WEBINAR SERIES | SESSION 3

PRACTICAL EDUCATION ON BLEEDING DISORDERS

Knowledge for All

Medical educational webinar series on global topics surrounding bleeding disorders.

TUESDAY, OCTOBER 12, 2021, 8–10 A.M. EDT

English with simultaneous translation into Arabic, French, Russian and Spanish.

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WELCOME

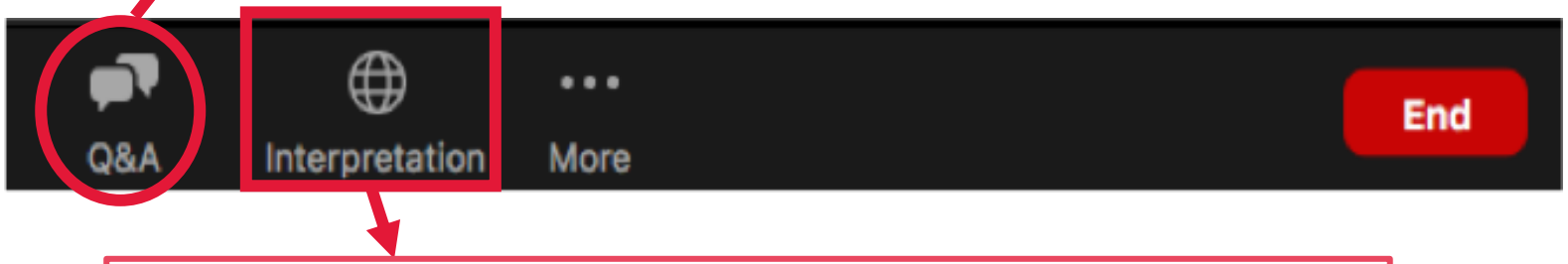
GLENN PIERCE, MD PhD

WFH VICE PRESIDENT, MEDICAL

QUESTIONS AND TRANSLATION

FOR COMPUTERS OR TABLETS

Please submit your questions in the Q&A box



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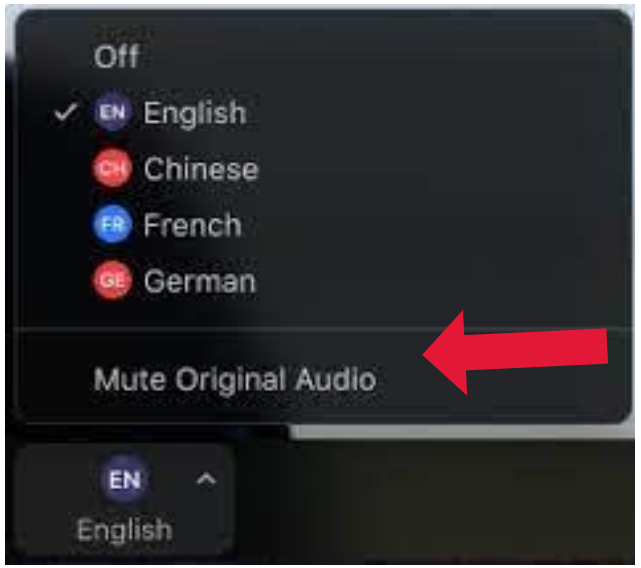
الرجاء اختيار لغتك المفضلة الآن

Пожалуйста выберите язык



Option to mute the original English audio

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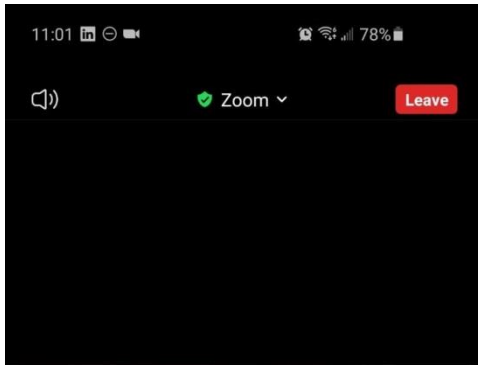
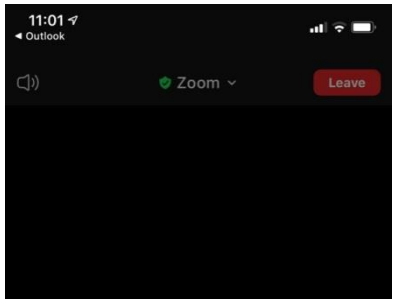
QUESTIONS AND TRANSLATION

FOR MOBILE PHONES





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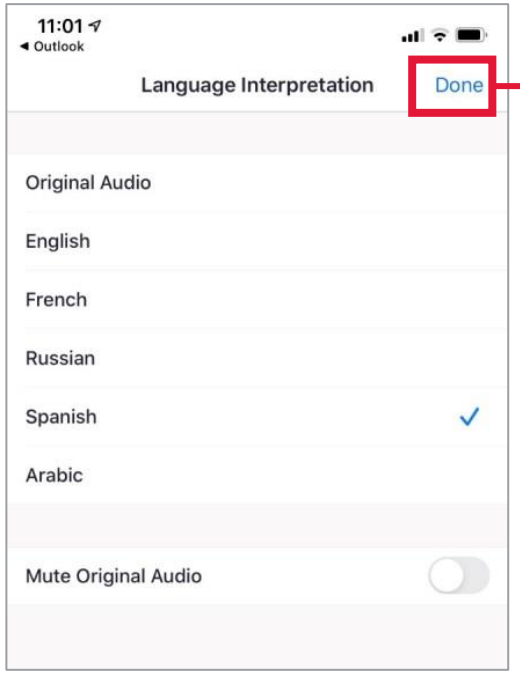

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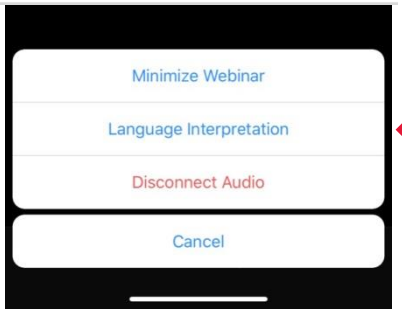

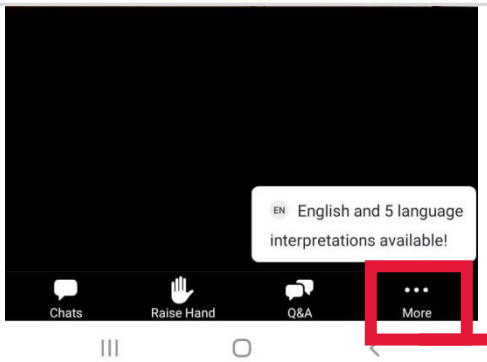

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AGENDA

1. Opening & welcoming remarks
2. MSK Comorbidities
    - Medical
    - Rehabilitation
    - Surgery
3. Q&A
4. Cardiovascular comorbidities
    - Hypertension & renal disease
    - Atrial fibrillation & anticoagulants
    - Ischemic heart disease
5. Q&A
6. Closing remarks

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SPEAKERS

Gianluigi Pasta, MD
Chair of WFH MSK Committee
Italy

Paul McLaughlin, MD
Clinical Specialist Physiotherapist
U.K.

Adolfo Llinás Volpe, MD
Medical Director, Fundación Santa Fe de Bogotá
Colombia

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SPEAKERS

Robert Klamroth , MD
Head of the Department and Director of Comprehensive Care
Germany

Roger Schutgens, MD
Van Creveldkliniek University Medical Center
Utrecht, The Netherlands

Gerard Dolan , MD
Consultant Haematologist and Director, St Thomas' Haemophilia Comprehensive Care centre
U.K.

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MSK Comorbidities – Osteoporosis, pain management, associated medical conditions and surgery

Gianluigi Pasta, MD
Chair of WFH MSK Committee
Fondazione IRCCS Policlinico San Matteo Pavia
Italy

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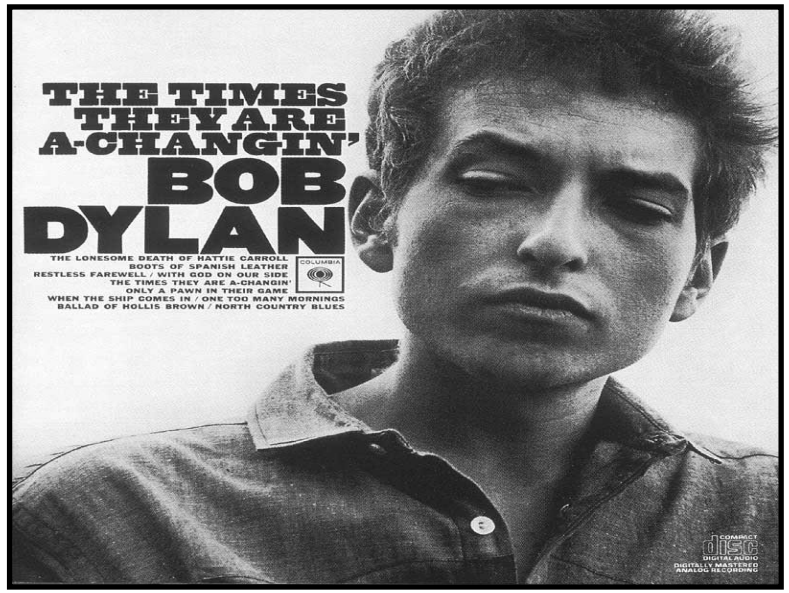
Haemophilia and MSK comorbidities



- Associated medical conditions and surgery
- Pain management
- Osteoporosis

Haemophilia and MSK comorbidities

Accepted: 11 June 2017

DOI: 10.1111/hae.13308

ORIGINAL ARTICLE

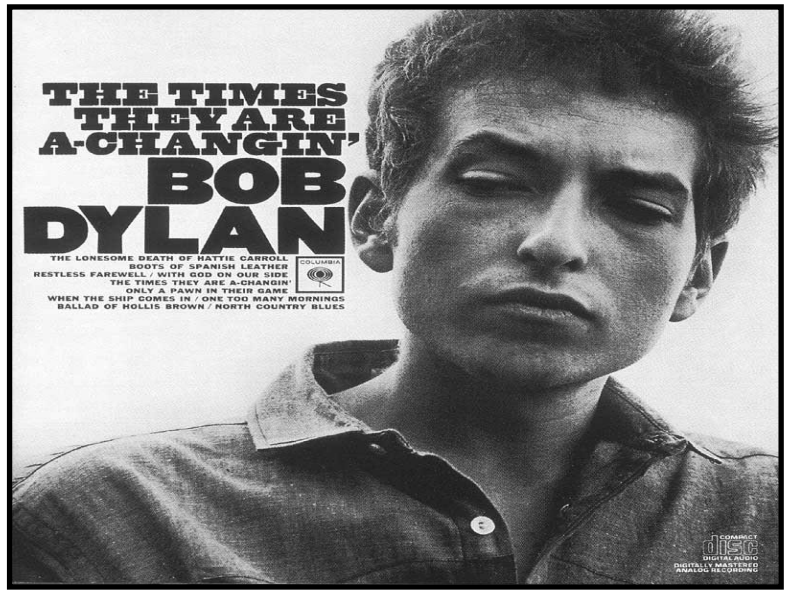
Clinical haemophilia

WILEY Haemophilia

Ageing successfully with haemophilia: A multidisciplinary programme

E. Boccalandro[1] | M. E. Mancuso[1] | S. Riva[1,2] | D. M. Pisaniello[1] | F. Ronchetti[3] | E. Santagostino[1] | F. Peyvandi[1] | L. P. Solimeno[4] | P. M. Mannucci[1] | G. Pasta[4]

Haemophilia and MSK comorbidities



- Associated medical conditions and surgery
- Pain management
- Osteoporosis

Associated medical conditions and surgery

Haemophilia
The Official Journal of the World Federation of Hemophilia,
European Association for Haemophilia and Allied Disorders and
the Hemostasis & Thrombosis Research Society

Haemophilia (2016), **22**, e275–e285 DOI: 10.1111/hae.12885

ORIGINAL ARTICLE *Musculoskeletal*

Meta-analysis: outcomes of total knee arthroplasty in the haemophilia population

M. F. MOORE,*† P. TOBASE‡ and D. D. ALLEN†
Physical Medicine and Rehabilitation, The Johns Hopkins Hospital Baltimore, MD; †Graduate Program in Physical Therapy, University of California San Francisco/ San Francisco State University; and ‡University of California, San Francisco Medical Center, San Francisco, CA, USA

[0.80–2.21]). A 31.5% complication rate was calculated with 106 reported in 336 TKAs. **Conclusions:** TKA is an effective procedure for improving ROM and decreasing functional deficits resulting from haemophilic arthropathy. Knee score data shows TKA improves overall function. This study guides clinicians regarding outcome expectations post-TKA in PWH.

Associated medical conditions and surgery

Infected joint replacements in HIV-positive patients with haemophilia

J. L. Hicks, W. J. Ribbans, B. Buzzard, S. S. Kelley, L. Toft, G. Torri, J. D. Wiedel, J. York

From Northampton General Hospital NHS Trust, England

J Bone Joint Surg [Br] 2001;83-B:1050-4.
Received 6 April 2000; Accepted after revision 30 March 2001

Associated medical conditions and surgery

bjh research paper

Factors influencing the long-term outcome of primary total knee replacement in haemophiliacs: a review of 116 procedures at a single institution

	Infected TKR (n = 9)	Uninfected TKR (n = 107)	Crude HR (95% CI)	Adjusted HR* (95% CI)
Age at surgery				
≤39 years (%)	6 (64)	54 (50)	1 (ref)	1 (ref)
>39 years (%)	3 (33)	53 (50)	0·5 (0·1–2·1)	1·1 (0·2–6·1)
Presence of inhibitors (%)	3 (33)	4 (4)	9·0 (2·2–36·3)	4·7 (0·3–67·2)
Human immunodeficiency virus infection (%)	3 (33)	39 (36)	0·8 (0·2–3·2)	0·3 (0·03–2·8)
Primary surgeon other than LPS (%)	3 (33)	7 (6)	5·0 (1·2–20·2)	9·8 (1·0–95·3)
Cementless implant (%)	6 (67)	20 (19)	5·7 (1·4–23·1)	3·7 (0·8–17·7)
Continuous infusion (%)	4 (44)	8 (7)	7·3 (1·9–27·1)	2·2 (0·2–22·8)

*Each variable was adjusted for all the others.

