD¹⁰¹.

Many studies have and are investigating the impact of treatments on changing the risk for CVD. The findings point to different types of treatment having different outcomes on CVD. Here, we will describe some of the main takeaways from the research done in the field.

DMARDs have different effects on the cardiovascular system. While some seem to have no impact on or decrease the incidence of CVD and CVE, others increase the likelihood of developing CVD¹⁰²⁻¹⁰⁵. The increase in risk for some DMARDs, for example when taking cyclosporin, is because it can impair renal function and cause hypertension or hyperlipidemia, risk factors for CVD. On the contrary, methotrexate is a DMARD that decreases the risk for CVD, even at low doses or in combination with other treatments. The risk was reported to decrease by 21% at a standard dose, and by 50% when prescribed at low doses¹⁰⁶. A possible explanation given by the authors for this interesting fact is that people taking methotrexate at higher doses may have had a more severe form of psoriatic disease or living with it for longer, which on its own increase the CVD risk. Other studies reported similar reductions in the risk for CVD, between 20 and 47%^{102,107,108}. Moreover, methotrexate therapy resulted in a 63% reduction in the levels of CRP, already mentioned in this report as being associated with CVD¹⁰⁹.

Similarly to DMARDs, biologics also have different effects on the risk of developing CVD. Studies on IL-17 inhibitors seem to point to this treatment having no impact on the risk of MACE¹⁰⁵. However, one study showed that flow mediated dilation, an assessment for endothelial function, is significantly improved with anti-IL-17 treatment¹¹⁰, suggesting a benefit to the cardiovascular system. Results from treatment with IL-12/23 blockers are contradictory. While some studies show no effect of treatment on the risk for MACE^{102,111,112}, others report an increase in the risk for CVD, as high as twice that of the control group^{105,113}. Concerning TNF- α blockers, research is aligned in showing they provide the best protection against CVE. Several studies have shown a decrease in the risk for MACE and CVD in people taking TNF- α blockers when compared to topicals and other systemics, such as methotrexate, different classes of biologics or phototherapy^{62,102,114-117}. Moreover, a study by Wu et al showed treatment with TNF- α blockers is associated with an 11% reduction in CV risk for every 6 months of additional treatment¹¹⁷. Anti-TNF therapies also seem to reduce inflammation¹¹⁸, slow down atherosclerosis and coronary artery disease progression^{119,120}, improve the flow mediated dilation¹²¹ and decrease the amount of GlycA, CRP, homocysteine, among other biomarkers^{88,122}. These are important findings that show an improvement in the risk factors associated with CVD.

The knowledge of how treatment designed towards improving psoriatic disease affects the incidence of comorbidities is necessary and should be taken into account at the time of prescription. Evaluating the family history for comorbidities such as CVD and the individual's health beyond the symptoms associated with psoriatic disease should be implemented on the guidelines for HCPs.



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Recommendations for reducing the risk of CVD in people with psoriatic disease

Reducing the risk for CVD in people with psoriatic disease is of extreme importance. Working groups such as that of EULAR (European League Against Rheumatism) have created a list of principles and recommendations for CV risk management in people with rheumatoid diseases, that include psoriatic arthritis¹²³. Implementing such recommendations into guidelines can result in an improvement of psoriatic disease and a decrease in the incidence of CVD. This, in turn, may decrease the burden of disease and comorbidities for those living with psoriatic disease and for the health care system.

Here we present recommendations categorized by their intended audience.

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Psoriatic disease is an independent risk factor for the onset of CVD. It is, therefore, recommended that people living with psoriatic disease have the disease under control.

Recommendations for people living with psoriatic disease

As mentioned in this report, there are several factors that increase the risk for CVD. Risk factors such as smoking, bad eating habits and a sedentary lifestyle (low physical activity) should be changed, and healthier habits should be implemented. Unfortunately, there isn't a one-size fits all approach for diet and active lifestyle. Nevertheless, **changes such as eating less processed foods and more vegetables and fruits, and an increase in the number or length of daily walks are good ways to start implementing healthier behaviors.**

Changes in lifestyle can help reduce the extra weight that is prevalent in people with psoriatic disease. Overweight and obesity seem to not only increase the severity of psoriatic disease¹²⁴⁻¹²⁶, but also to increase the risk for other comorbidities such as diabetes, high cholesterol, dyslipidemia, hypertension and others that, in turn, also increase the risk for CVD. Several studies have shown that reduction in body weight was associated with an improvement of psoriatic disease and its comorbidities^{127,128}. In one study, some individuals that experienced weight reduction were able to stop taking systemic medication¹²⁷.

In today's world there is an overwhelming amount of information and recommendations about diets, some that have little to no scientific evidence of their potential benefits. This type of information may not be beneficial to everyone. At the same time, adopting dietary changes can be very challenging as the access or affordability of fresh food is limited in many countries or regions. These recommendations can be difficult to follow for many people, therefore having support from trained professionals is very important.

