Pharma Nord
Academy

WELCOME

Thank you for coming

Today's talk will
begin soon

Afterwards,
please come to see us at

Stand: B53

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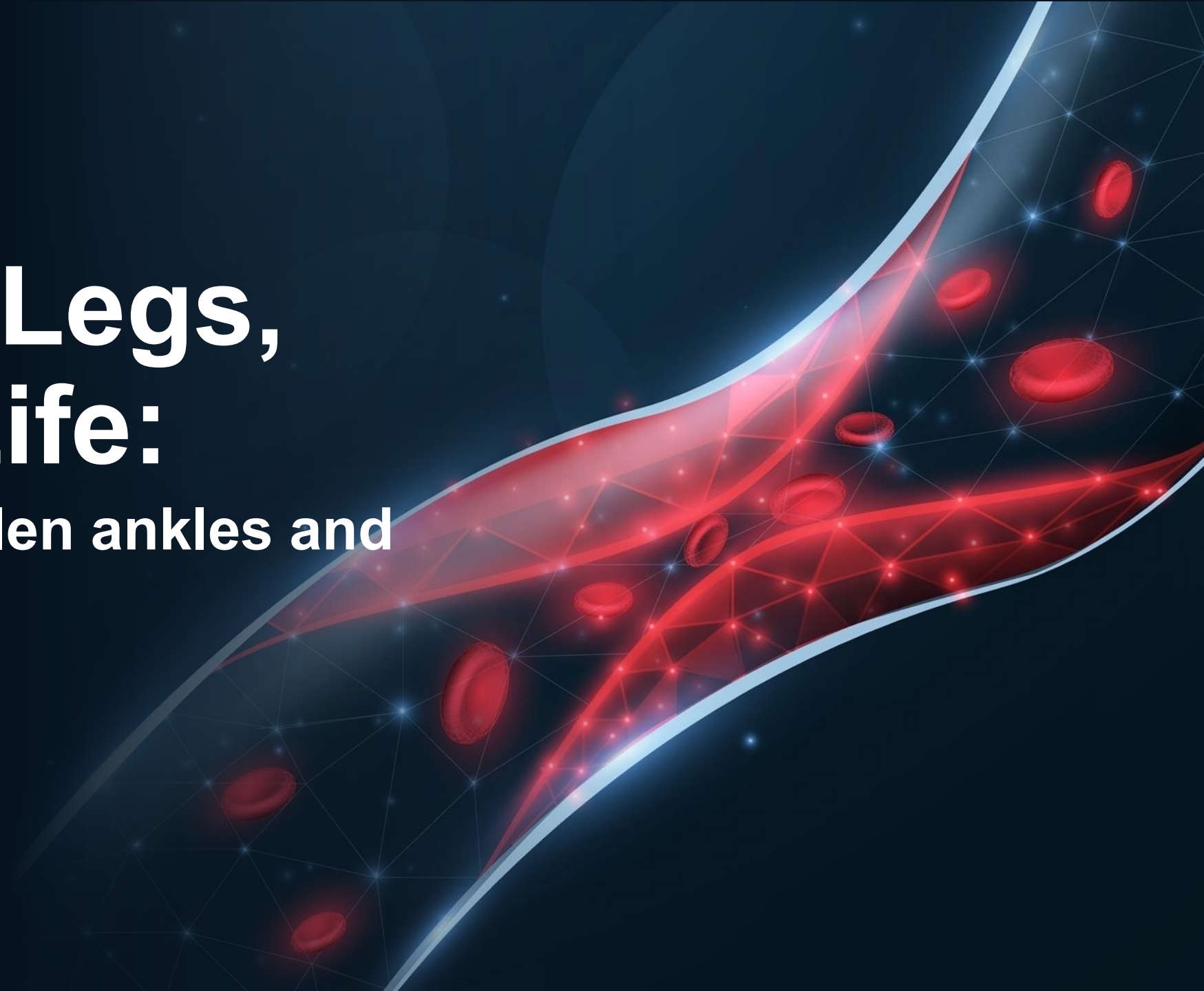
Healthy Legs, Happy Life:

Managing swollen ankles and varicose veins

19 June 2025



Lorraine Nicolle

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Dip. CIM, Dip. BCNH

- Nutrition Education Lead, Pharma Nord UK
- Registered Nutritionist (MBANT)
- Registered Nutritional Therapist (CNHC)
- Functional Medicine and Healthy Ageing Specialist
- In clinical practice for 20+ years
- Higher education teacher (nutrition science & practice)
- Author/editor of several nutrition books
- Accredited clinical supervisor and mentor for nutrition practitioners

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What we're covering today

1. Circulatory system: revision
2. Veins and capillaries: what can go wrong
3. Common venous conditions
4. Prevention and management: diet, lifestyle and supplements

The circulatory system comprises 5 types of blood vessels

They work together in a closed circuit with the heart…

… to bring oxygen and nutrients to the body…

… and eliminate waste products e.g. CO^2

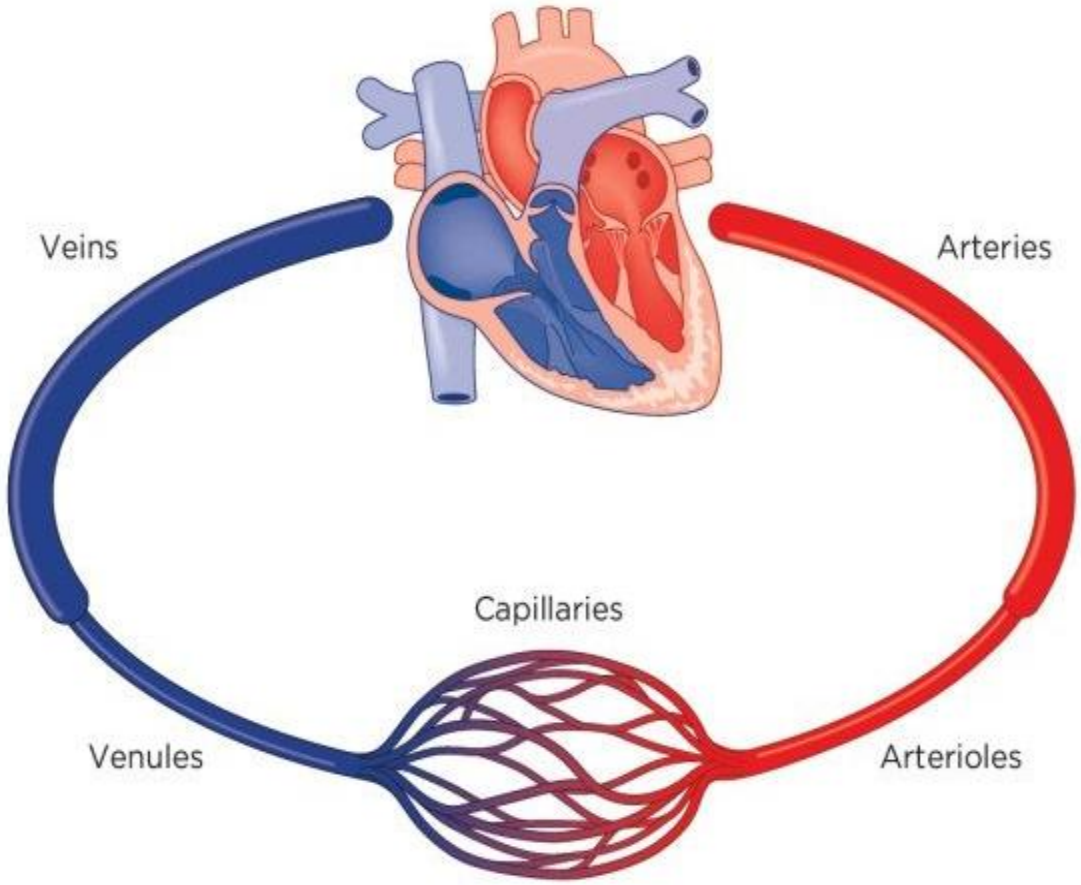


Image from www.nursingtimes.net

In reality there are **2 systems**

- The **pulmonary circulation** is a short loop that takes blood from the heart to the lungs to pick up O2 and off-load CO2; then goes back to the heart
- The **systemic circulation** carries the oxygenated blood via the aorta to other arteries and then smaller and smaller blood vessels to all parts of the body and brain
- At the capillary beds nutrients and O2 are delivered to cells and waste products collected
- The de-oxygenated blood flows from capillaries to larger and larger veins back to the heart
- This is a one-way system thanks to unidirectional valves
- Once back at the heart, the blood re-enters the pulmonary circulation

Arteries

- Have strong muscular walls to withstand pressure
- Carry *oxygenated* blood from the heart to the organs (except pulmonary artery)
- Have no valves (except pulmonary artery) because the pressure of the blood pumping from the heart prevents back-flow

Veins

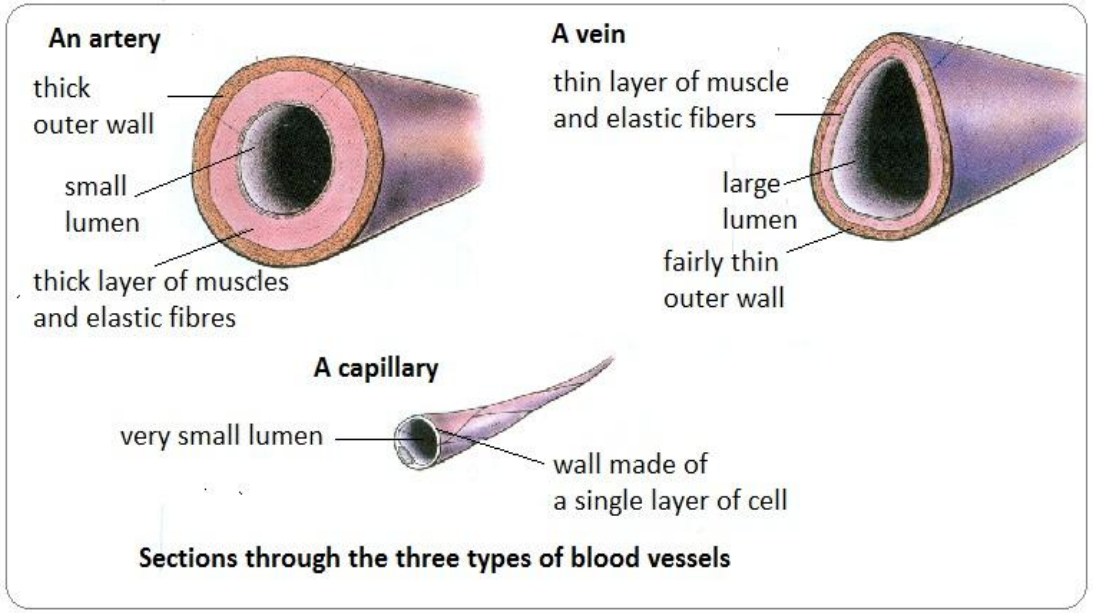
- **Carry *deoxygenated* blood back to the heart**
- **3 types: deep, superficial,perforated**
- **Contain most of the body's blood at any one time**
- **Have thin walls (little smooth muscle) as blood is at lower pressure**
- **Contain valves to keep blood flowing in one direction**