Associated medical conditions and surgery

■ KNEE

The preoperative management of Hepatitis C may improve the outcome after total knee arthroplasty

Correspondence should be sent to R. Schwarzkopf; email: ran.schwarzkopf@nyumc.org

doi:10.1302/0301-620X.101B6.BJJ-2018-0723.R3 $2.00

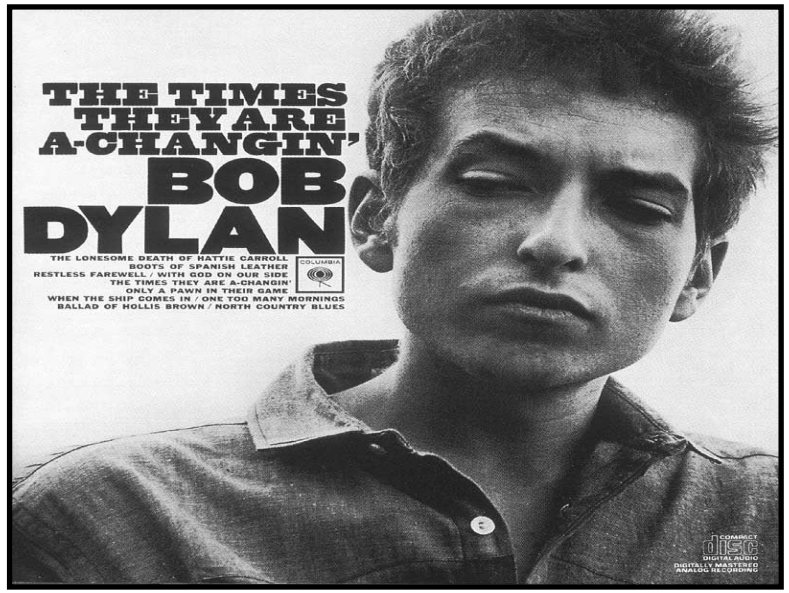
Bone Joint J
2019;101-B:667–674.

Table VI. Postoperative surgical outcomes

Characteristic	Cured (64 patients; 70 knees)	Untreated (63 patients; 71 knees)	p-value
Infection, n (%)	3 (*4.3*)	11 (*15.5*)	0.03*‡
Deep infection	3 (*4.3*)	7 (*9.9*)	
Superficial infection	0 (*0.0*)	4 (*5.6*)	
Stiffness requiring MUA, n (%)	2 (*2.8*)	1 (*1.4*)	0.55*
Wound drainage, n (%)	0 (*0.0*)	2 (*2.8*)	0.16*
Intraoperative fracture, n (%)	0 (*0.0*)	0 (*0.0*)	N/A
Postoperative fracture, n (%)	0 (*0.0*)	0 (*0.0*)	N/A
Revision total knee arthroplasty, n (%)	1 (*1.4*)	9 (*12.7*)	< 0.01*‡
Infection	1 (*1.4*)	6 (*8.5*)	
Arthrofibrosis	0 (*0.0*)	1 (*1.4*)	
Improper component sizing	0 (*0.0*)	1 (*1.4*)	
Persistent wound drainage	0 (*0.0*)	1 (*1.4*)	
All surgical complications, n (%)	5 (*7.1*)	15 (*21.1*)	0.02*‡

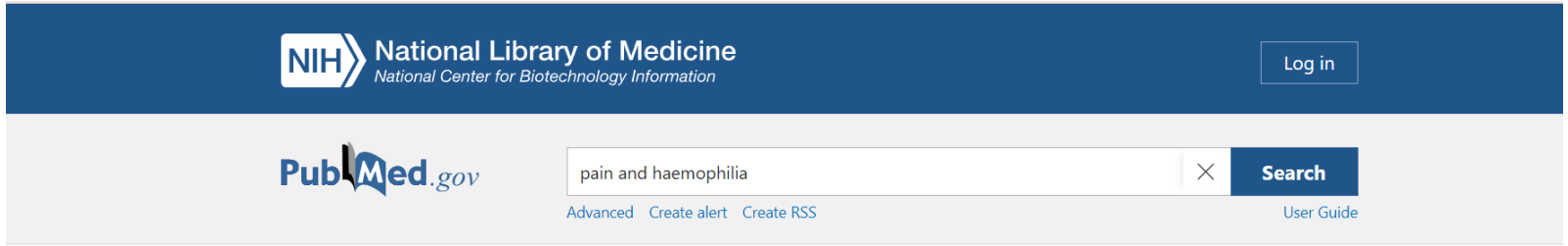
*Chi-squared test
‡Statistically significant
MUA, manipulation under anaesthesia; N/A, not applicable

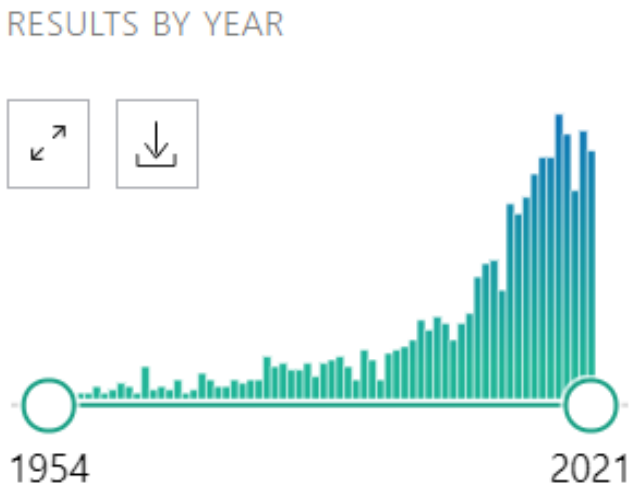
Haemophilia and MSK comorbidities



- Associated medical conditions and surgery
- Pain management
- Osteoporosis

Haemophilia and pain





Haemophilia and pain

Contents lists available at ScienceDirect

Blood Reviews

journal homepage: www.elsevier.com/locate/issn/0268960X

Review

Improving assessment and management of pain in hemophilia: an Italian Delphi consensus statement☆

Cristina Santoro[a,1], Matteo Nicola Dario Di Minno[b,*,1], Antonio Corcione[c], Giovanni Di Minno[d], Marco Martinelli[e], Maria Elisa Mancuso[f], Benedetto Acone[g], Angelo Claudio Molinari[h], Emilio Valter Passeri[e], Angiola Rocino[i], Rita Carlotta Santoro[j], Annarita Tagliaferri[k], Consalvo Mattia[l], On Behalf of the HAEMODOL Study Group

Haemophilia and pain

Improving assessment and management of pain in hemophilia: an Italian Delphi consensus statement☆

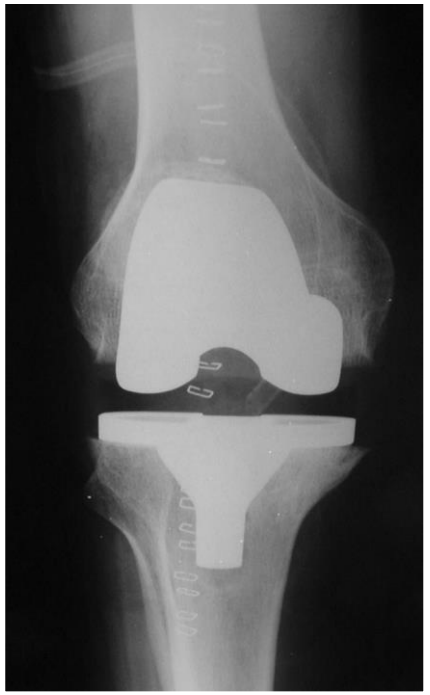
Joint pain, both acute (caused by hemarthrosis) and chronic (caused by hemophilic arthropathy), is a major problem in PwH, including children and adolescents [12–19]. Up to 50% of adult PwH have chronically painful joints that cause disability and impair quality of life (QoL) [10,20], and in a multinational study, 89% of PwH experienced at least one pain exacerbation episode during a 4-week observation period [21]. Chronic and acute pain are frequently experienced concurrently, which causes unique challenges in the assessment and management of pain in PwH [12,22,23].

Appropriate pain assessment and effective management strategies are essential to improve the functionality and QoL of PwH [20,24,25].

Thus, there is an urgent need to improve and standardize both pain assessment and pain management in PwH [25]. To this end, the HAE-

Haemophilia and pain

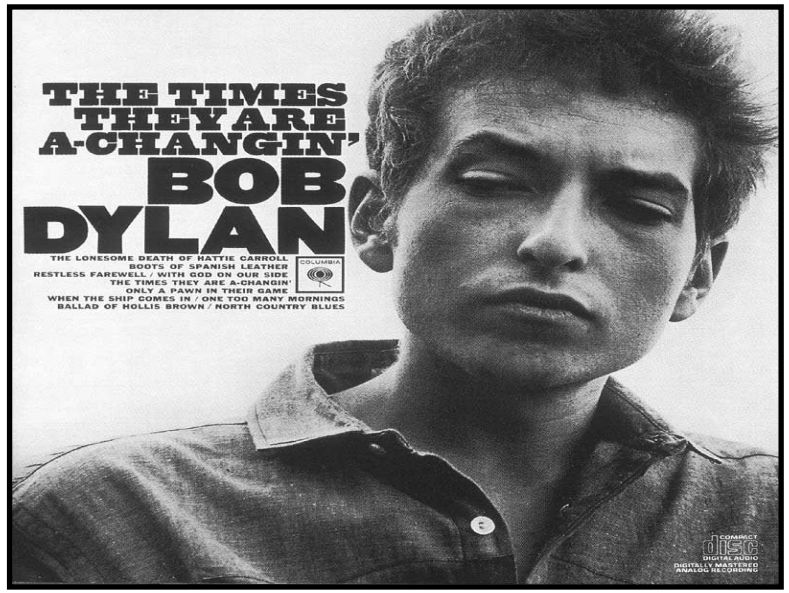
Multimodal management



Haemophilia and pain

- Sylent bleedings
- Chronic synovitis
- Chronic arthropathy

Haemophilia and MSK comorbidities



- Associated medical conditions and surgery
- Pain management
- Osteoporosis

Haemophilia and osteoporosis

Several original articles published after 1994 have suggested a relationship between osteoporosis.

Iorio A et al. Thromb Haemost. 2010

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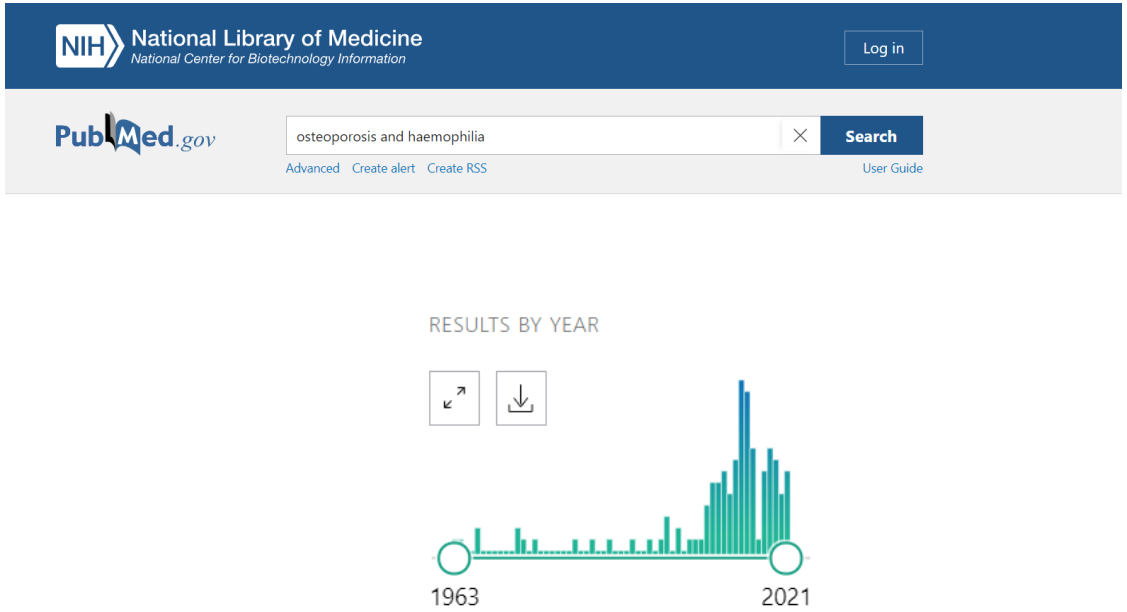
Haemophilia and osteoporosis



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Haemophilia and osteoporosis

Type of change	Finding	Score
Osteoprosis	Absent	0
	Present	1
Enlargement of epiphysis	Absent	0
	Present	1
Irregularity of subchondral bone	Absent	0
	Surface partially affected	1
	Surface completely affected	2
Narrowing of joint space	Absent	0
	Joint space>1 mm	1
	Joint space<1 mm	2
Subchondral cyst formation	Absent	0
	1 cyst	1
	>1 cyst	2
Erosions at joint margins	Absent	0
	Present	1
Incongruence between joint surfaces	Absent	0
	Slight	1
	Pronounced	2
Articular deformity (angulation and/or displacement of articulating bones)	Absent	0
	Slight	1
	Pronounced	2

Pettersson, *Clin Orthop 1980*

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Haemophilia and osteoporosis

Bone mineral density in haemophilia patients

A meta-analysis

Alfonso Iorio[1]; Gianluigi Fabbriciani[2,3]; Maura Marcucci[1]; Matteo Brozzetti[4]; Paolo Filipponi[2]

[1]Hemophilia Centre – Internal and Vascular Medicine, Department of Internal Medicine, University of Perugia, Perugia, Italy; [2]U.O. Medicina Generale, Azienda A.S.L. n. 1 dell'Umbria – Città di Castello and Umbertide, Italy; [3]Institute of Internal Medicine, Angiology and Arteriosclerosis, Department of Clinical and Experimental Medicine, University of Perugia, Perugia, Italy; [4]Ospedale di Norcia, Azienda A.S.L. n. 2 dell'Umbria, Perugia, Italy

BMI or with the percentage of HCV-infected patients. This meta-analysis confirms the association between severe haemophilia and low BMD.