Psoriatic disease is an independent risk factor for the onset of CVD. It is, therefore, recommended that people living with psoriatic disease have the disease under control. **Avoid stress triggers, follow the treatment plan, find support on family members and patient organizations, are a few strategies that can be taken up.**



weight loss:

reducing PASI
and DLQI by
2 points each

Article from the
World Heart Federation
highlighting the importance of recognizing obesity as one of the main drivers of CVD



Recommendations for health care professionals (HCPs)

Discuss risks and lifestyle changes

One important way to engage people with psoriatic disease is to discuss the details of their disease, including the risks for developing other comorbidities and what can be done to reduce such risks¹²⁹. HCPs often mention refraining from such conversations to avoid causing discomfort or damaging the relationship with their patient. However, people living with psoriatic disease report wishing to be able to discuss more about the disease, comorbidities, and how to best manage them with their doctor.

Concerning changes in lifestyle, HCPs play an important role in advising people with psoriatic disease to choose to eat a healthier diet, reduce smoking and alcohol intake, if applicable, exercise regularly and be mindful of their own mental health. Ideally, referral to nutritionists, psychologists and physical therapists would provide the personalized support needed for people with psoriatic disease to achieve their health goals.

Some treatments for psoriatic disease increase the risk for CVD. Taking this into consideration is essential when prescribing such treatments to people who may already have a predisposition or increased risk for CVD. When the risk factors are present, referral to a cardiologist for specialized care may be beneficial. Importantly, key preventive drugs for heart disease do not seem to have any negative effect on psoriatic disease, such as statins^{131,132}. Increasing monitoring becomes even more crucial to ensure safety for those taking the treatment.

Implement routine surveillance programs

This report has listed the main tools and biomarkers that can give insight into the risk of developing CVD. Routine checks of cholesterol (LDL and HDL) and glucose levels, blood pressure and BMI (body mass index) are relatively simple ways to monitor disease progression and, by using risk calculation scores such as the Framingham Risk Score, the overall risk for CVD^{129,130}. Other methodologies, even though more expensive and less available in a clinical setting, can be used to evaluate the risk for CVD. Some can be monitored by blood tests, such as CRP or IL-17, and others using ultrasound such as carotid intima-media stiffness or coronary artery calcification. An accurate monitoring of disease progression would help make informed decisions concerning disease management and treatment.



CVD comorbidity affects people with psoriatic disease in several life dimensions:

CVD results in significant lower mental and physical well-being, higher impact on work productivity and general activity.

It is also associated with more resource use, including **1.9 more HCP visits** in the 6 months prior to the survey. Likewise, ER visits and hospitalizations were two to three times greater for the CV comorbidity group.

Recommendations to policymakers

Improve access and quality of care

Psoriatic disease and CVD are associated with a significant burden for those living with these diseases. CVD still is the number one killer worldwide, therefore the need for better prevention and care for CVD globally is urgent. The proven association between psoriatic disease and CVD reinforces the need for the implementation and investment in multidisciplinary care. This would include primary care doctors, dermatologists, rheumatologists, cardiologists, psychologists, nutritionists, physical therapists and others. Better care and support for those living with psoriatic disease in managing the disease and the associated comorbidities such as CVD, reducing the incidence, the burden and associated costs should be prioritized.

In alignment with the World Heart Federation, in this report we reinforce the call to action from policy makers to, for example, increase the implementation of CVD prevention and care units in primary healthcare settings.

Facilitate the access to advanced therapies

Research has shown that treatment, in particular some systemic therapies, reduce the risk of CVD. Access to the most adequate treatments that not only improve psoriatic disease but also the well-being of those being treated as well as reducing the risk for other comorbidities should be a priority.

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State of the heart
cardiovascular
diseases report



Increase awareness of psoriatic disease and associated comorbidities

There is still an overwhelming need to disseminate information about psoriatic disease and the increased risk for comorbidities. Awareness can facilitate the adoption of changes in lifestyle and care that reduces the incidence of such comorbidities. Awareness and education campaigns should be disseminated and readily available, for example, in primary care facilities.

Implement compulsory education and training for HCPs

The knowledge on psoriatic disease is continuously being updated. The same is valid for the understanding of the impact of psoriatic disease in other diseases. For those reasons, there is an urgent need for HCPs that care for people with psoriatic disease to be updated on the latest knowledge about the disease, treatment options and how these affect the risk for comorbidities. Complement training with guidelines for easy access to information would also be beneficial.

Conclusions

There is an unequivocal link between psoriatic disease and CVD, that is stronger the more severe psoriatic disease is. When local inflammation, believed to be the first trigger for the onset of psoriatic disease, expands systemically and settles in the cardiovascular system, it can trigger the onset of CVD and increase the risk for CVE. Importantly, good psoriatic disease management, including effective treatment, can reduce systemic inflammation and, consequently, the risk for CVD.

Reducing the incidence of CVD in psoriatic disease is a shared responsibility between people living with the disease, who should follow a healthy lifestyle, the HCPs, who should explain the risks for comorbidities and provide support, and the policymakers, who should create and implement the infrastructures and guidelines for adequate disease management. By engaging and uniting people living with psoriatic disease, healthcare providers, and policymakers we aim to influence healthcare policies, promote integrated care strategies and ensure that screening for comorbidities becomes a standard practice.

In addressing the dual health challenge of psoriatic disease and CVD, we can improve outcomes, enhance quality of life, and reduce the long-term burden of these interconnected conditions.

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