Capillaries

- Located inside all tissues
- Thin wall: one cell only
- Carry blood between veins and arteries
- Diffuse nutrients & wastes to and from tissues
- Carry both oxygenated and deoxygenated blood
- Don't have muscle tissue
- Don't have valves

Veins and arteries comprise 3 layers

- **Tunica intima**: in direct contact with the blood, a single layer of epithelial cells (the endothelium)
  - Can easily be damaged by hypertension, oxidation, glycation, etc.
  - Produces chemicals e.g., endothelial nitric oxide
- **Tunica media**: ***very thick in arteries, very thin in veins: smooth muscle fibres and elastin***
  - Sympathetic NS contracts the SM fibres → vasoconstriction; parasympathetic NS opposes
- **Tunica externa**: connective tissue fibres that protect and attach the blood vessels
- Capillaries have only the media layer



Sections through the three types of blood vessels

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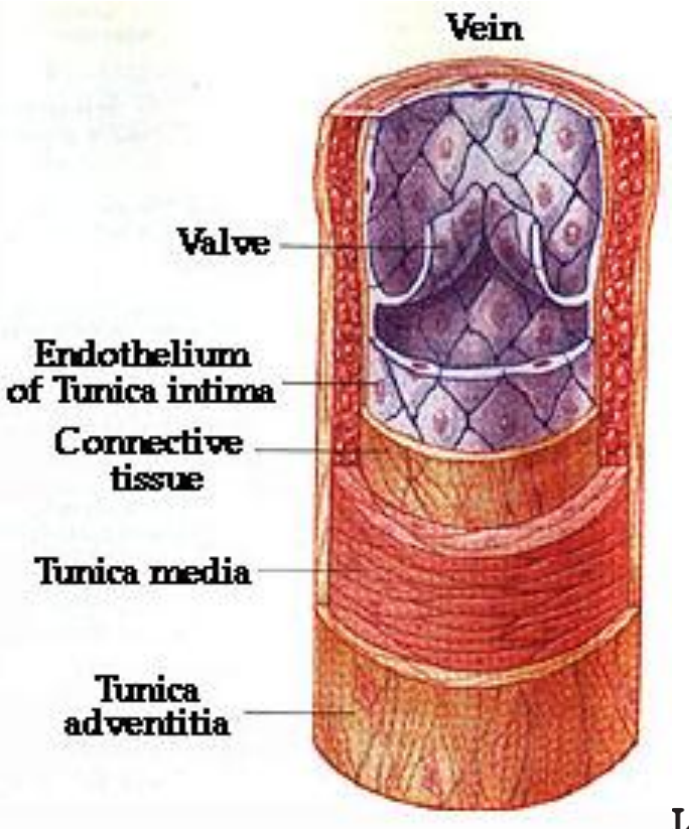
Veins have less smooth muscle and so they circulate the blood via valves

- Bicuspid flap-like structures made of elastic tissue
- Unidirectional and non-refluxing: allow blood to return to the heart, but not to fall back into the legs or arms again
- Need to remain healthy because they are moving blood back to the heart *against the force of gravity*
- (Arteries are helped by the force of the *heart* pumping the blood through)



How venous valves work

- As the leg and arm muscles contract, the valves in the veins open to allow blood to flow back towards the heart
- Each valve has two opposing flaps that act like gates opening in one direction, stopping blood from moving back down
- Lower leg movement is crucial

Healthy venous return requires:

- **Peripheral pump (calf, thigh and foot pump)**
- Breathing: suction force from lungs expanding and diaphragm moving
- Sympathetic NS activity
- Integrity of entire venous system:
  - Superficial veins, capillaries, deep veins and perforating veins

What happens when the valves fail?

- Blood can pool in the lower legs due to gravity
- Can cause a range of symptoms that together are known as *chronic venous insufficiency (CVI)*

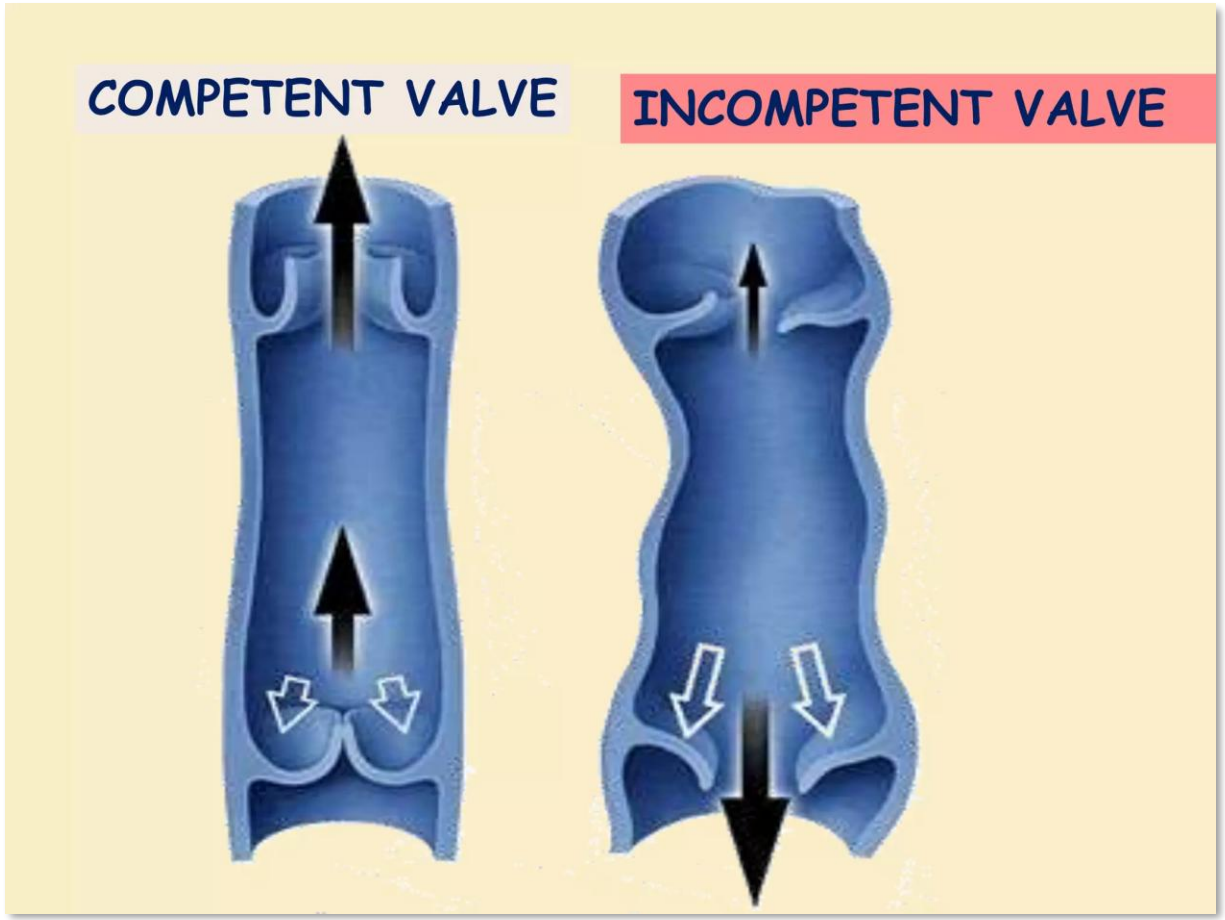
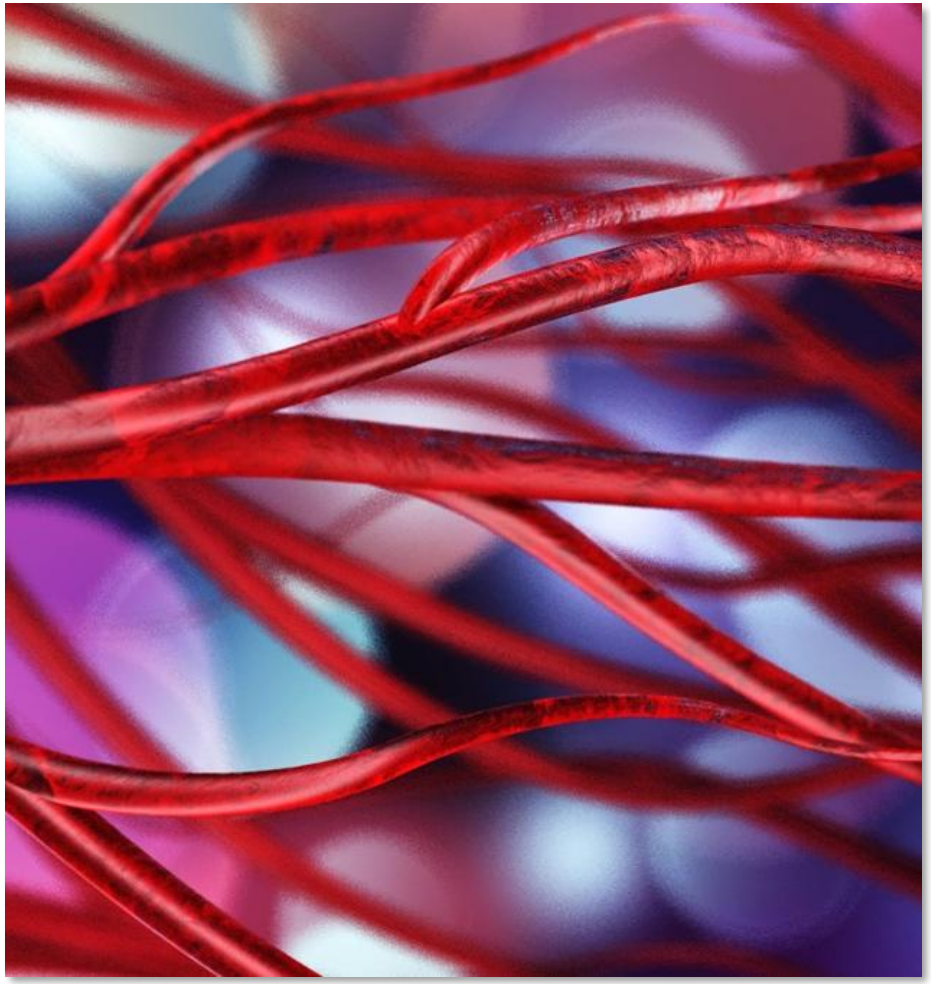


Image: https://www.slideshare.net/BharathiPriya5/pathophysiology-of-varicose-veins

Chronic venous insufficiency

Can manifest as…



Manifestations of CVI

- Tired, heavy, achy legs and feet
  - Worse after prolonged sitting/standing
- Easy bruising
- Spider veins / thread veins
- Oedema
  - Capillaries become ‘leaky’ due to pressure of pooled blood
- Haemorrhoids
- Varicose veins
  - Elongated, tortuous, protuberant superficial veins
- Pigmentation under the skin’s surface
- Eczema and ulceration of the legs (later stages).

Varicose veins

- Enlarged, dilated veins, overfilled with blood
- Often painful, common in the lower legs

Caused by:

- Venous obstruction (e.g. DVT)
- Muscle pump dysfunction *or disuse* from being sedentary, leading to…
- …venous wall stress, over-stretching and venous valve incompetency → pooling → further dilation

Image: ucihealth.org

A: Varicose veins B: Hyperpigmentation and severe lipodermatosclerosis (subcutaneous fat inflammation) with oedema. C: Venous ulcers with eczema and inflammation

American Heart Association.