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Haemophilia and BMD

BMD in any given individual is determined by peak bone mass and the rate of bone loss. Peak bone mass is achieved around the mid-20s and is determined by several factors (genetic, nutrition, body weight, and weight-bearing physical activity)

Nelson DA et al., 2006

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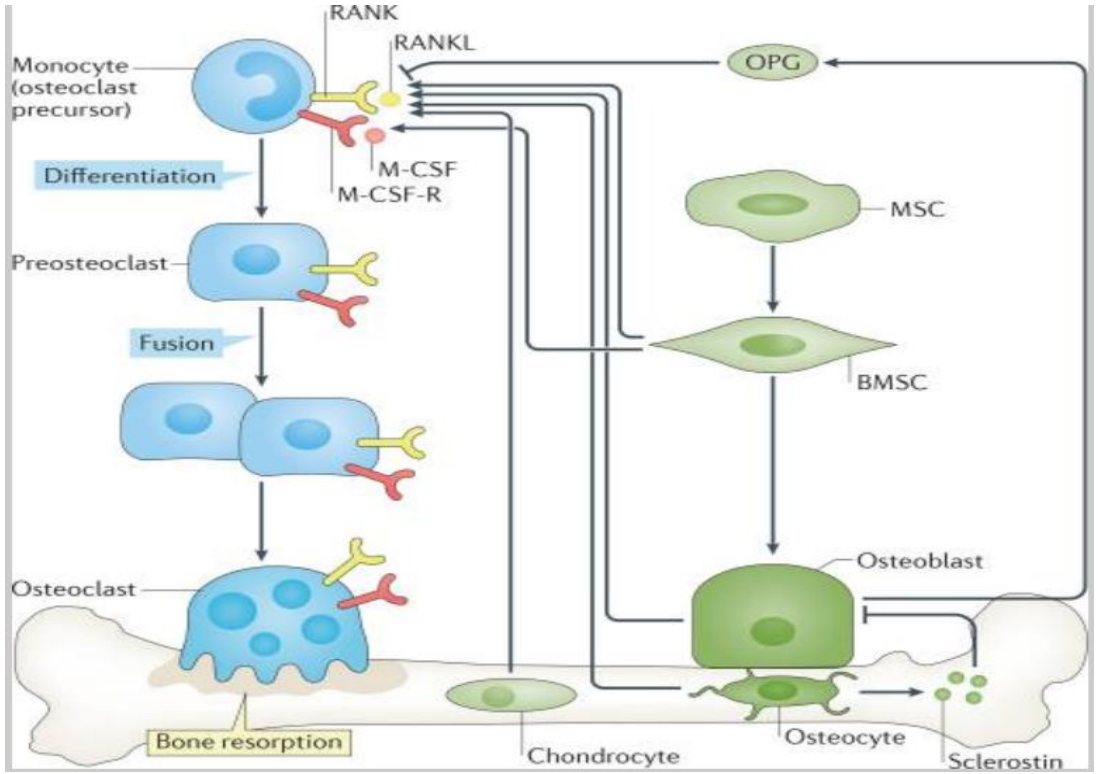
Haemophilia and osteoporosis

Osteoporosis is a skeletal disorder characterised by decreased bone strength and increased risk of fracture. Bone mineral density (BMD) is the most important factor in bone strength.

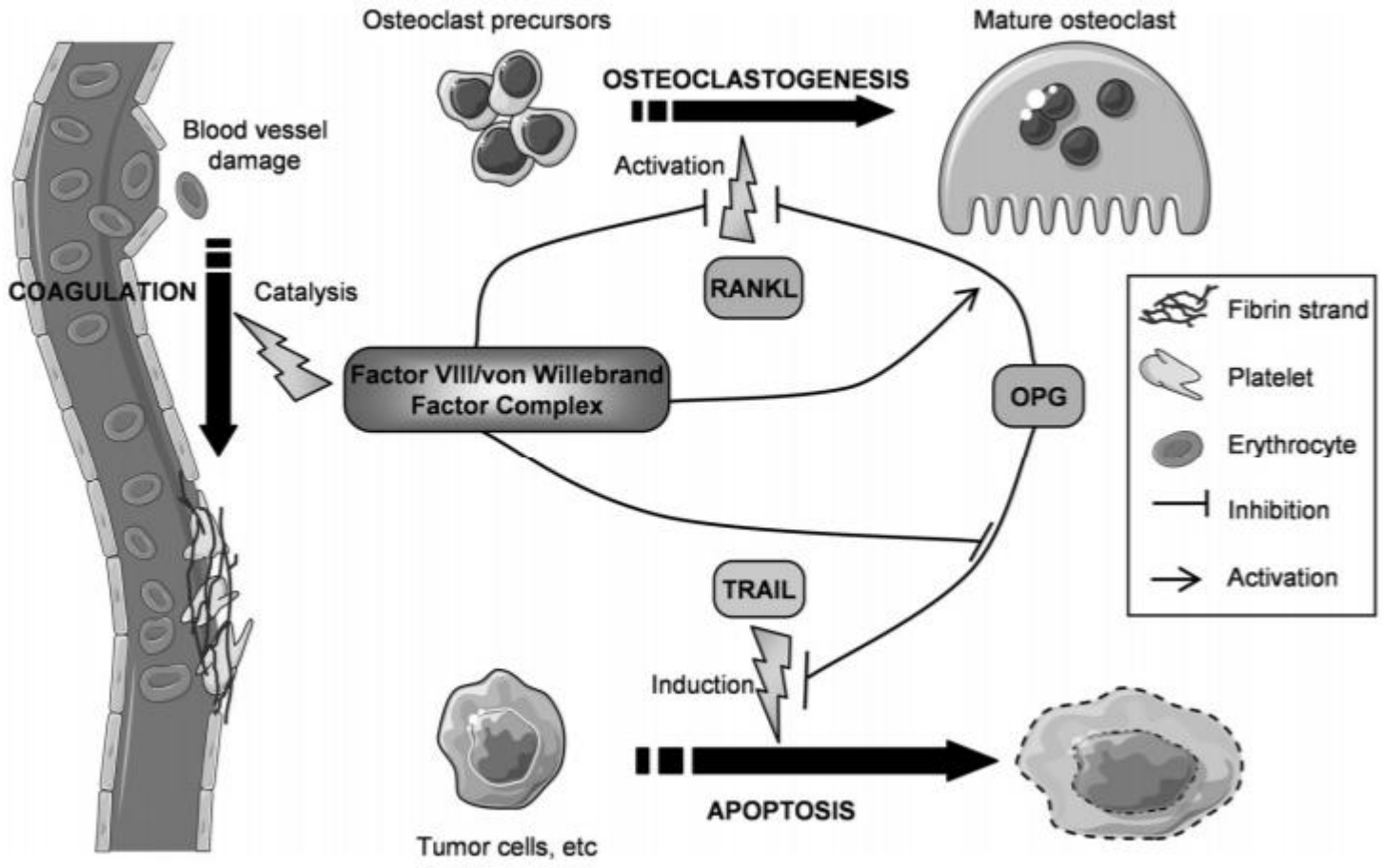
NIH consensus on Osteoporosis Prevention 2001

Haemophilia and bone turnover

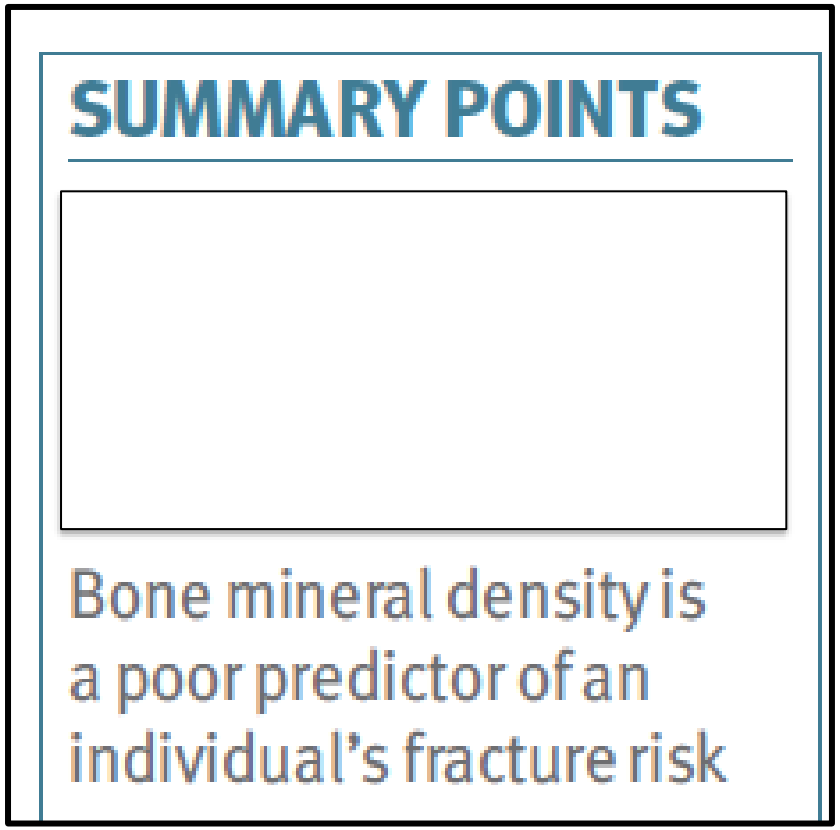


M. Neale Weitzmann, Physiological and pathophysiological bone turnover — role of the immune system, Malkiet Kaur, Osteoblast-n-Osteoclast: Making Headway to Osteoporosis Treatment

Haemophilia and bone turnover



Haemophilia and osteoporosis



BMJ, 2008

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Haemophilia and osteoporosis

Surrogate endpoints

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Haemophilia and osteoporosis

Received: 7 June 2018 | Revised: 1 August 2018 | Accepted: 26 August 2018

DOI: 10.1111/hae.13611

ORIGINAL ARTICLE

Musculoskeletal

WILEY Haemophilia

Usefulness of bone microarchitectural and geometric DXA-derived parameters in haemophilic patients

Fabio Massimo Ulivieri[1] | Giulia Antonella Angela Rebagliati[2] | Luca Petruccio Piodi[3] | Luigi Piero Solimeno[4] | Gianluigi Pasta[5] | Elena Boccalandro[4] | Maria Rosaria Fasulo[6] | Maria Elisa Mancuso[7] | Elena Santagostino[7]

	TBS			BS		
Age (pts. number)	Mean	SD	Median	Mean	SD	Median
≤30 (11)	1.42	0.07	1.41	3.20	1.32	3.06
31-40 (20)	1.37	0.09	1.37	2.59	0.89	2.49
41-50 (20)	1.38	0.39	1.31	3.02	1.46	2.56
51-60 (11)	1.33	0.12	1.36	2.63	1.20	2.38
61-70 (5)	1.21	0.11	1.22	1.83	0.39	1.85
≥71 (3)	1.15	0.11	1.20	4.87	3.48	3.40

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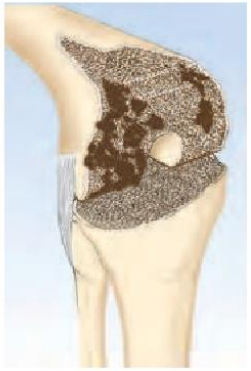
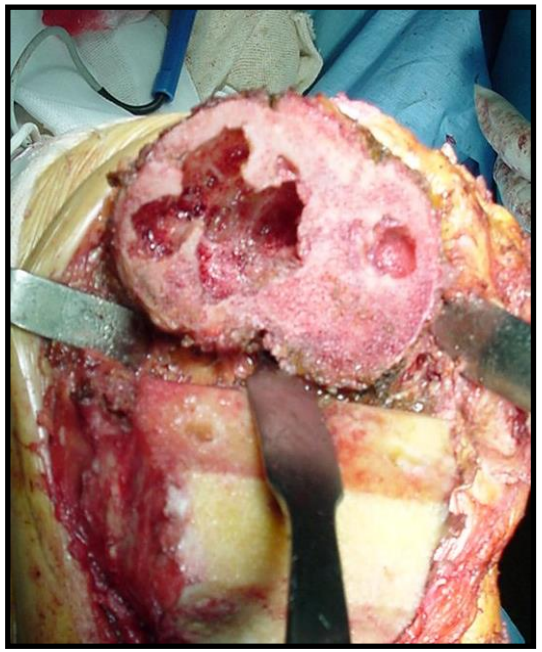
Haemophilia and osteoporosis

Femoral defect			
F1	F2a	F2b	F3
			
Small amounts of bone loss not compromising component stability (contained, minor defects)	Damaged unicondylar structural bone (noncontained)	Damaged bicondylar structural bone (noncontained)	Significant bone loss compromising a major portion of the condyles with ligamentous instability (noncontainec



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Haemophilia and osteoporosis

Bone mineral density in haemophilia patients

A meta-analysis

Alfonso Iorio[1]; Gianluigi Fabbriciani[2,3]; Maura Marcucci[1]; Matteo Brozzetti[4]; Paolo Filipponi[2]

[1]Hemophilia Centre – Internal and Vascular Medicine, Department of Internal Medicine, University of Perugia, Perugia, Italy; [2]U.O. Medicina Generale, Azienda A.S.L. n. 1 dell'Umbria – Città di Castello and Umbertide, Italy; [3]Institute of Internal Medicine, Angiology and Arteriosclerosis, Department of Clinical and Experimental Medicine, University of Perugia, Perugia, Italy; [4]Ospedale di Norcia, Azienda A.S.L. n. 2 dell'Umbria, Perugia, Italy

Future studies should investigate fracture rates and interventions to prevent bone loss in persons with haemophilia

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Haemophilia and osteoporosis

“ It takes a child 1 year to acquire independent movement and 10 years to acquire indipendent mobility. An old person can lose both in a day”.