Robert T. Eberhardt, and Joseph D. Raffetto Circulation. 2014;130:333-346

Factors that increase risk

- Being female (oestrogen and progesterone; pregnancy)
- Strong family history
- Older age
- Being overweight
- Having a job that involves long periods of standing

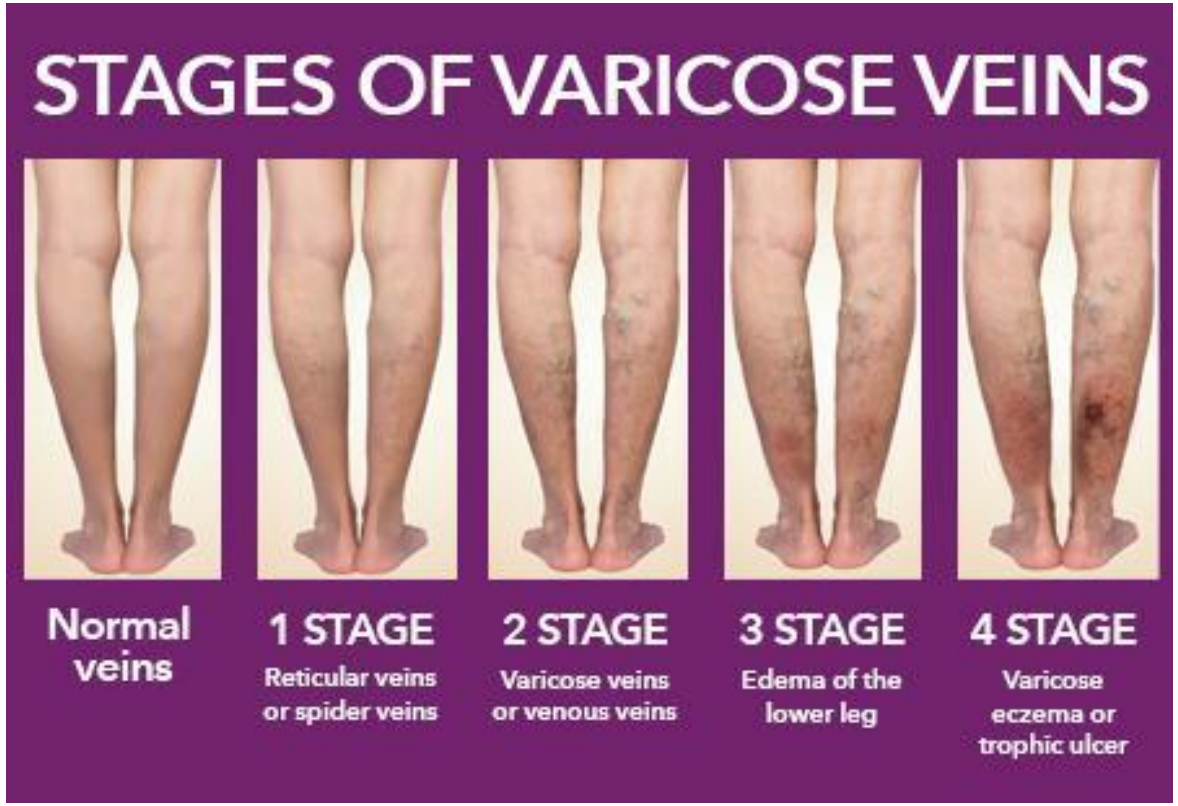
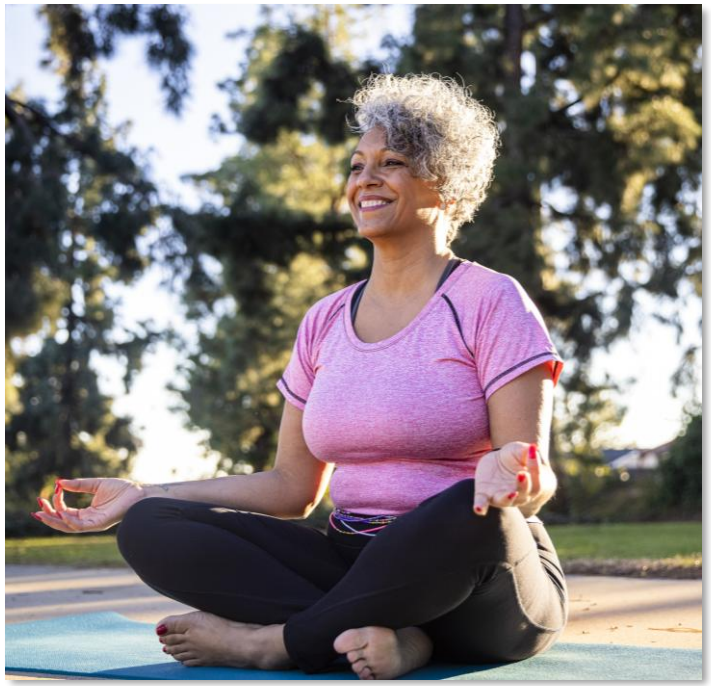


Image: honorhealth.com

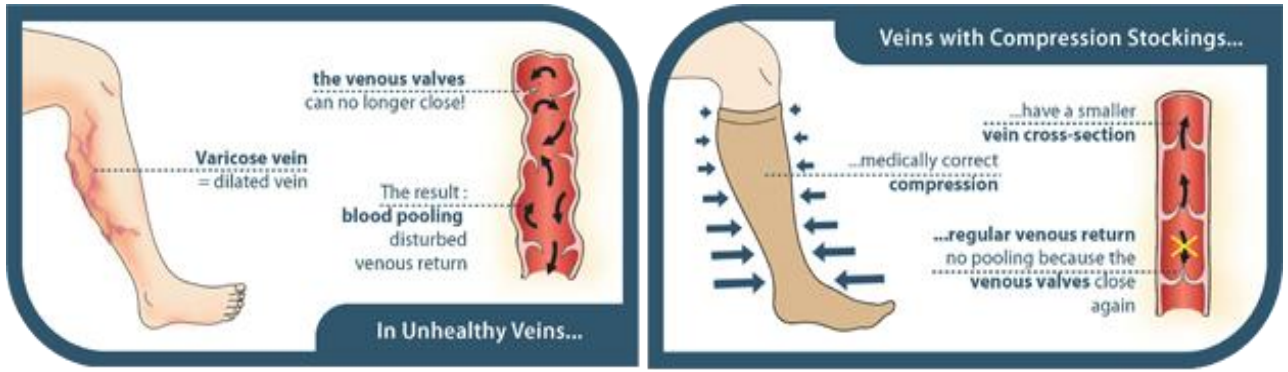
Medical management

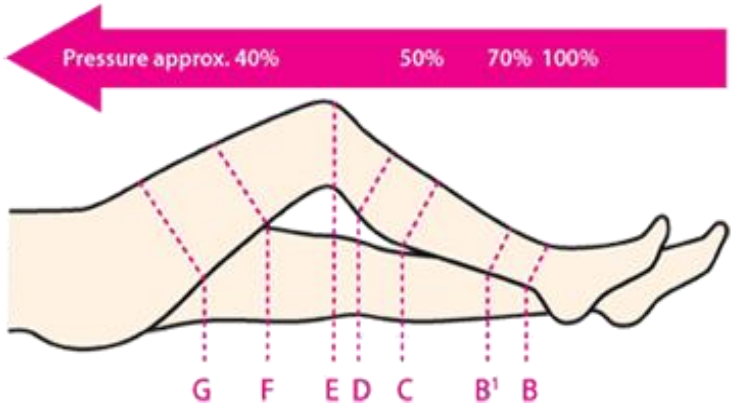
- Exercise for the peripheral pump (calf raises, lunges, bicycle kicks, walking, cycling, yoga…)
- Tailor-made graded pressure, triple-layer compression *dressings*
  - Zinc oxide paste gauze wrap, in contact with the skin to promote healing of *ulcers*
- Compression stockings/socks (see next →)
- Minimally invasive techniques (sclerotherapy, laser therapy)
- Surgery (e.g. vein stripping)
- Medications for swelling



Compression

- Compression stockings/ socks press down on surface veins, arteries and muscles
- This reduces the diameter of distended veins, increasing venous blood flow velocity and valve effectiveness
- Medical-grade stockings have graded pressure, increasing further down the leg





(Image: https://medi-life.com.my/compression/)

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Venous leg ulcers

Worldwide problem: esp. India and Africa

- Prevalence: 2% increases to 5% over age 65 years
- Incidence: 70-80% of all clinical ulcers
- Recurrence rates: 50-70% at 6 months
- Chronic disorder: significant debilitating disease with isolation
- Recurrent and chronic nature indicates underlying drivers must be at play (see later)

Complex pathophysiology:

- Endothelial dysfunction
- Inflammation
- Oxidation
- Metabolic problems
- Proteolytic pathway activation (e.g. MMPs)

Haemorrhoids

- A form of CVI characterised by congested, swollen veins around the anal canal
- Can be internal or external
- Community-based studies in the UK reported that haemorrhoids affect 13 to 36% of the general population

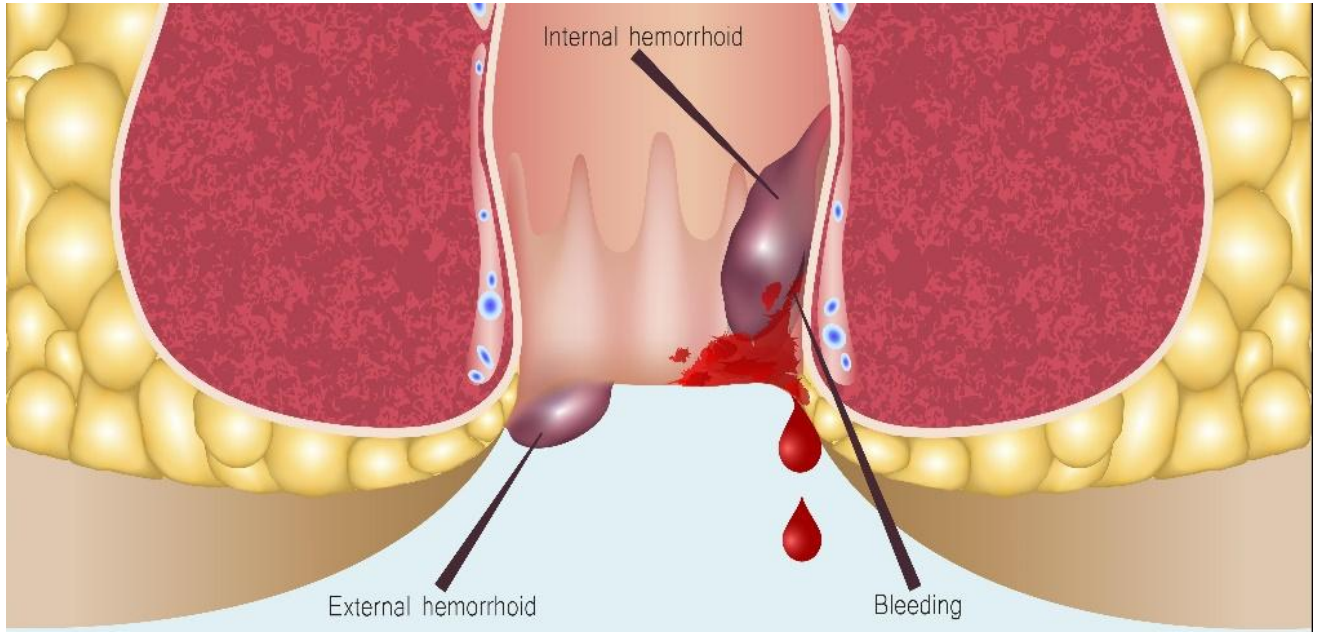


Image from pharmacytoday.co.nz

NICE 2021: https://cks.nice.org.uk/topics/haemorrhoids

Haemorrhoid symptoms

- External haemorrhoids are covered by an epithelium richly innervated with pain fibres, so can be itchy and painful
- Internal haemorrhoids tend to be painless (unless they become strangulated) because they are covered with an epithelium without pain fibres
    - Internal haemorrhoids are graded by degree of prolapse
- Most common symptom = bright red, painless rectal bleeding
- Occurs with defecation; seen as streaks on the toilet paper, in the bowl, and/or on the surface of the faeces

Other possible symptoms:

- Anal itching or irritation
- A feeling of rectal fullness, discomfort and/or incomplete evacuation
- Anal pain (with complications: prolapsed, strangulated internal haemorrhoids, or thrombosed external haemorrhoids).

 NICE 2021: https://cks.nice.org.uk/topics/haemorrhoids

Risk factors for haemorrhoids

- Straining during defecation
- Chronic constipation
- Frequent diarrhoea
- Antibiotics (that change bowel habit)
- Anal intercourse
- Heavy lifting
- Obesity
- Ageing
- Chronic cough
- Sitting all day
- Conditions that cause raised intra-abdominal pressure:
- Pregnancy
- Childbirth
- Space-occupying lesions

Primary and secondary medical management

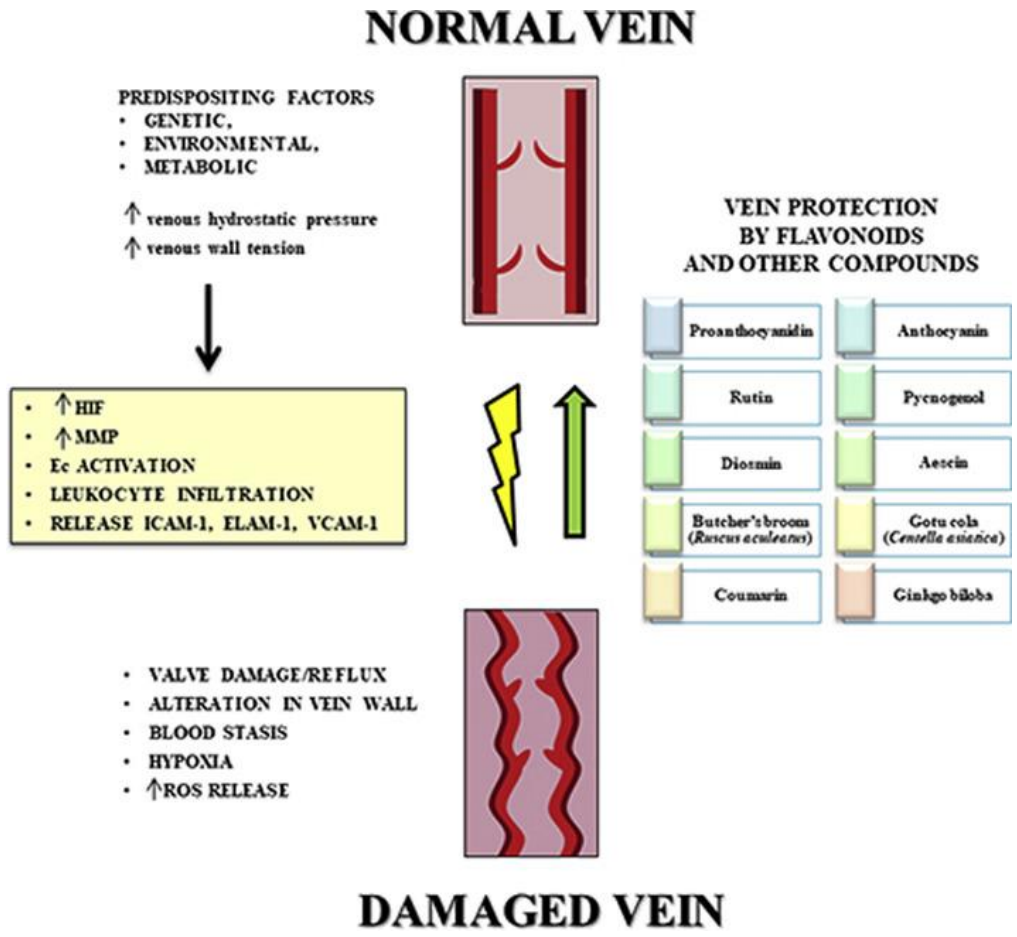
- Constipation treatment (water, fibre, laxatives)
- Avoiding straining and optimising anal hygiene for healing
- Symptomatic relief with topical creams/suppositories
  - Anti-inflammatory steroids
  - Astringent agents
- Referral in cases of non-response; or complications: ulceration; skin tags; maceration of the skin; ischaemia, thrombosis, or gangrene; and rarely, perianal sepsis and anaemia from bleeding
- **Non-surgical**: rubber band ligation, injection sclerotherapy, electrotherapy and others
- **Surgical**: haemorrhoidectomy; haemorrhoidal artery ligation

Antecedents, triggers and mediators to consider for *all types* of CVI: summary

- Hereditary weaknesses
- Destruction of valves (e.g. from deep vein thrombosis)
- Obstruction to blood flow:
  - Pregnancy
  - Constipation
  - Pelvic fibroids / tumours
- Associated with prolonged standing (gravity and lack of muscle pump)
- Chronic oxidation (smoking ↑es risk)
- Chronic inflammation
- Glycation
- Poor collagen integrity
- Hormonal imbalances
- Obesity (glycation + inflammation)
- High homocysteine

Oxidative stress and inflammation

- Blood from varicose veins tends to be higher in oxidative stress markers and lower in antioxidants
- Thus a call for identifying all drivers of free radical activity
- And to increase antioxidant capacity
- Antioxidant flavonoids are well-studied in varicose veins (see later)



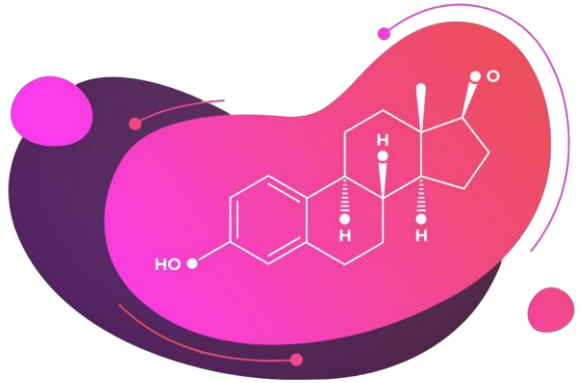
Lichota A, Gwozdzinski L, Gwozdzinski K. Therapeutic potential of natural compounds in inflammation and chronic venous insufficiency. Eur J Med Chem. 2019 Aug 15;176:68-91.

Excess weight and dysglycaemia: ‘Phlebesity’

- Involves **glycation, oxidation** and **inflammation** that can damage veins**:**
  - Improving *glucose* control → ↓ glycation + oxidation
  - Improving *insulin* control → ↓ inflammation (via PLA2; D5D)
- **Normalising weight:**
  - Reduces hypertension within the venous system that then…
  - …reduces the extra pressure on the vein walls and valves
- Action starts with a *personalised* low-GL, wholefoods diet (as everyone here knows)

Hormonal influence

- CVI more common in women and especially during pregnancy, perhaps not only due to obstruction:
- Progesterone stabilises uterus by relaxing smooth muscle fibres → venous dilation → valvular dysfunction
- Oestrogen may have even more of an effect because it relaxes smooth muscle and softens collagen fibres
- Expression of oestrogen and progesterone receptors has been shown to correlate with the severity of CVI in subjects
- Conversely, oestrogen supports collagen integrity
- Thus: consider all types of sex hormone imbalance



García-Honduvilla N, Asúnsolo Á, Ortega MA, et al. Increase and Redistribution of Sex Hormone Receptors in Premenopausal Women Are Associated with Varicose Vein Remodelling. Oxid Med Cell Longev. 2018 Sep 3;2018:3974026; Serra R, Gallelli L, et al. Estrogen Receptors and Chronic Venous Disease. Eur J Vasc Endovasc Surg. 2016 Jul;52(1):114-8

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High homocysteine (HHcy) in CVI

- Prospective study of 166 patients with CVI
  - HHcy was present in 54.22% of the CVI patients and was higher in the patients who'd had CVI the longest
  - The metabolic profile was altered in almost half of CVI cases and inflammation contributed to 23% of CVI cases
  - Concluded: HH contributes to CVI alongside the chronic inflammation that is well known in CVI, which increased thrombogenic risk
- Retrospective study of 611 patients without ulcers (control group) and 106 with ulcers (case group)
  - 46.2% of patients with ulcer had Hhcy compared with only 17.5% of control
  - Concluded HHcy is a key factor in the development of venous ulceration in patients with CVI

Rotaru M, Mariana Iancu G, Baldovin I. A prospective study on hyperhomocysteinemia as an aggravating factor in chronic venous insufficiency. Exp Ther Med. 2022 May 17;24(1):449, Guo Z, Li X, Wang T, Yang X, Fan L. Elevated serum homocysteine levels are associated with the development of chronic venous ulcers. Vasc Med. 2022 Aug;27(4):358-364..