Isaacs B, Challenge of Geriatric Medicine 1992

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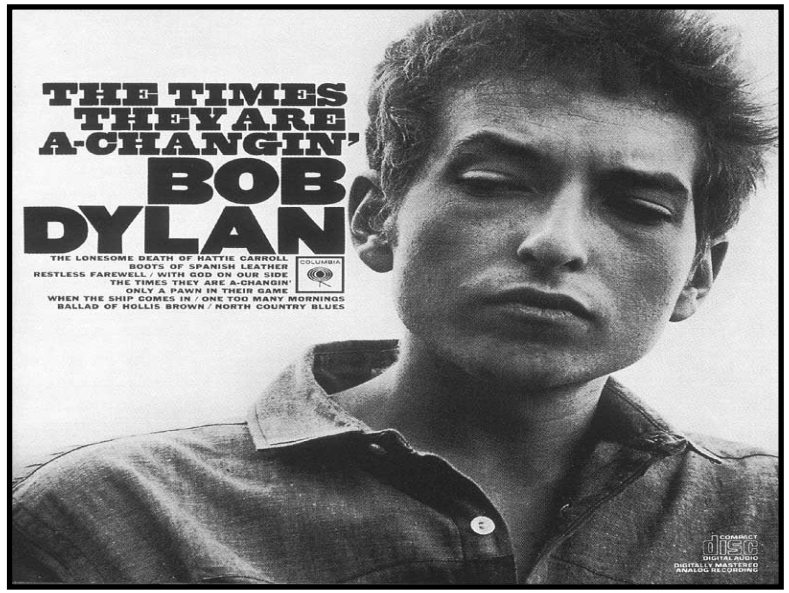
Haemophilia and osteoporosis



During the last decade, the approach to the patients with low bone mass has shifted from a simple BMD measurement to a more comprehensive evaluation of fracture risk.

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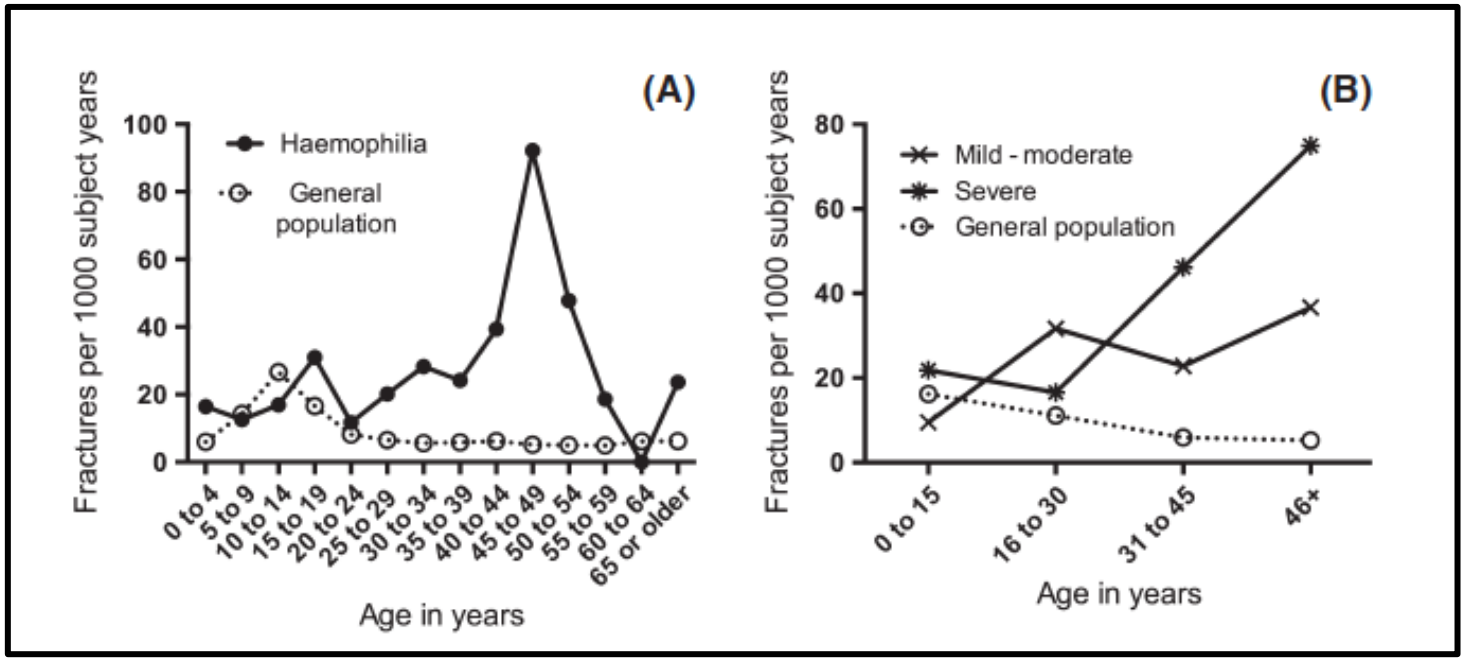
Haemophilia and fracture rate

bjh correspondence

Increased fracture rates in people with haemophilia: a 10-year single institution retrospective analysis



Gay ND et al. 2015

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Haemophilia and fracture rate

Epidemiology of fractures in patients with haemophilia

H. Caviglia [a,b,*], M.E. Landro [a], G. Galatro [a,b], M. Candela [b], D. Neme [b]

[a] Department of Orthopaedic Surgery and Traumatology, Dr. Juan A. Fernández General Hospital, Cerviño 3356, 3rd floor, (C1425APF), Buenos Aires, Argentina
[b] Haemophilia Foundation, Soler 3485, (C1425BWE), Buenos Aires, Argentina[1]

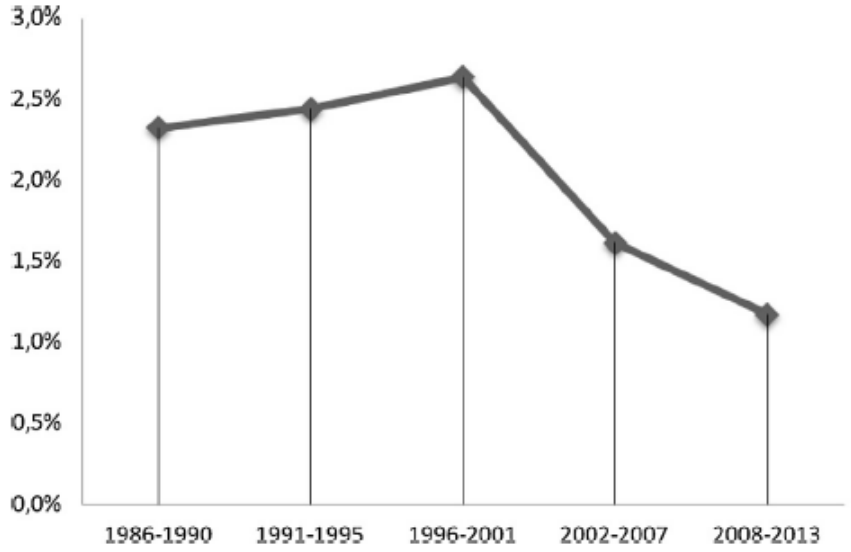

Fig. 2. Fracture incidence depending on the periods analysed.
The maximum peak of the fracture incidence was in the period 1996–2001, in concordance with the availability of prophylaxis in our country. We compared the incidence of fracture in the population of PWH before (2.5%) and after (1.4%) 2001, the difference between the two groups was statically significant ($p = 0.0003$).

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Haemophilia and fracture rate

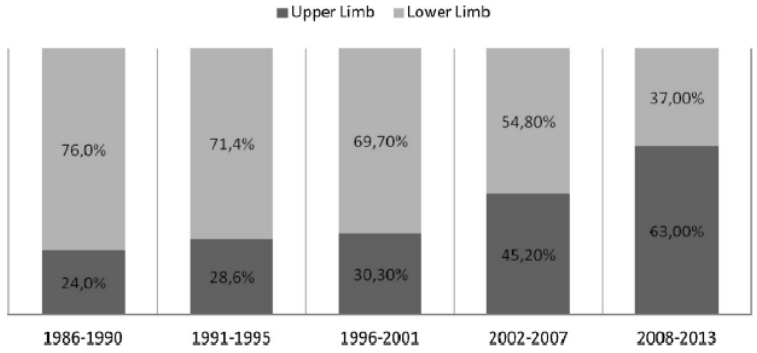

Fig. 3. Incidence of fractures in the UL y LL along the years.
The incidence of presentation of the fractures of the upper limb and lower limb changed through the years, being more frequent in the lower limb in the first period analysed and in the upper limb in the last one. This difference was statically significant ($p = 0.0168$).

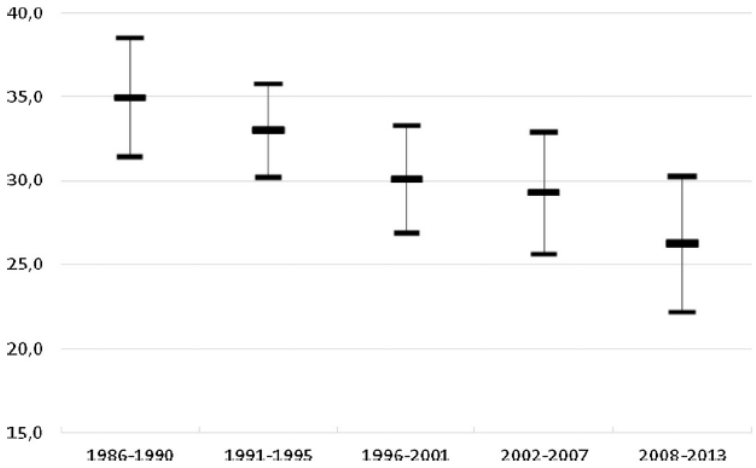

Fig. 4. Patient age when fractured according to the periods analysed.
The total mean age was 32 years old, ranging from 2 to 66 years old, as in the period 1986–1990 the average age was 35 (ranging 15–55 years old, SD 12.6), in 1991–1995 was 33 (ranging 12–57 years old, SD 11.6), 1996–2001 was 30 (ranging 2–59 years old, SD 14.3), 2002–2007 was 29 (ranging 7–55 years old, SD 15.8) and 2008–2013 was 26 (ranging 2–66 years old, SD 16.1). Difference was statistically significant between the first period and last period analysed, ($p = 0.035$).

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Haemophilia and osteoporosis

Osteoporosis is a skeletal disorder characterised by decreased bone strength and ***increased risk of fracture***.

NIH consensus on Osteoporosis Prevention 2001

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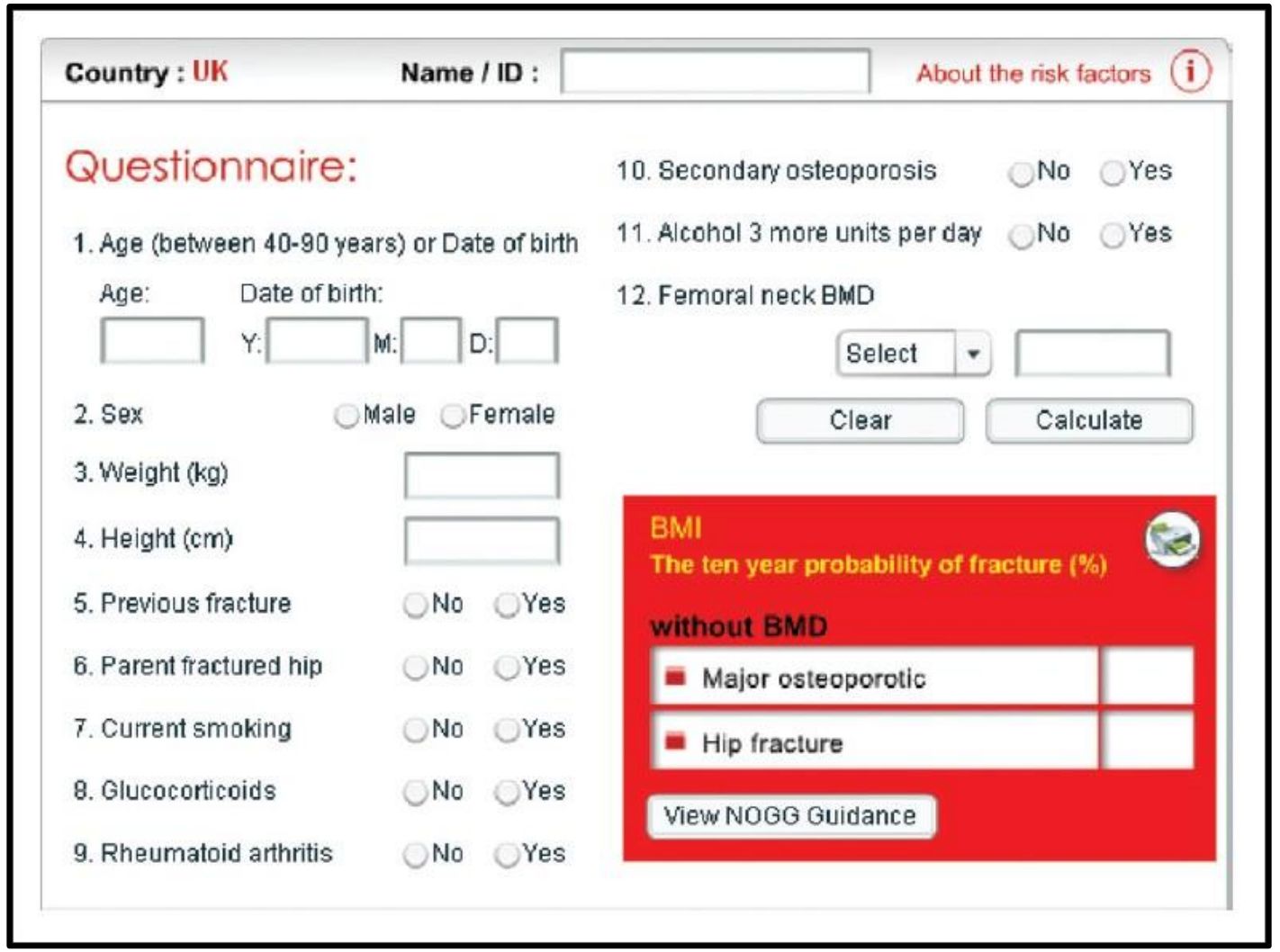
Haemophilia and fracture risk



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Haemophilia and fracture risk

Haemophilia A and B as a cause for secondary osteoporosis and increased fracture risk

Panagiotis Anagnostis[a,b], Spyridon Karras[a], Stavroula A. Paschou[a] and Dimitrios G. Goulis[a]

"It can be speculated that fracture risk in patients with haemophilia should be higher than in the general population."