Thus, in summary, for all types of CVI

- Consider family history
- Be alert for any history of DVT
- Look for any obstruction to blood flow:
  - Pregnancy
  - Constipation
  - Pelvic fibroids / tumours
- Look for factors like prolonged standing/sitting (gravity and lack of muscle pump), constipation…

Identify and work on any:

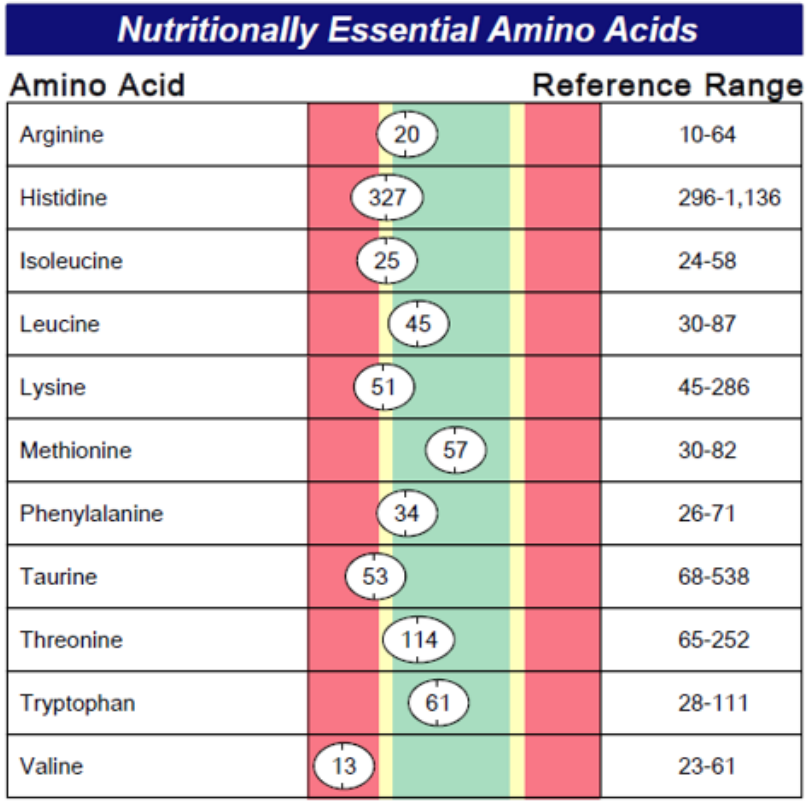
- Chronic oxidation
- Chronic inflammation
- Glycation
- Poor collagen integrity
- Hormonal imbalances
- Obesity (glycation + inflammation)
- High homocysteine

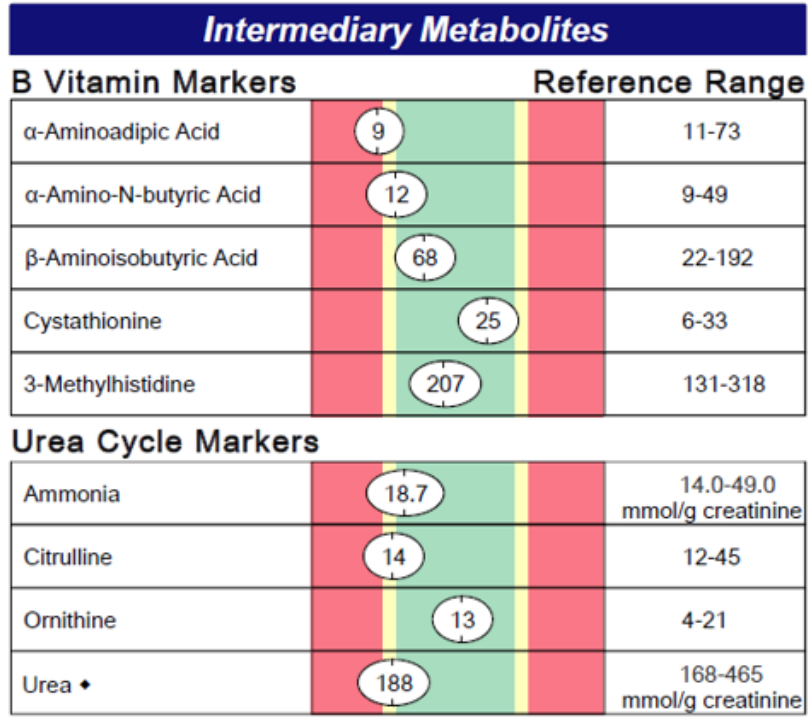
Specific nutrients to consider

Supporting healthy veins

Collagen integrity requires

- Precursors (protein sufficiency)
- Co-factors (vitamin C and Cu)





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‘Complete’ proteins come from animals, apart from soy

Incomplete proteins need to be combined to become ‘complete’

Grains and most seeds are extremely low in lysine but are good sources of tryptophan and methionine

Beans, pulses and most nuts are rich in lysine but are not good sources of tryptophan or methionine

'Anabolic resistance' may require a higher protein intake as we age

- Concept used to describe reduced muscle building ability that is common in older adults
- Caused by:
  - Impaired signalling pathways (e.g. MTOR1)
  - Reduced vascular health (we're discussing today!)
  - Reduced muscle protein synthesis
- Because of this, many experts recommend **a higher protein intake as we age**, such as 1-1.3g/kg body weight, vs the RDA of 0.8g

Nowson C, O'Connell S. Protein Requirements and Recommendations for Older People: A Review. Nutrients. 2015 Aug 14;7(8):6874-99, Paulussen KJM, McKenna CF, Beals JW, Wilund KR, Salvador AF, Burd NA. Anabolic Resistance of Muscle Protein Turnover Comes in Various Shapes and Sizes. Front Nutr. 2021 May 5;8:615849.

Vitamin C in blood vessel health

- Anti-inflammatory and antioxidant
- Co-factor for collagen synthesis
  - Deficiency results in scurvy (collagen catabolism)
- Increases blood flow in instances of impaired flow (smoking, obesity, etc.)
  - Slows oxidation of nitric oxide
- Prevents decline in endothelial function during prolonged sitting:
  - RCT of 11 healthy men sitting for 3 hours. 1g and 500mg at 30 min and 1 h 30 min, respectively
  - Superficial femoral artery flow-mediated dilation declined during sitting but this was prevented by vit C
- Used successfully in a licenced drug for CVI (with ruscus extract and hesperidin methyl chalcone)

Thosar SS, Bielko SL, et al (2015). Antioxidant vitamin C prevents decline in endothelial function during sitting. Med Sci Monit. 21:1015-21Fernandes et al 2011, Thosar et al 2015; Pompilio G, Nicolaides A, et al. Systematic literature review and network Meta-analysis of sulodexide and other drugs in chronic venous disease. Phlebology. 2021 Oct;36(9):695-709; Fernandes PR, Lira FA, Borba VV, et al (2011). Vitamin C restores blood pressure and vasodilator response during mental stress in obese children. Arq Bras Cardiol. 96(6):490-7.

Pharma Nord Formulations

Vitamin C

- 750 mg of vitamin C in each tablet
- Non-acidic vitamin C source (calcium ascorbate)
- Blister pack ensures that the vitamin C content is not damaged by oxygen and moisture
- Pharmaceutical-grade vitamin C
- Manufactured under Danish pharmaceutical control

Available in **UK**

Available in **ROI**

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Vitamin D, folate and flavonoids

- A systematic review of 20 studies of the nutritional status of patients with active and/or healed venous ulcers
- The majority of patients were overweight or obese; and this was associated with delayed wound healing
- Dietary intakes of omega-3 fatty acids, vitamin C and zinc were low for some patients
- **Vitamin D, folic acid and flavonoids** were associated with beneficial effects on ulcer healing

Barber GA, Weller CD, Gibson SJ. Effects and associations of nutrition in patients with venous leg ulcers: A systematic review. J Adv Nurs. 2018 Apr;74(4):774-787.

Flavonoids

- Phytochemicals from fruits, vegetables, flowers, nuts, seeds, herbs and spices
- Support blood vessels and blood flow, and have antioxidant and anti-inflammatory properties
- **Quercetin, anthocyanins and oligomeric proanthocyanidins (OPCs), rutin, aescin, coumarin, ginkgo biloba extract** are all being studied in CVI with promising results

Lichota A, Gwozdzinski L, Gwozdzinski K. Therapeutic potential of natural compounds in inflammation and chronic venous insufficiency. Eur J Med Chem. 2019 Aug 15;176:68-91

Flavonoid absorption:

- Many flavonoids are absorbed after interaction with microbes in the intestine
- Active metabolites are created by the gut microbiome
- Thus, always a good idea to **look after gastrointestinal health** to get the most from flavonoid consumption

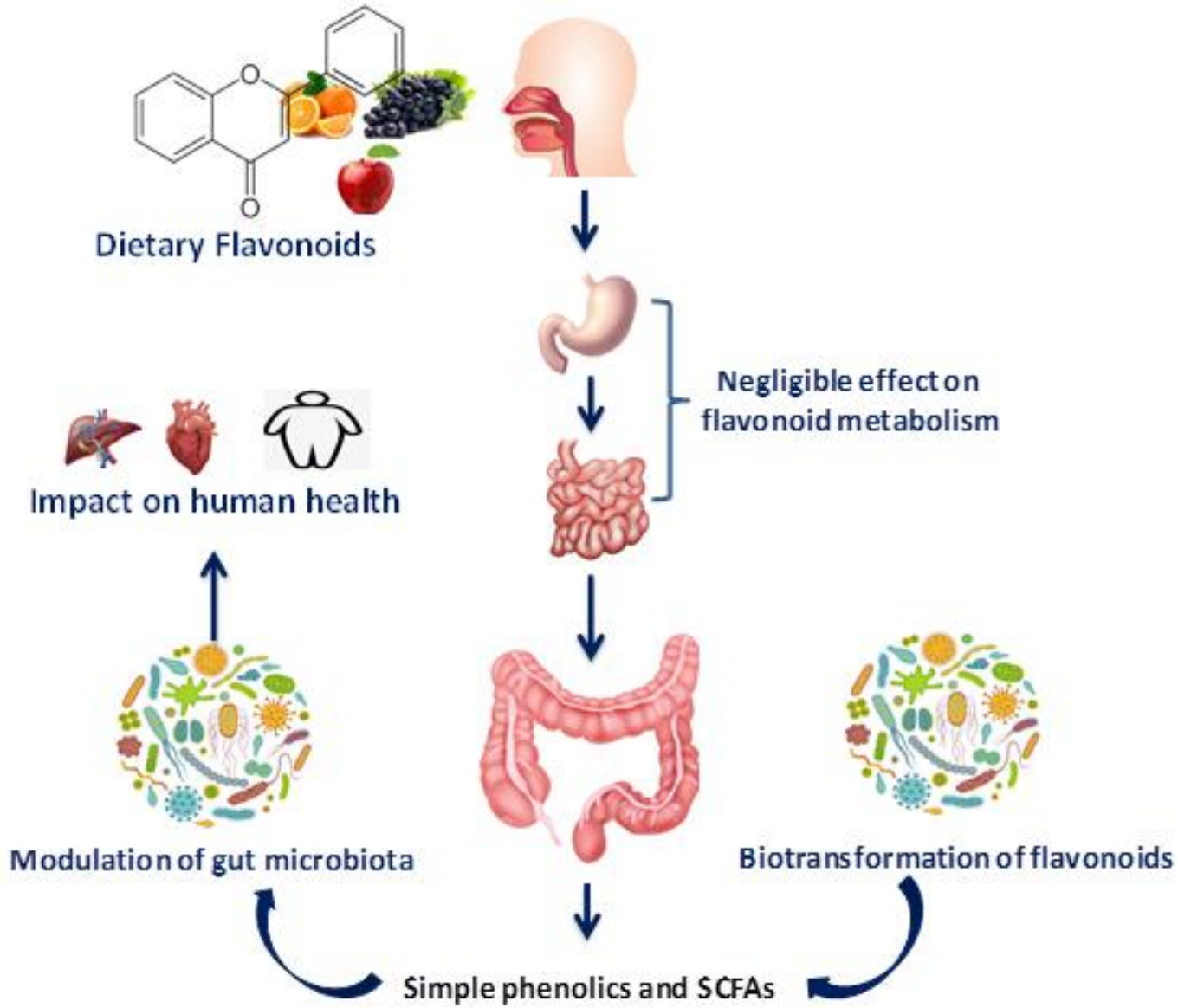


Image: Baky MH, Elshahed M, Wessjohann L, Farag MA. Interactions between dietary flavonoids and the gut microbiome: a comprehensive review. Br J Nutr. 2022 Aug 28;128(4):577-591

Pycnogenol

- A sustainably grown pine-bark extract with a consistent content of polyphenols
  - A by-product of the timber industry
- Grown in Southwest France without pesticides or fertilizers
- 40+ years of evidence with actions in many areas of health including CVI

What exactly is **Pycnogenol?**

- The patented extract comprises phenols known as OPCs (oligomericproanthocyanidins)
- Standardized to 65-75% procyanidin compounds by weight
- Have a strong affinity for blood vessels
- Diets low in these flavonoids → damaged and ‘leaky’ capillaries

- OPCs are also found in apples, berries, plums, tea, cocoa, wine, grape seed
- Pycnogenol has more consistent levels of OPCs than other plant extracts
  - Thus recent OPC studies tend to use Pycnogenol

Key **mechanisms** in venous health

- Strengthens capillary walls and makes them more resistant against internal blood pressure
    - This reduces the leakage of fluid into surrounding tissues
- Improves endothelial function with enhanced nitric oxide synthesis
    - This widens the blood vessels, releasing constriction

Cesarone MR, Belcaro G, et al. Chronic venous insufficiency and venous microangiopathy: management with compression and Pycnogenol®. Minerva Cardioangiol. 2019 Aug;67(4):280-287

How pycnogenol does this

- Binds to collagen and elastin and prevents their breakdown by inhibiting MMP enzymes (matrix metallo-proteases) involved in venous degradation
- Traps free radicals to prevent oxidative injury endothelium
- Supports vitamin C function: At least two studies have shown a synergistic effect between Pycnogenol and ascorbic acid in reducing oxidative damage and in regenerating vitamin C
- Anti-inflammatory through inhibition of NF-kB activation
- Inhibits platelet aggregation, improving circulation

Cesarone MR, Belcaro G, et al. Chronic venous insufficiency and venous microangiopathy: management with compression and Pycnogenol®. Minerva Cardioangiol. 2019 Aug;67(4):280-287

Found to be helpful in CVI

as early as 1999

- A 1999 review of 15 clinical studies, including double-blinded, placebo-controlled studies, showed…
- Pycnogenol (300mg/day for 60 days) → a significant improvement in CVI patients:
  - Improved oedema, leg pain, and the feeling of heavy legs
- Concluded the effect is most likely achieved through the improvement of the circulation as well as through a strengthening of the capillary walls
- And in another RCT in the 1990s Pycnogenol was shown to reduce the extent of thrombocyte aggregation in the microcirculation induced by cigarette smoking

Rohdewald P & Gulati OP. (1999). Proceedings of the 6th International Symposium on Pycnogenol, May 30 - June 2, 1999, Biarritz, France; European Bulletin of Drug Research; 7(2): 1-36

More effective for improving leg swelling than compression stockings

- 2024 trial of 2 comparable groups of 30 CVI patients
- One group took pycnogenol (150mg/day) and the other had compression stockings
- Pycnogenol relieved oedema (reduced leg volume by 18.3% in the evening compared to 4.4% with compression)
- PYC improved microcirculation of nutrient and waste exchange; and reduced local oxidative stress
- At the study end, 4 ulcerations and skin breaks were observed in the compression group (none in the PYC group)

Belcaro G, Cesarone MR, Cox D, et al. Improvements in edema and microcirculation in chronic venous insufficiency with Pycnogenol® or elastic compression. Minerva Surg. 2024 Aug;79(4):448-453.

Follows an earlier human trial (2019)

- 142 patients with CVI assigned to one of three groups:
  1. Pycnogenol 150 mg/day
  2. Compression stockings
  3. Compression + 150 mg/day Pycnogenol
- **At eight weeks**: combined Pycnogenol plus compression produced the best improvements in microcirculation (e.g. ankle swelling, symptom score, venous disability & severity, oxidative stress markers)
  - Also, Pycnogenol alone was more effective than compression alone
- Concluded Pycnogenol has a significant clinical role in CVI (both as a single treatment and in association with compression)

Cesarone MR, Belcaro G, et al. Chronic venous insufficiency and venous microangiopathy: management with compression and Pycnogenol®. Minerva Cardioangiol. 2019 Aug;67(4):280-287

CVI in a trial of 58 diabetic CVI patients (2024)

- PYC (150mg/day) vs. compression for 8 weeks
- Venous pressures, microcirculatory and clinical measurements of the patients were comparable at inclusion
- After 8 weeks, the PYC group had significantly less ankle swelling and microcirculatory perfusion vs. the compression group
- Clinical symptoms were also significantly lower in the PYC group vs. the compression group
- PYC also showed antioxidant properties and lowered oxidative stress
- Note that, as with the 2024 trial above, compression was less well tolerated

Belcaro G, Cesarone MR, Scipione C, et al. Pycnogenol® relieves chronic venous insufficiency (CVI) in diabetics: a supplement registry study. Minerva Surg. 2024 Sep 11.

Comparison of Pycnogenol with a widely used agent in venous health

166 CVI patients comparable in age, symptoms, venous incompetence, and microcirculation at baseline were assigned to take either 100mg Pycnogenol/day or 360mg red grape vine leaf extract (Antistax) 2/day, or compression stockings

Outcomes at 8 weeks:

- The rate of swelling and skin flux decreased toward normal values; the changes were greatest with Pycnogenol
- The oxygen level of tissue below the skin was increased more with Pycnogenol
- Ankle circumference was decreased more with Pycnogenol
- Pain and oedema were decreased with Pycnogenol and elastic compression, with prevalence for Pycnogenol ($p < 0.05$).
  - Oedema with Pycnogenol was reduced by 40%
- Hardening of tissue (with loss of elasticity and pliability) was reduced only in the Pycnogenol group

Belcaro G. A Clinical Comparison of Pycnogenol, Antistax, and Stocking in Chronic Venous Insufficiency. Int J Angiol. 2015 Dec;24(4):268-74.

Pycnogenol in comparison with 9 other products and compression in CVI

- In 2017, researchers compared the efficacy of ten interventions (nine products and compression) used to control symptoms of chronic venous insufficiency (see next slide →)
- 1051 subjects with CVI (typically varicose veins and/or ankle swelling)
- The endpoints of the study (at 12 months) were: microcirculation, effects on volume changes, symptoms (analogue scale)

Belcaro G, Dugall M, et al. Management of Varicose Veins and Chronic Venous Insufficiency in a Comparative Registry with Nine Venoactive Products in Comparison with Stockings. Int J Angiol. 2017 Sep;26(3):170-178.

- The best performers overall were Venoruton, Pycnogenol, the combination of the 2 (Venoruton and Pycnogenol), and compression
- The best improvement in *symptoms* score was obtained with Pycnogenol and compression
- *'The efficacy of Pycnogenol and the combination are competitive with stockings that do not have the same tolerability in warmer climates'*

Table 1

The nine venoactive products used in the study

	Dosage	Doses per day
Venoruton (Novartis)	1,500 mg	0-(β-hydroxyethyl)-rutosides
Pycnogenol (Horphag)	150 mg	French Maritime Pine bark extract
Troxerutin	1,000 mg	several preparations available
Diosmin + hesperidin		diosmin mg 450 flavonoids (esperidine = mg 50)
Antistax (Boehringer Ing)	750 mg	*360 mg extract red grape leaf*
Mirtaven (*Mirtoselect*) Indena	600 mg	*Mirtoselect* (*standardized bilberry extract* with 36% anthocyanins)
Troxerutin generic	800 mg	troxerutin 300 mg
E SSAVEN-Escin (Aventis-Sanofi, generic)	100 g dry extract of horse chestnut	Triterpene glycosides (triterpene 22.5%)
Ve-Pycno (Novartis and Horphag; noncombined preparation)	150 + 1,500 mg	*Supercompound*

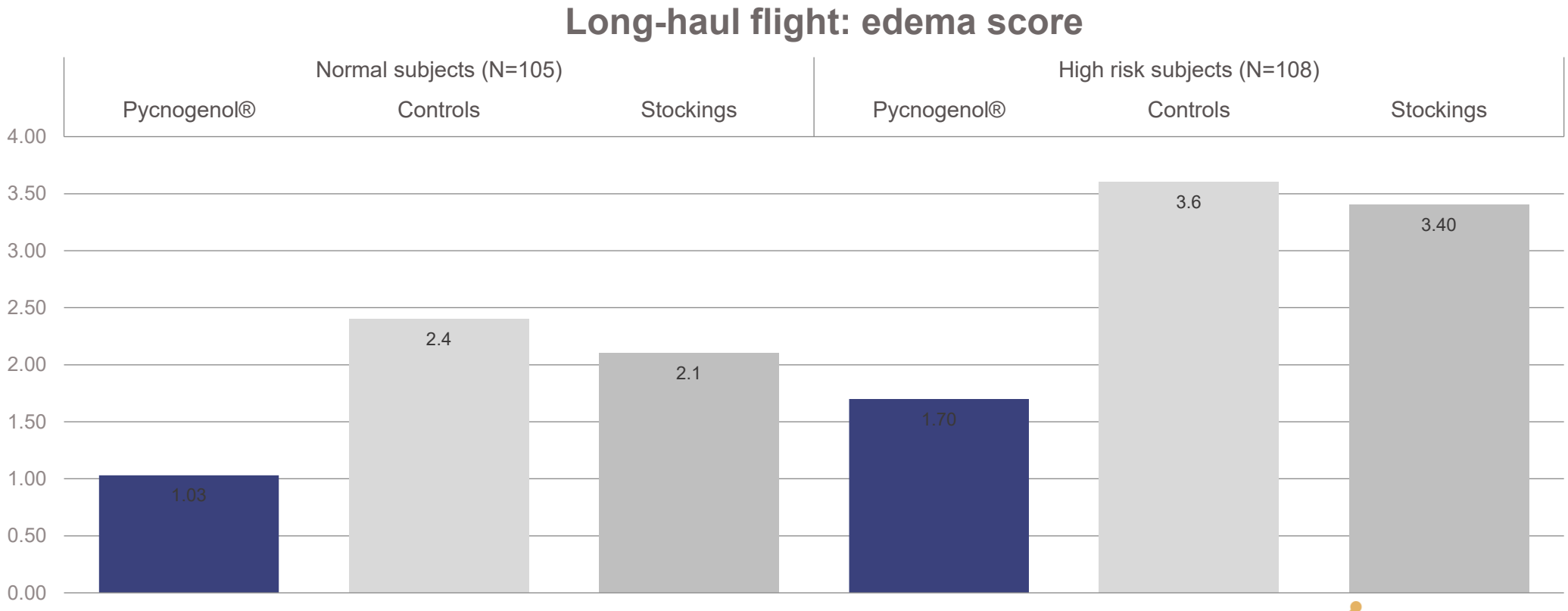
Belcaro G, Dugall M, et al. Management of Varicose Veins and Chronic Venous Insufficiency in a Comparative Registry with Nine Venoactive Products in Comparison with Stockings. Int J Angiol. 2017 Sep;26(3):170-178

Human trial in long-haul flight complications (2018)