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Haemophilia and fracture risk

Royal Free London NHS
NHS Foundation Trust

The current National Osteoporosis Foundation Guide recommends treating patients with FRAX 10-year risk scores of > or = 3% for hip fracture or > or = 20% for major osteoporotic fracture, to reduce their fracture risk. Our patients FRAX 10 year risk scores are below those levels.

Agapidou A et al. 2016

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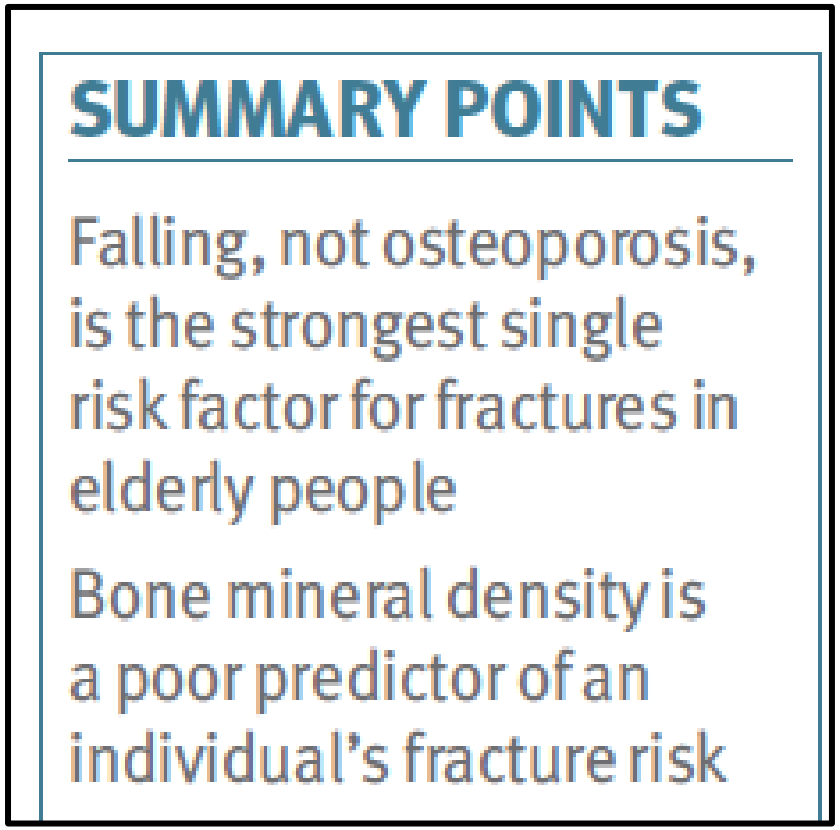
Haemophilia and disease mongering



SUMMARY POINTS

Falling, not osteoporosis, is the strongest single risk factor for fractures in elderly people

Bone mineral density is a poor predictor of an individual's fracture risk

BMJ, 2008

Haemophilia and fracture risk

Joint deformity, muscle weakness and impaired proprioception. Such conditions may cause difficulty with mobility, pain, increased risk of falls.

Dolan G. Haemophilia 2010

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Haemophilia and MSK comorbidities

Accepted: 11 June 2017

DOI: 10.1111/hae.13308

ORIGINAL ARTICLE

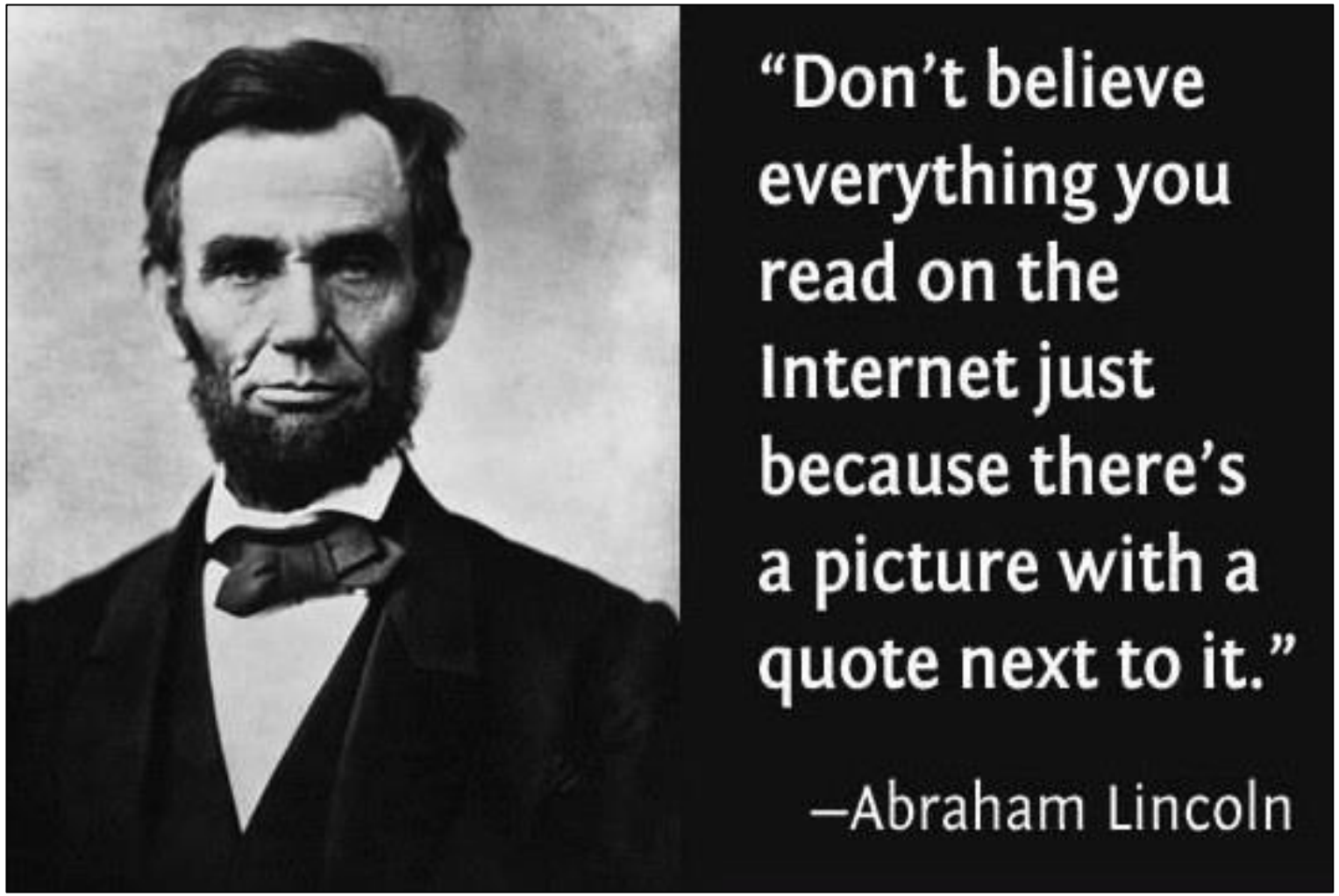
Clinical haemophilia

WILEY Haemophilia

Ageing successfully with haemophilia: A multidisciplinary programme

E. Boccalandro[1] | M. E. Mancuso[1] | S. Riva[1,2] | D. M. Pisaniello[1] | F. Ronchetti[3] | E. Santagostino[1] | F. Peyvandi[1] | L. P. Solimeno[4] | P. M. Mannucci[1] | G. Pasta[4]

Haemophilia and MSK comorbidities



THANK YOU

gianluigipasta@yahoo.it

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MSK Comorbidities – Rehabilitation

Paul McLaughlin MSc, MMACP

Specialist Physiotherapist in Haemophilia

The Royal Free Hospital, London, UK

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Speaker disclosures

Shareholder	
Grant / Research Support	National Institute for Health Research (NIHR)
Consultant	
Employee	
Paid Instructor	
Speaker bureau	
Other	

Discussion points

- Case study
- Defining Rehabilitation
- What makes effective rehabilitation
- A bio-psycho-social view of rehabilitation
- Take home points

Case study

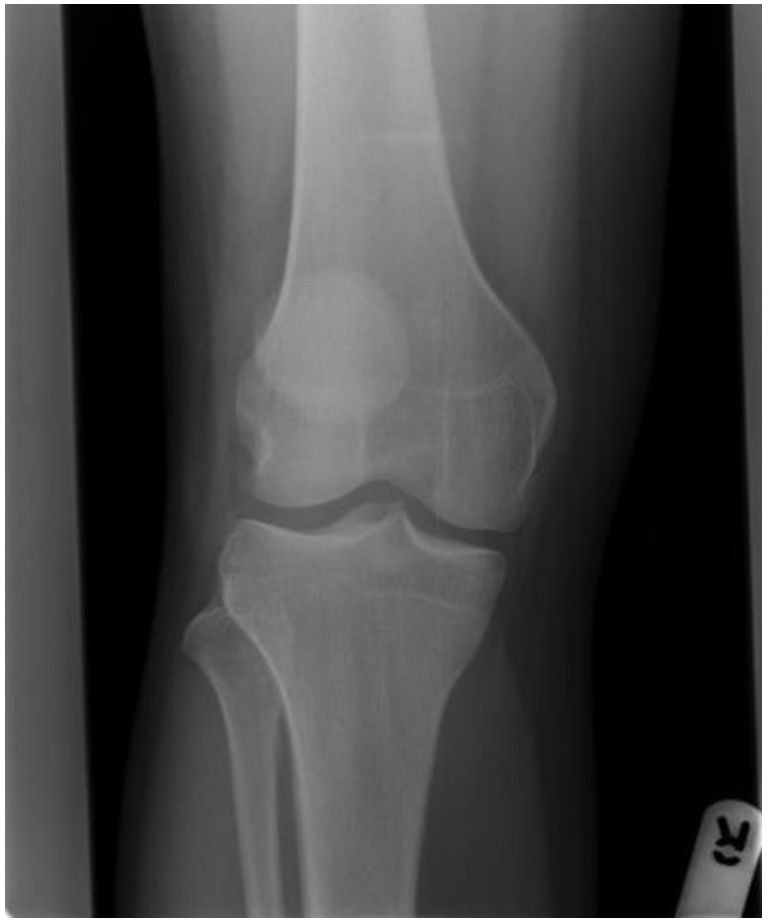
- 18 years old – SHA
- History bilateral ankle and Rt knee bleeding
- Prophylaxis – 2000iu/alt day

- 3/52 history Rt knee pain
- Locking and giving way
- No trauma/injury/recent bleed
- No change with extra FVIII
- ↓stairs and ↓ hills = ↑ pain

- No swelling
- Antalgic gait- protective
- Valgus Right knee
- Full ROM
- Tender anterolateral knee joint line
- Decrease quads strength
- HJHS Rt knee = 4
- HAL – 76.5 (LeisSport, house, lowcom)
- Trouble playing golf – his main hobby

Case study

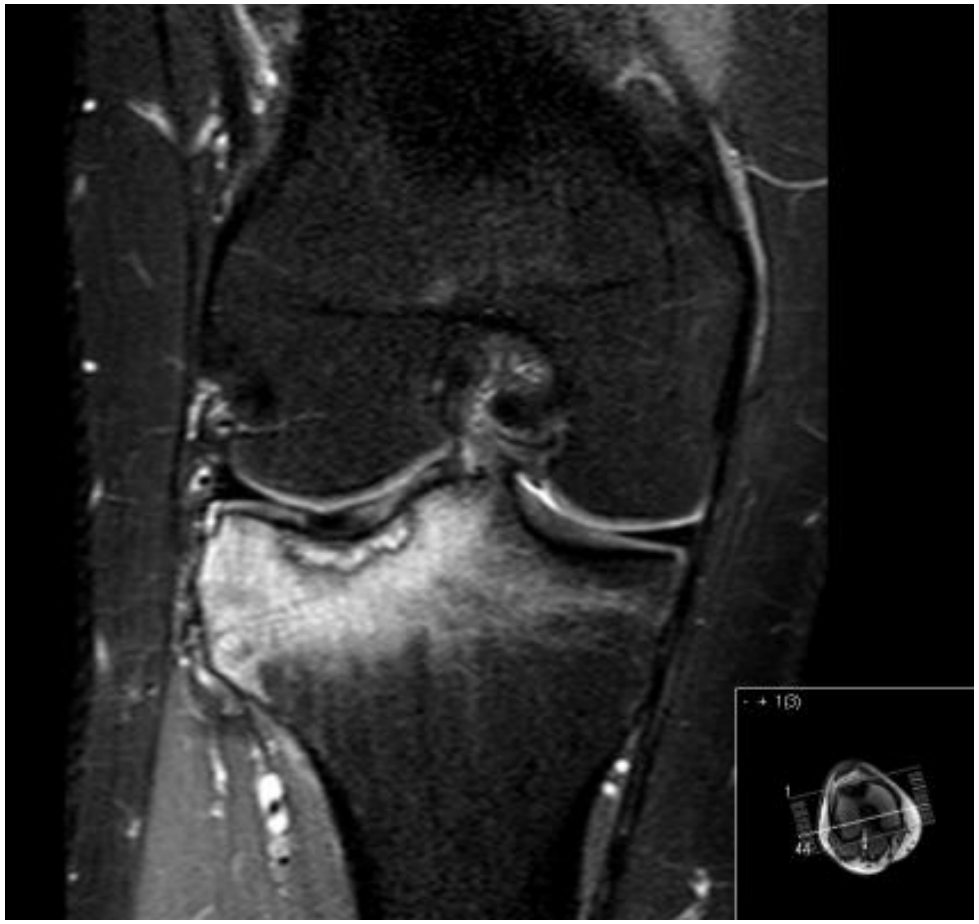
- ?? Possible meniscal pathology
  - Unusual due to age
- Quads strength and fear an issue:
  - Knee support
  - Quads exercises
- More pain – further visits in next few weeks
- X-Ray …