- 295 participants comparable in CVI symptoms at baseline, but at different risk levels for thrombosis, who were flying in economy class twice in one week for more than 8 hours
- Outcomes: oedema, thromboses, jet lag
- Assigned to different groups according to whether their levels of risk for thromobosis. (High-risk group also received Aspirin)
- Each group was further divided into:
  - Pycnogenol 150 mg/day from 5 days before until 2-7 days after the second flight (N = 90)
  - Compression stockings (N = 99)
  - Controls (N – 106)

Belcaro G, Cornelli U, Dugall M, Hosoi M, Cotellese R, Feragalli B. Long-haul flights, edema, and thrombotic events: prevention with stockings and Pycnogenol® supplementation (LONFLIT Registry Study). Minerva Cardioangiol. 2018 Apr;66(2):152-159

Results: **Pycnogenol reduced oedema** from long-haul flights



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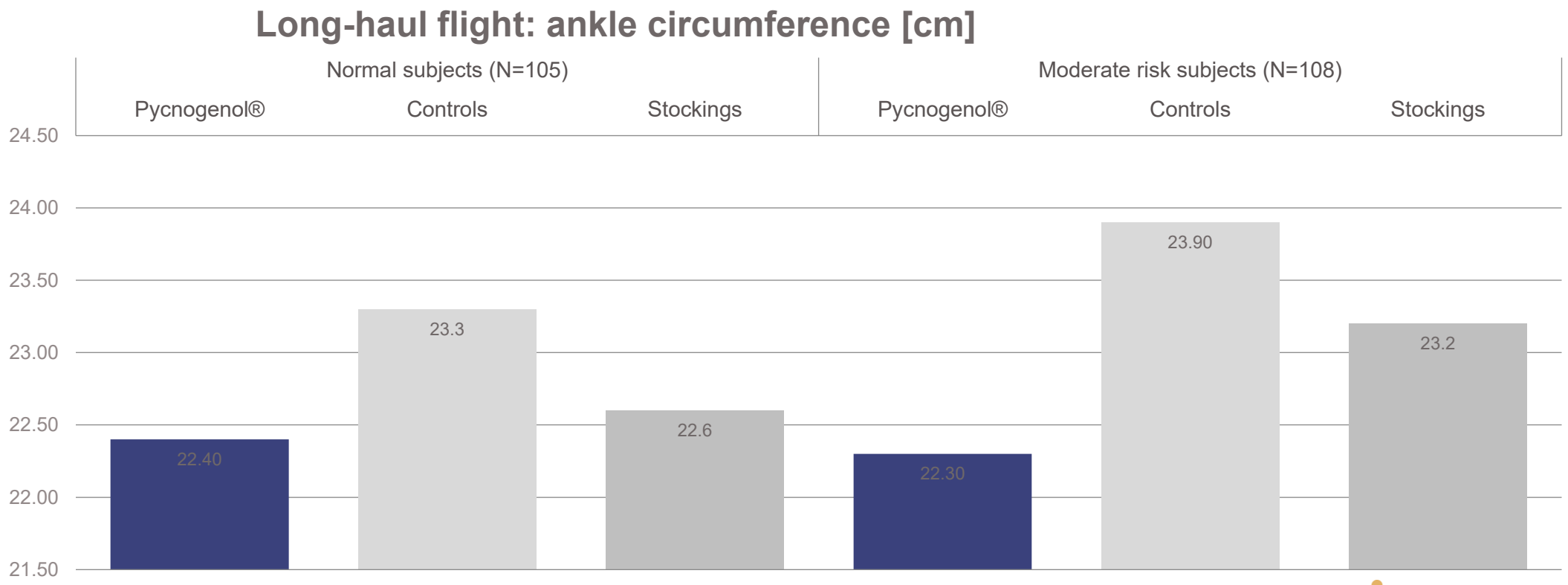
Results: **Pycnogenol reduced ankle circumference/swelling** from long-haul flights



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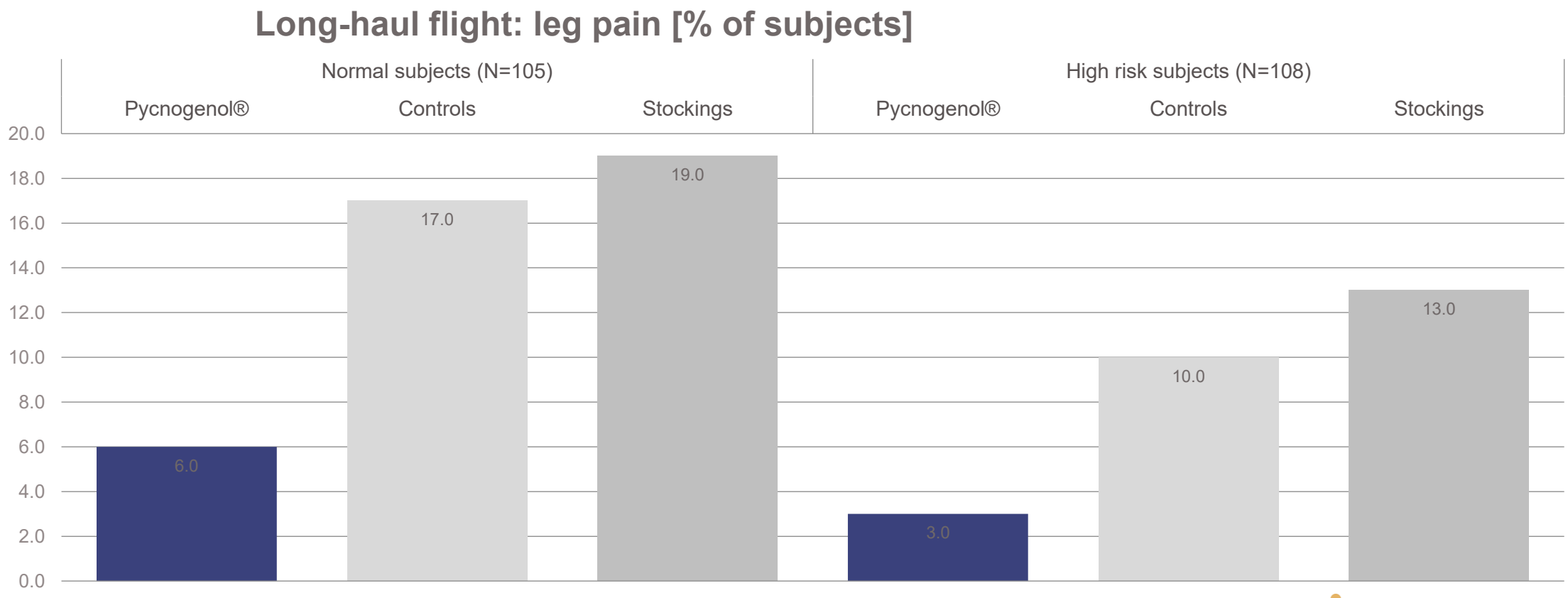
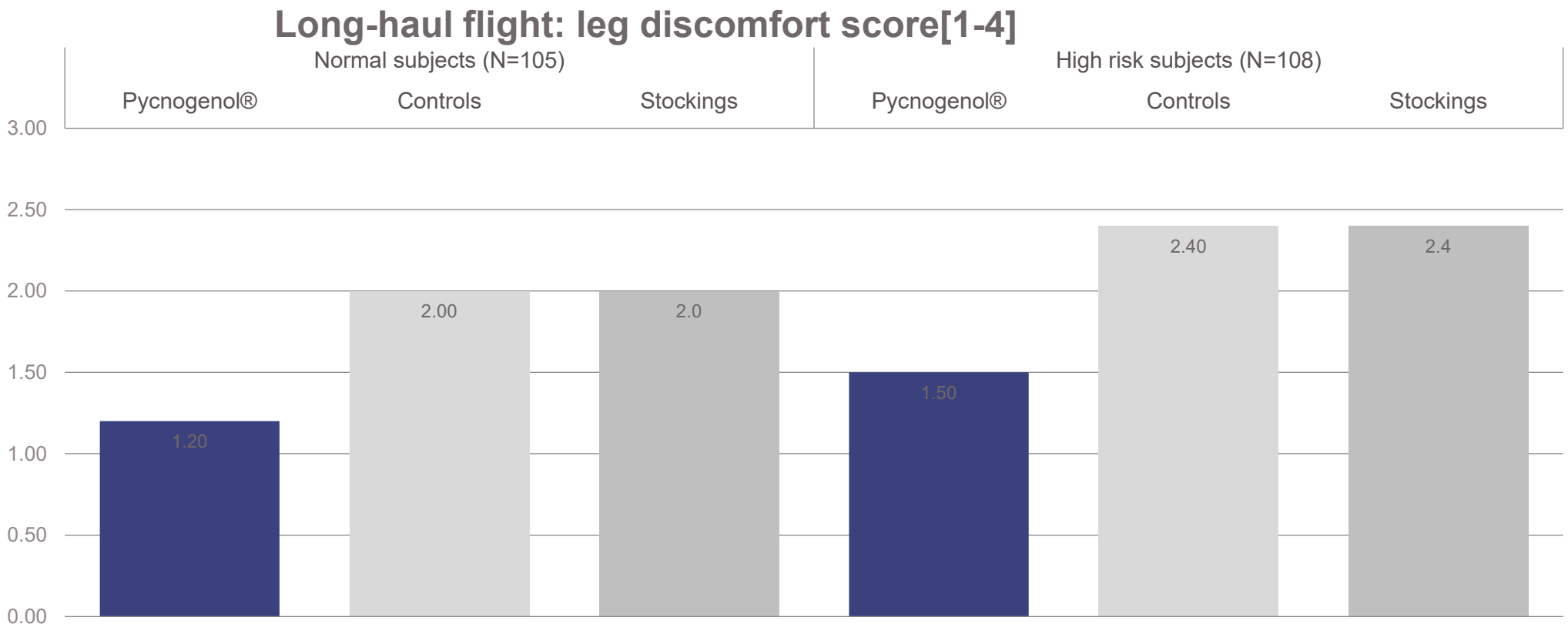
Results: **Pycnogenol reduced leg pain** from long-haul flights