Case study

- MRI examination
- Well defined subchondral lesion
- Marked bone marrow oedema
- Overlying cartilage intact
- ACL, PCL, menisci intact

- ‘AVASCULAR NECROSIS’



Case study

- Medical input
  - Cox-2 inhibitors and pain meds as needed
  - Daily prophylaxis (1500iu) – manage risk of bleed
- Physio rehab input
  - Lockable knee brace
  - Hydrotherapy – quads, hams, glutes strength
  - Gym based – closed chain progressing to open chain – golf specific activity



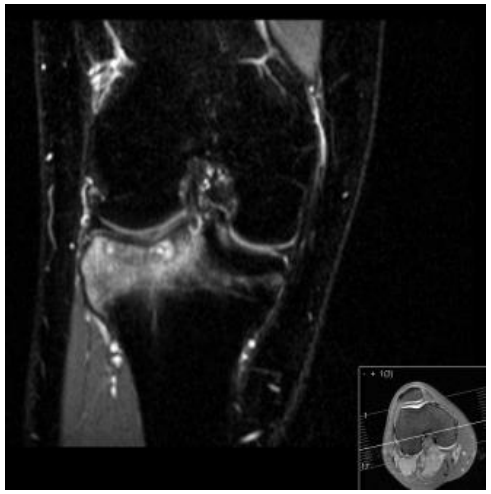


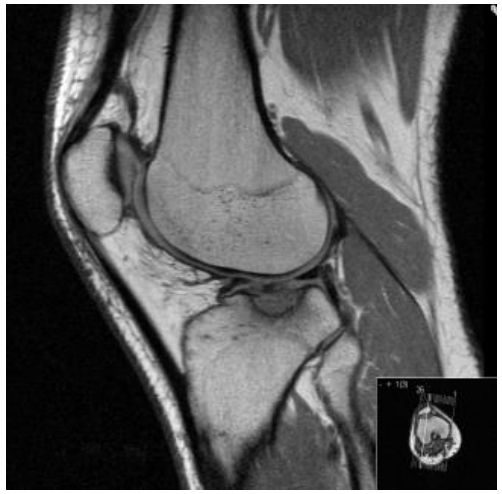


THIS IS ALL REHABILITATION – HAPPENING OVER A PERIOD OF MONTHS

Case study

- 6 months later - MRI:
  - Diagnosis reviewed as haemorrhagic subchondral cyst associated with haemarthropathy
  - Bone abnormality larger
  - Intense bone oedema remains

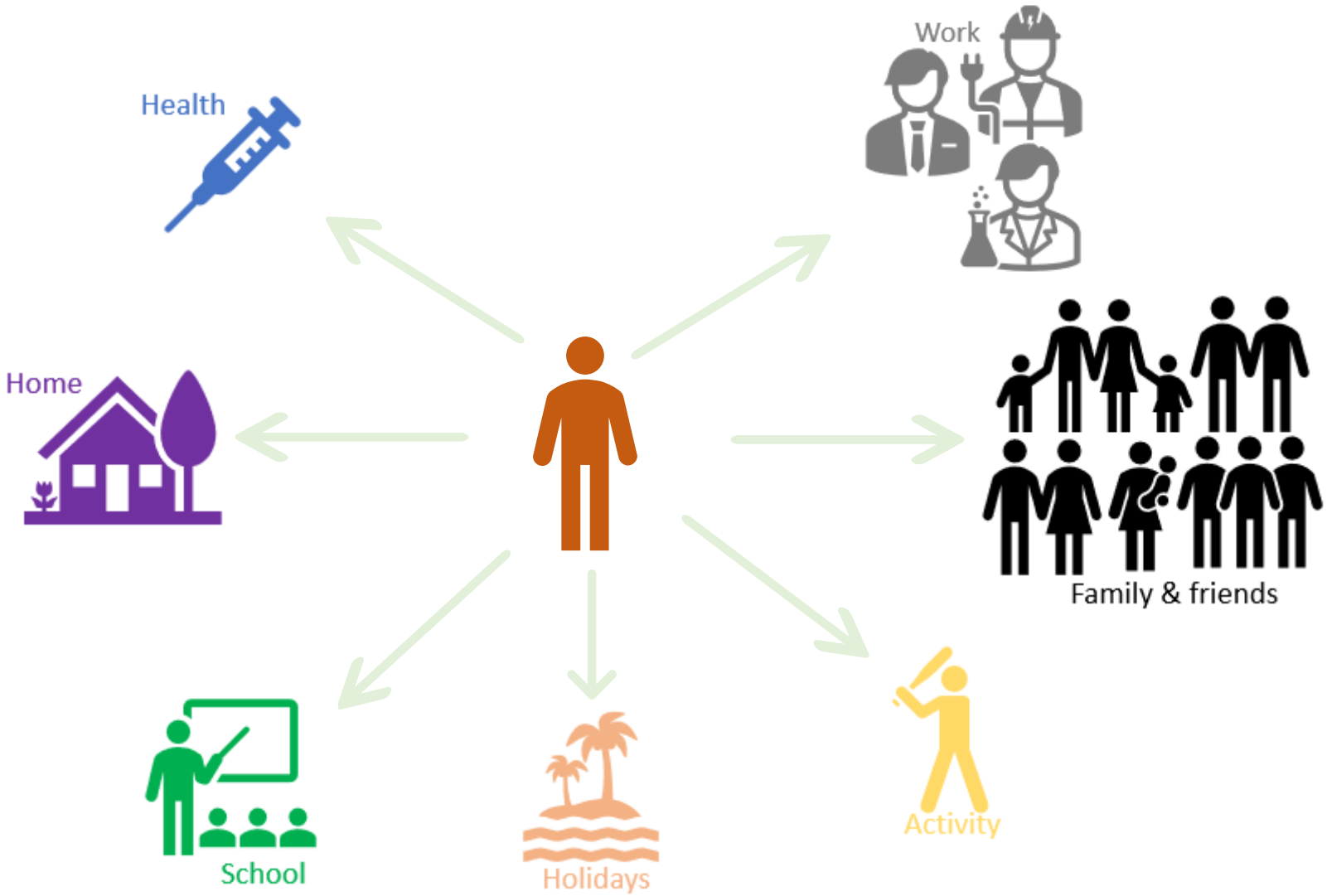




- 6 months later – Patient review:
  - Pain free
  - Back to 18 holes of golf
  - Knee subjectively feels better/safer
  - Minimal need for knee support
  - HJHS = 1 (was 4)
  - HAL = 90 (was 76.5)

- A rehab success – by which metric?

The person exists in a life

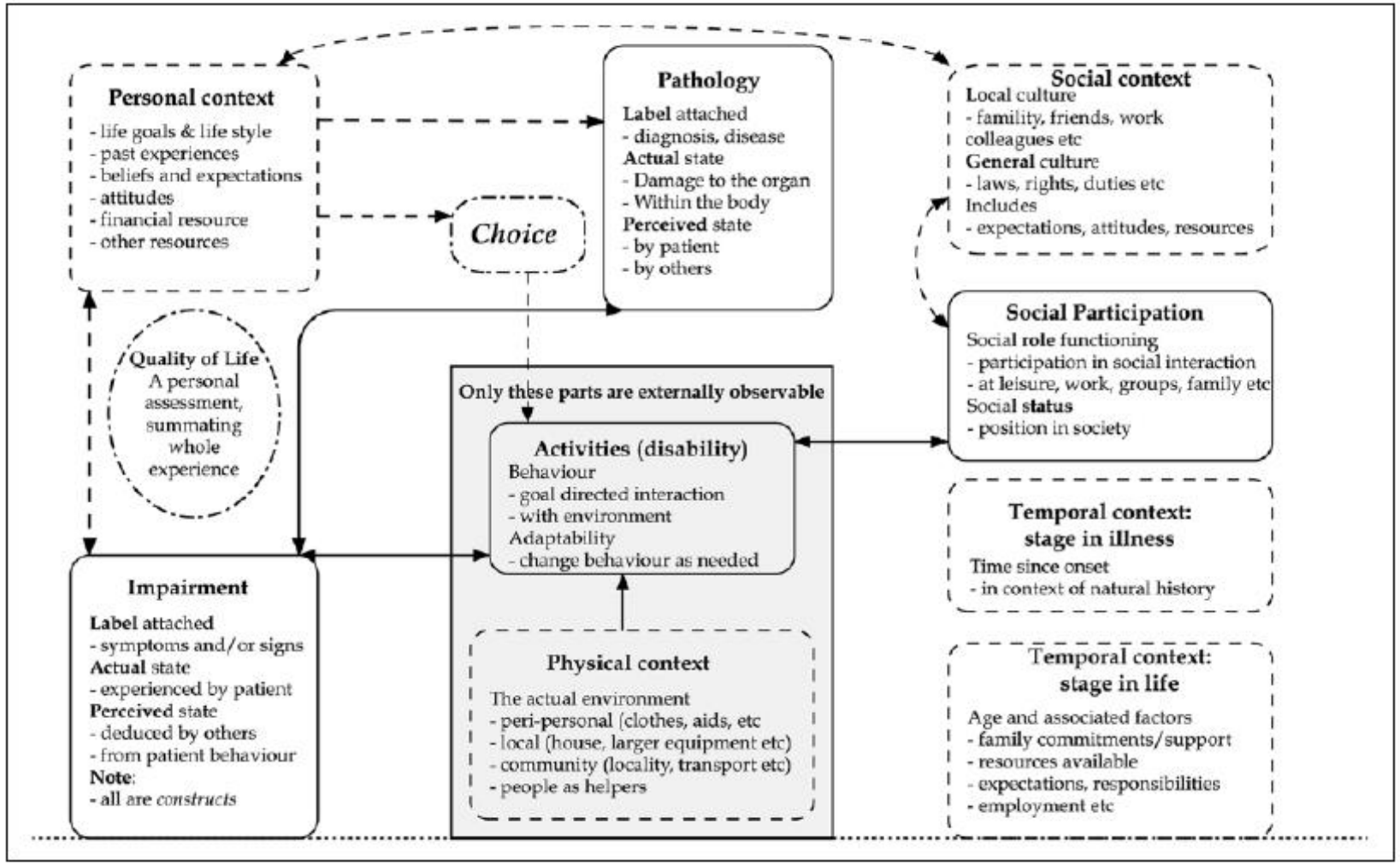


What is rehabilitation?

- Helps a person be as **independent as possible** in everyday activities
- Enables **participation** in education, work, recreation and **meaningful life roles**
- Is **Person centred** – with approaches chosen based on individual goals and preferences
- Can be in any setting – hospital, home, private clinic
- Can lessen the **impact and burden** of health conditions
- Is an **investment** – cost benefits to individuals and society
- **Is for anyone who needs it**

WHO 2021; https://www.who.int/news-room/fact-sheets/detail/rehabilitation

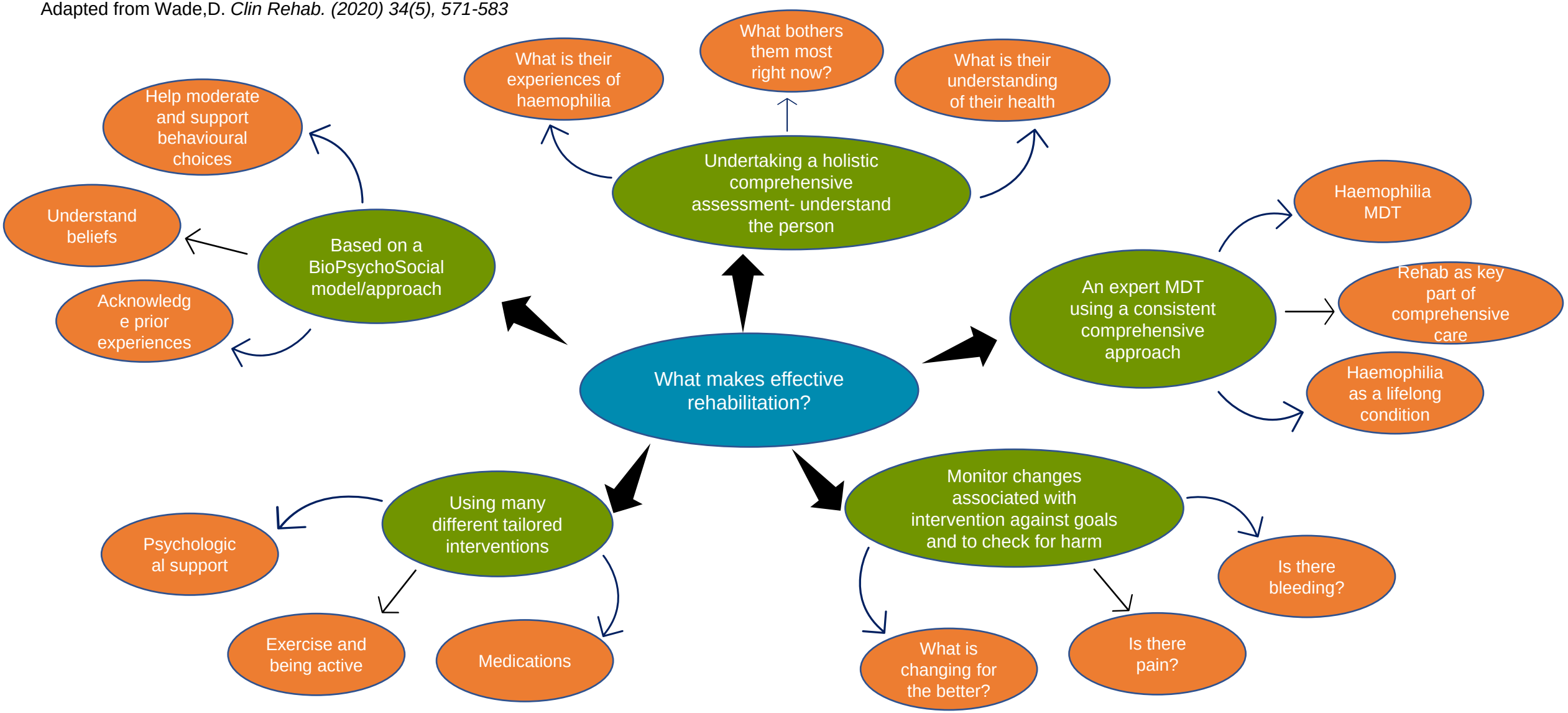
Rehabilitation – a whole person view



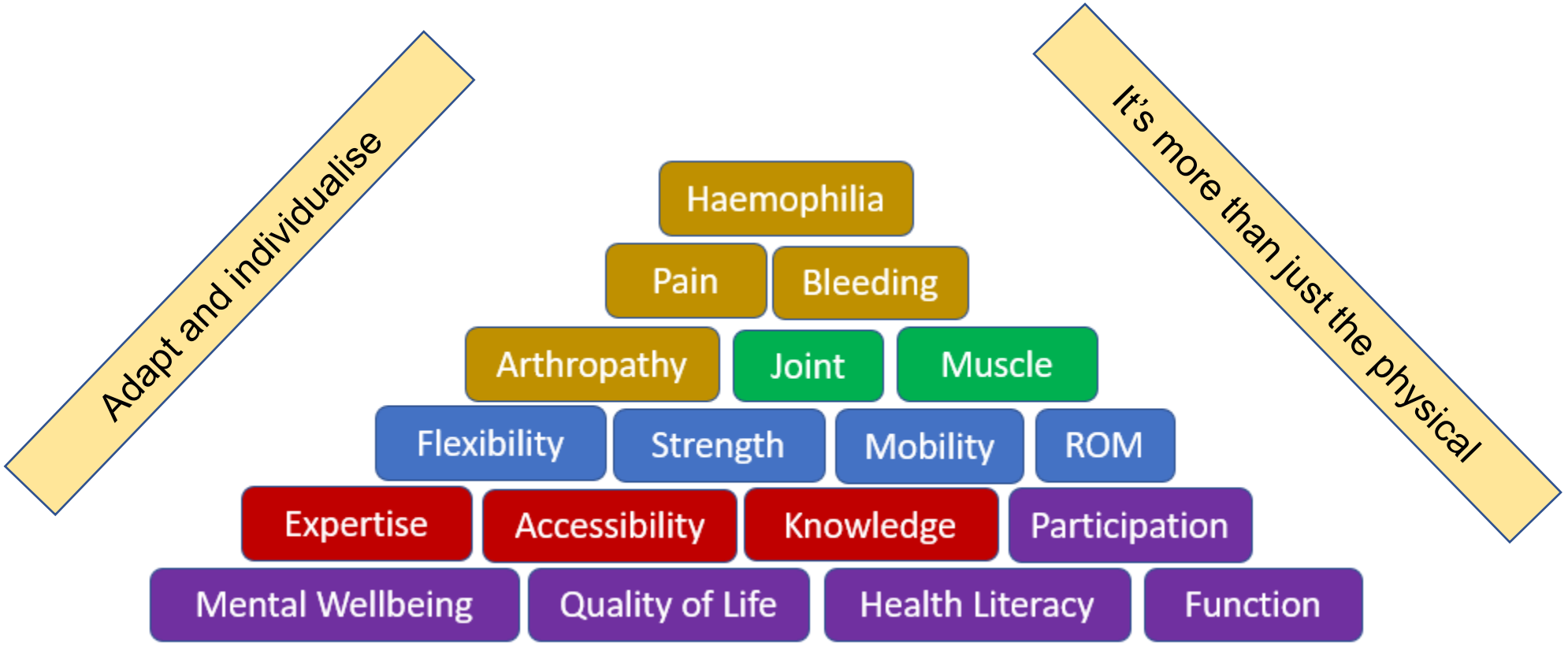
Wade and Halligan. *Clin Rehab*. (2017) 31(8), 995-1004

What makes effect rehabilitation?

Adapted from Wade,D. *Clin Rehab. (2020) 34(5), 571-583*



Take home message



Accept and recognise the complexity!

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MSK Comorbidities – Surgery

Synovitis & Residual Flexion Contracture of the Knee

Adolfo Llinás, MD
Chief Medical Officer & Department of Orthopedics and traumatology,
Fundación Santa Fe de Bogotá
Clinical Professor, Universidad de los Andes, School of Medicine
Colombia

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Speaker disclosures

Shareholder	None
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Consultant	Bayer, Takeda, HED
Employee	Fundación Santa Fe de Bogotá & Los Andes University, Bogotá
Paid Instructor	None
Speaker bureau	Takeda, Bayer, Novonordisk
Other	Board member, Centro Hospitalario Serena del Mar. Advisory Board CEVAXIN, Panama.

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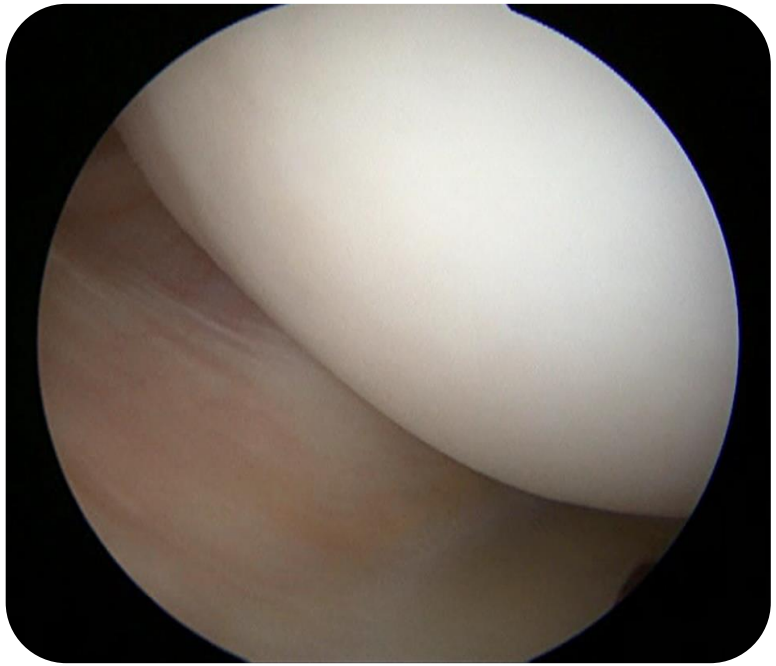
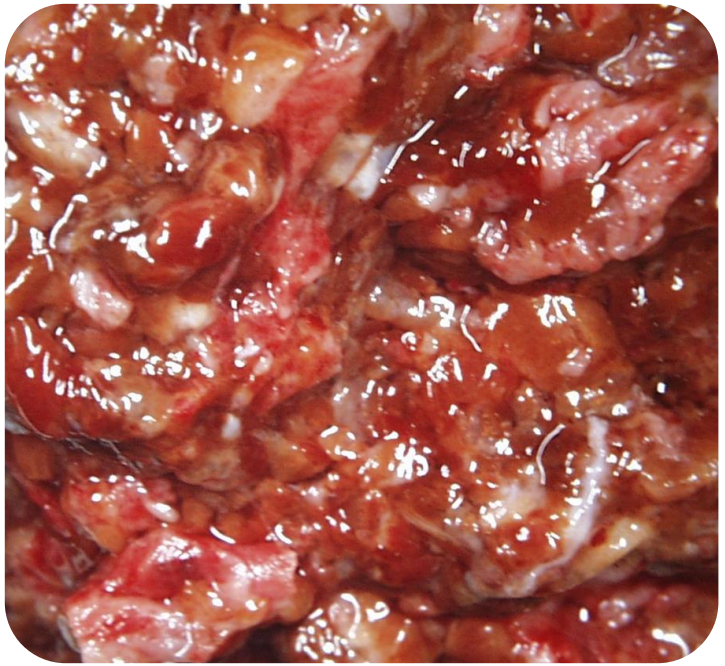
Synovitis

Acute & Chronic





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Synovitis

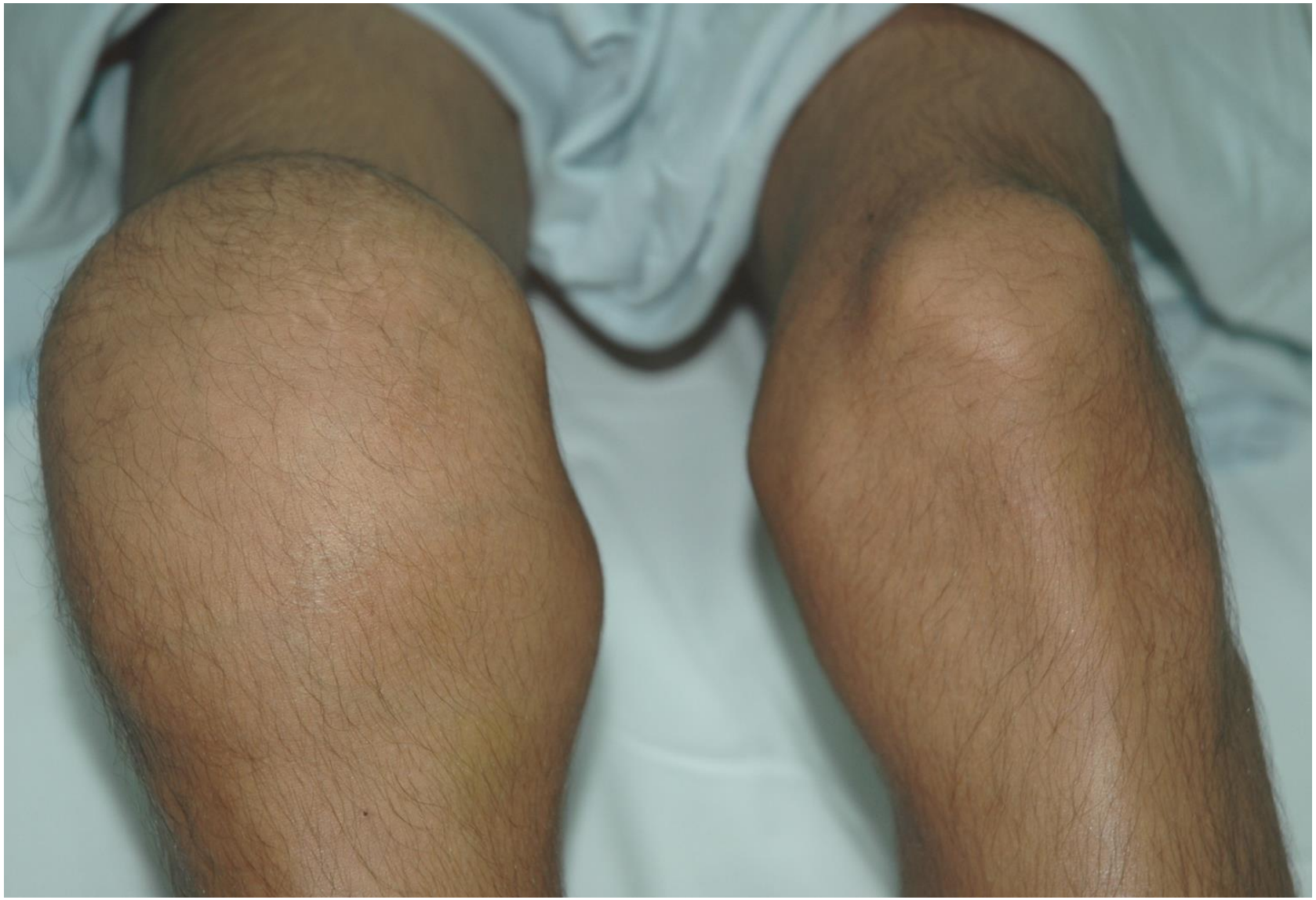
Recommendation 10.2.4:

For patients with hemophilia who have unresolved chronic synovitis, the WFH recommends nonsurgical synovectomy as a first-line treatment option using radioisotope synovectomy with a pure beta emitter (phosphorus-32, yttrium-90, rhenium-186, or rhenium-188). One dose of CFC per dose of isotope should be used.

Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020: 26(Suppl 6): 1-158. https://doi.org/10.1111/hae.14046