Pharma Nord Academy

Results: **Pycnogenol reduced leg discomfort** from long-haul flights



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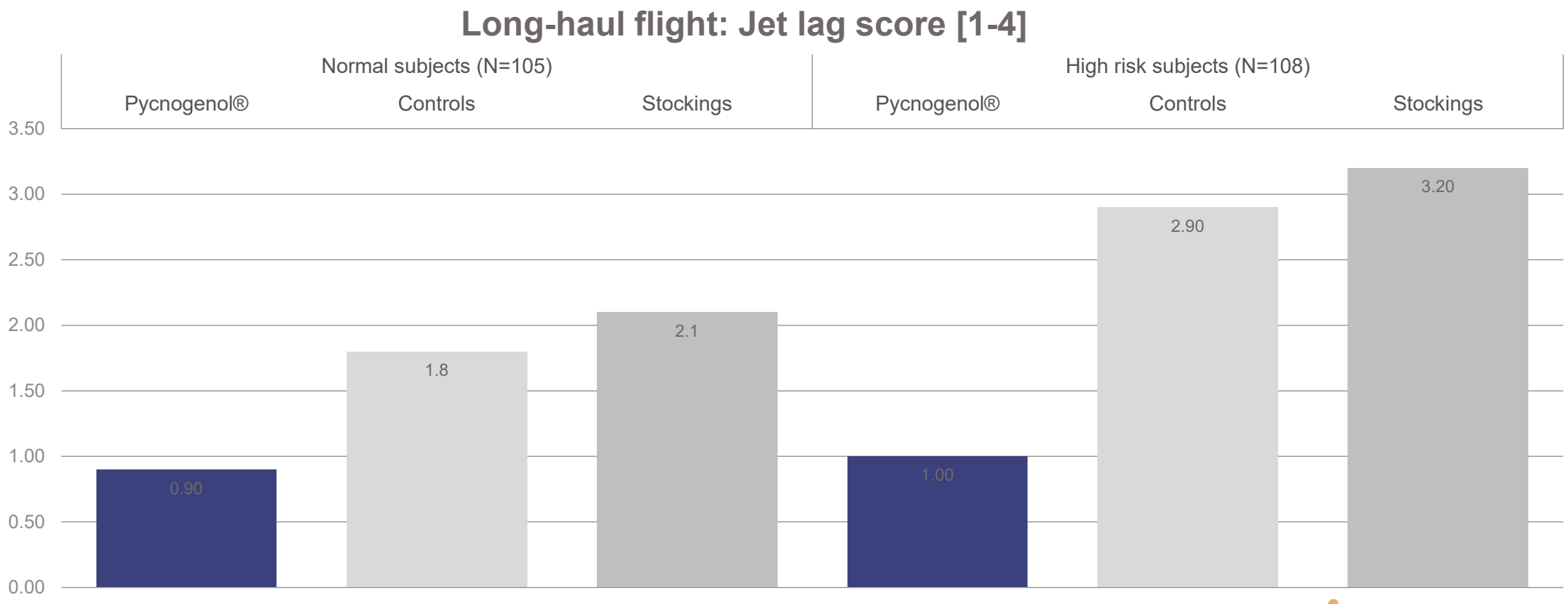
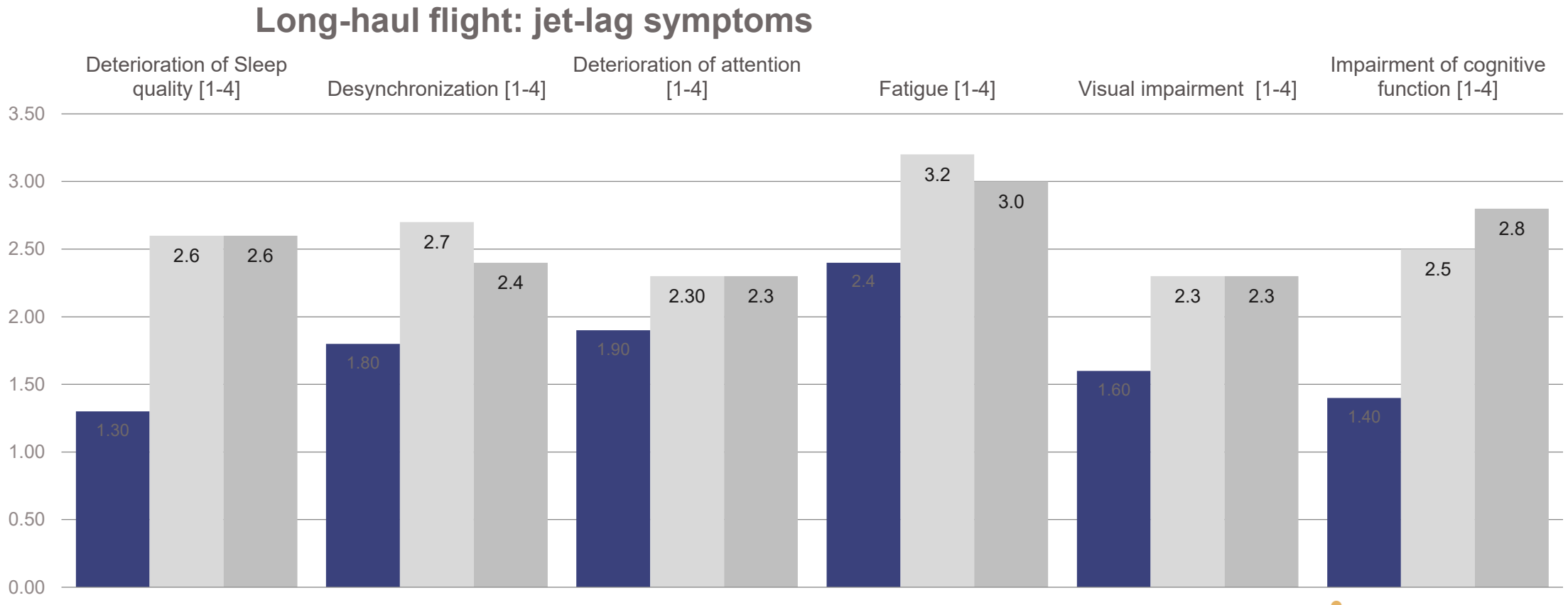
Results: **Pycnogenol reduced jet lag symptoms** from long-haul flights



Pharma Nord Academy

Results: **Pycnogenol reduced jet lag symptoms** from long-haul flights



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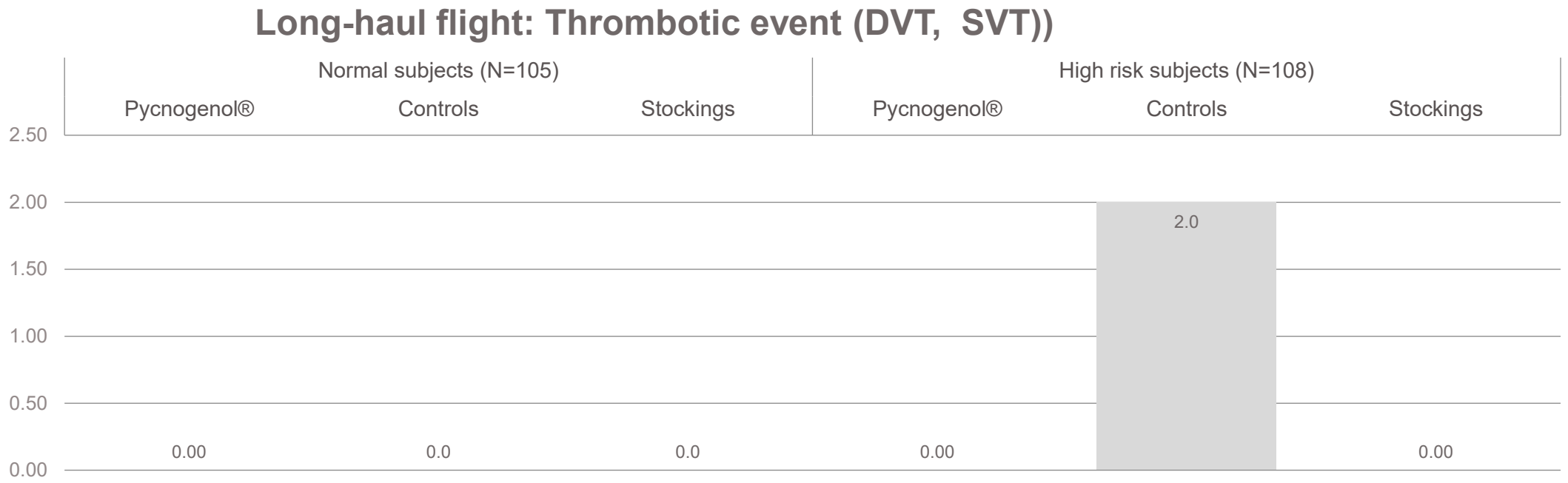
Pycnogenol prevented thrombosis from long-haul flights



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Researchers concluded (2018)

- Pycnogenol supplementation reduces oedema and may control some thrombotic events from long-haul flights
- These replicated the results of a similar trial in 2004 that concluded that Pycnogenol is effective in reducing the number of thrombotic events (both deep vein and superficial vein thrombosis) in moderate-to-high risk subjects during long-haul flights
  - 198 participants; average flight duration of 8 hours 15 minutes
  - Intervention group took two capsules (100mg per cap) 2-3 hours before flights; plus two capsules were taken 6 hours later; and one capsule the next day
  - Control group took comparable placebo at the same intervals

Belcaro G, Cesarone MR, et al. Prevention of venous thrombosis and thrombophlebitis in long-haul flights with pycnogenol. Clin Appl Thromb Hemost. 2004 Oct;10(4):373-7

Pycnogenol in venous ulcers

- A common complication of CVI
- 2017 longitudinal, prospective RCT of 30 patients with venous ulcers from a vascular surgery outpatient clinic
- Compared adjuvant treatment with Pycnogenol (50 mg orally, 3/day) to adjuvant treatment with diosmin/hesperidin - bioflavonoids widely used in venous disorders (450/50mg, 2/day)
- Assessed every 15 days for 90 days
- Both groups had a similar healing effect on the ulcers and had significantly reduced circumference of affected limbs
- Concluded Pycnogenol has an adjuvant effect on healing similar to diosmin/hesperidin

Toledo RR, Santos MERC, Schnaider TB. Effect of Pycnogenol on the Healing of Venous Ulcers. Ann Vasc Surg. 2017 Jan;38:212-219. doi: 10.1016/j.avsg.2016.04.014

Pycnogenol in haemorrhoids

- Trial of women with haemorrhoids within the third month following pregnancy
- Compared ‘standard best management’ (SBM) to SBM plus Pycnogenol 150 mg/day (intervention group) for 6 months. Results:
- Most severe cases: main symptoms were reduced at 6 months in all patients, but the group using Pycnogenol in addition to SBM showed more improvement
- 70% in the Pycnogenol group were symptom-free at 6 months in comparison with 36% of subjects in the ‘best management’ group

Belcaro G, Gizzi G, et al. Pycnogenol® in postpartum symptomatic hemorrhoids. Minerva Ginecol. 2014 Feb;66(1):77-84

Pycnogenol in haemorrhoids

- In more moderate cases: symptoms were reduced in both management groups at 6 months; with Pycnogenol the reduction in symptoms scores was significantly better
- 75% in the Pycnogenol group were symptom-free in comparison with 56% in controls.
- **Conclusion**: Pycnogenol appears to positively affect haemorrhoid signs and symptoms in the months after pregnancy.

Belcaro G, Gizzi G, et al. Pycnogenol® in postpartum symptomatic hemorrhoids. Minerva Ginecol. 2014 Feb;66(1):77-84

Pharma Nord Formulations

Pycnogenol

A research-driven & sustainable pine bark extract

- 40mg of Pycnogenol per tablet
- Consistent levels of plant compounds from batch to batch
- Over 40 years of research in various areas of health
- Suitable for vegetarians and vegans

Available in **UK**

Available in **ROI**

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Summary

1. Chronic venous insufficiency includes oedema, varicose veins and haemorrhoids
2. Lifestyle factors can reduce risk (e.g. keeping muscles working / weight management / compression)
3. Protein and vitamin C are core nutrients; also evidence for flavonoids, especially Pycnogenol

Any Questions?

Come and see us at stand:

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