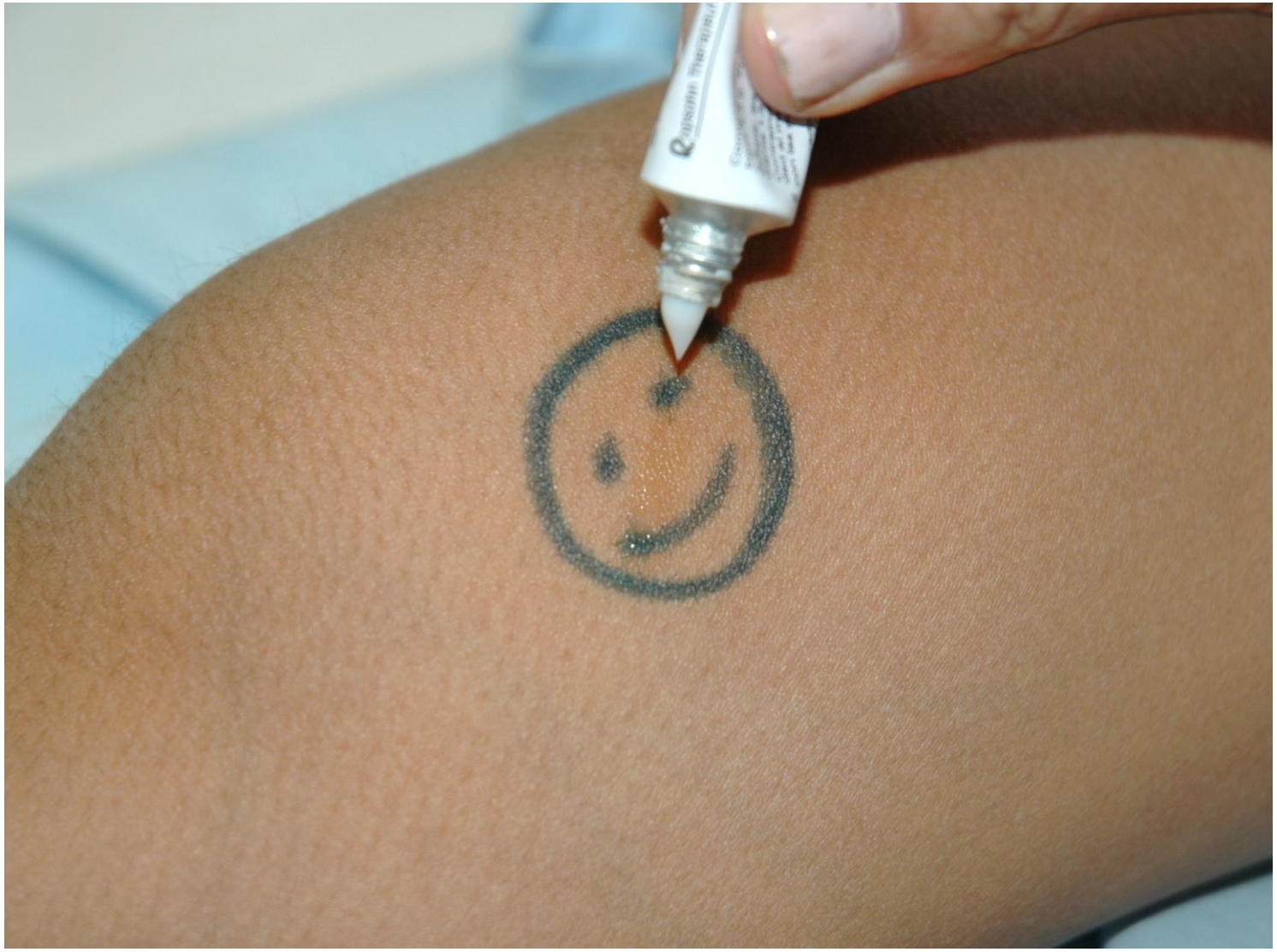
Synovitis

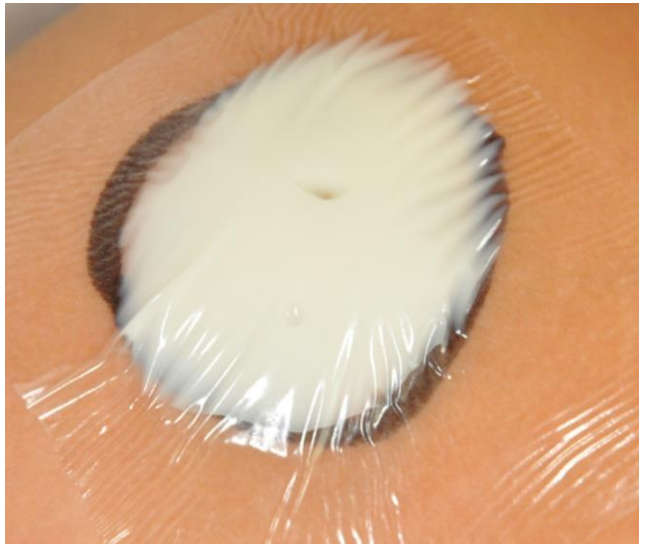
Chronic



Synovitis

Chronic





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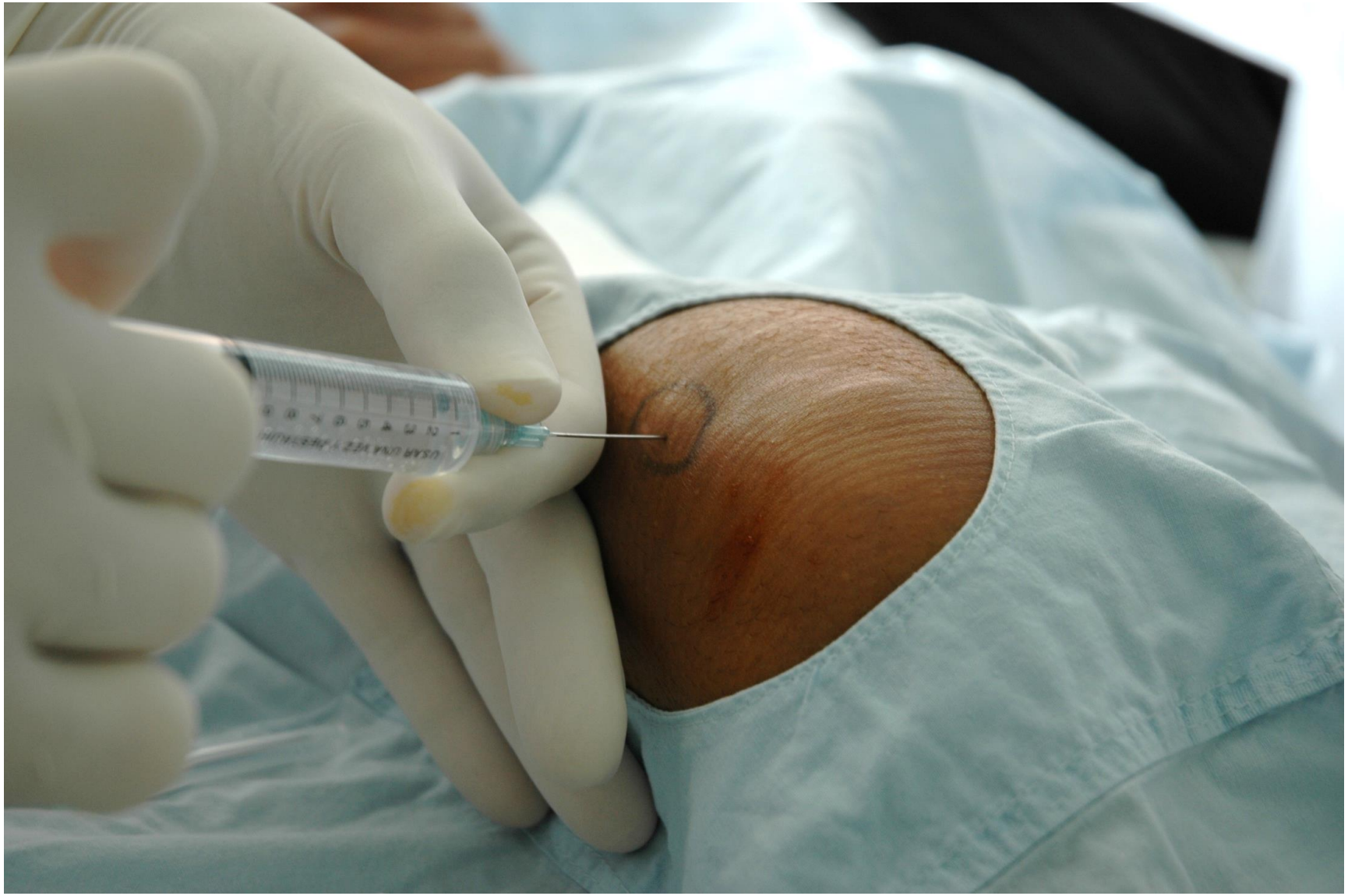
Synovitis

Chronic



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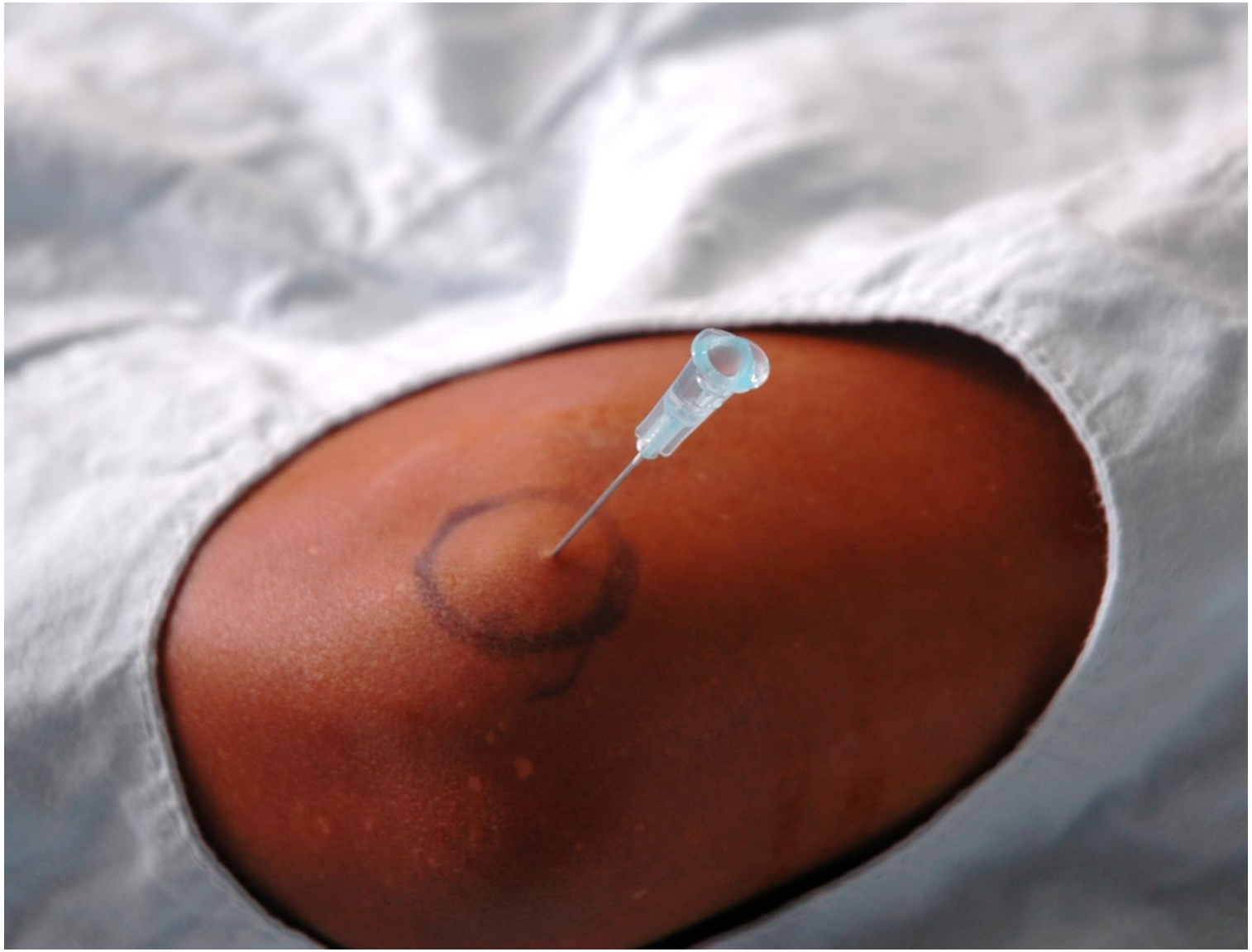
Synovitis

Chronic



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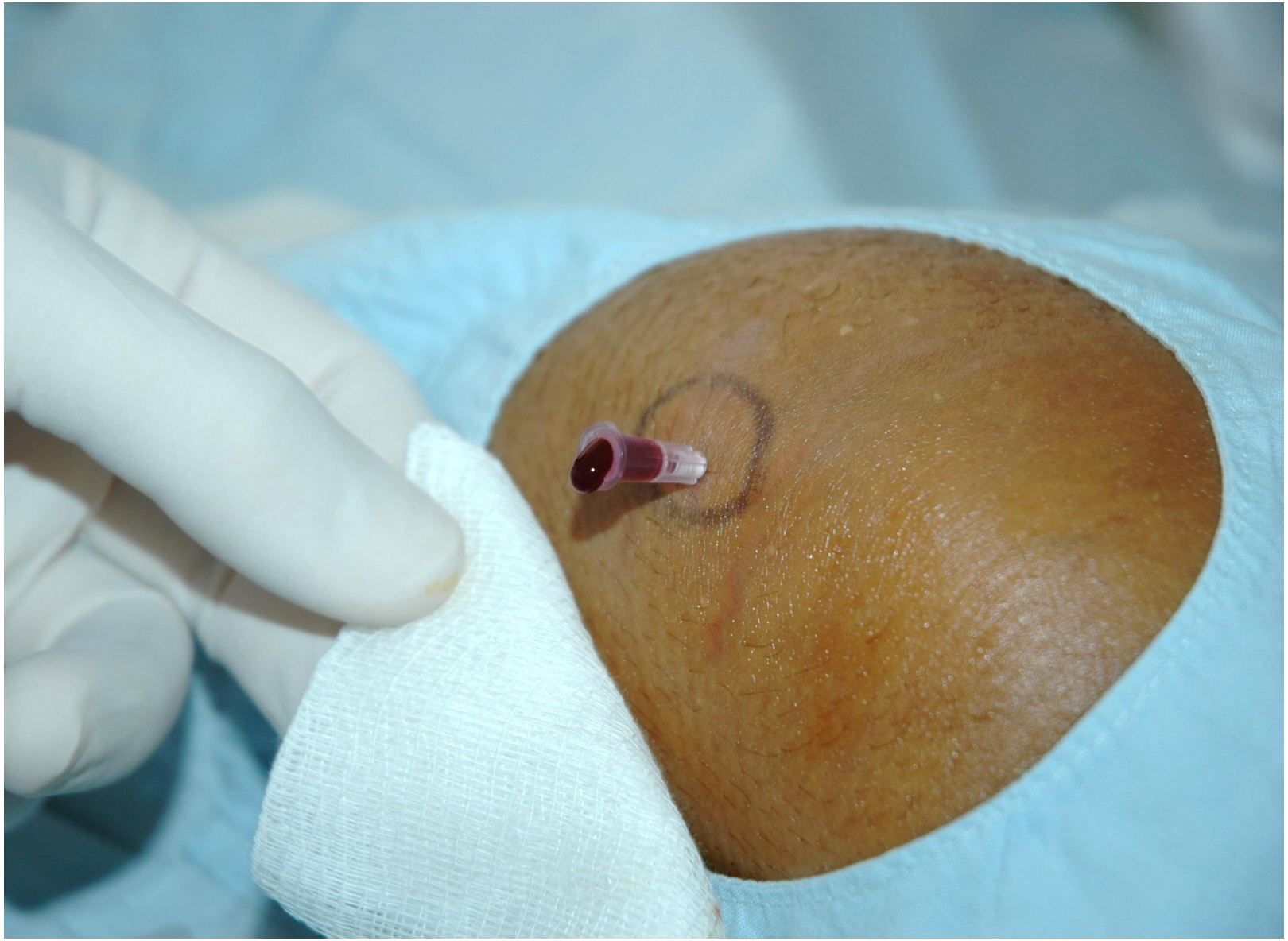
Synovitis

Chronic



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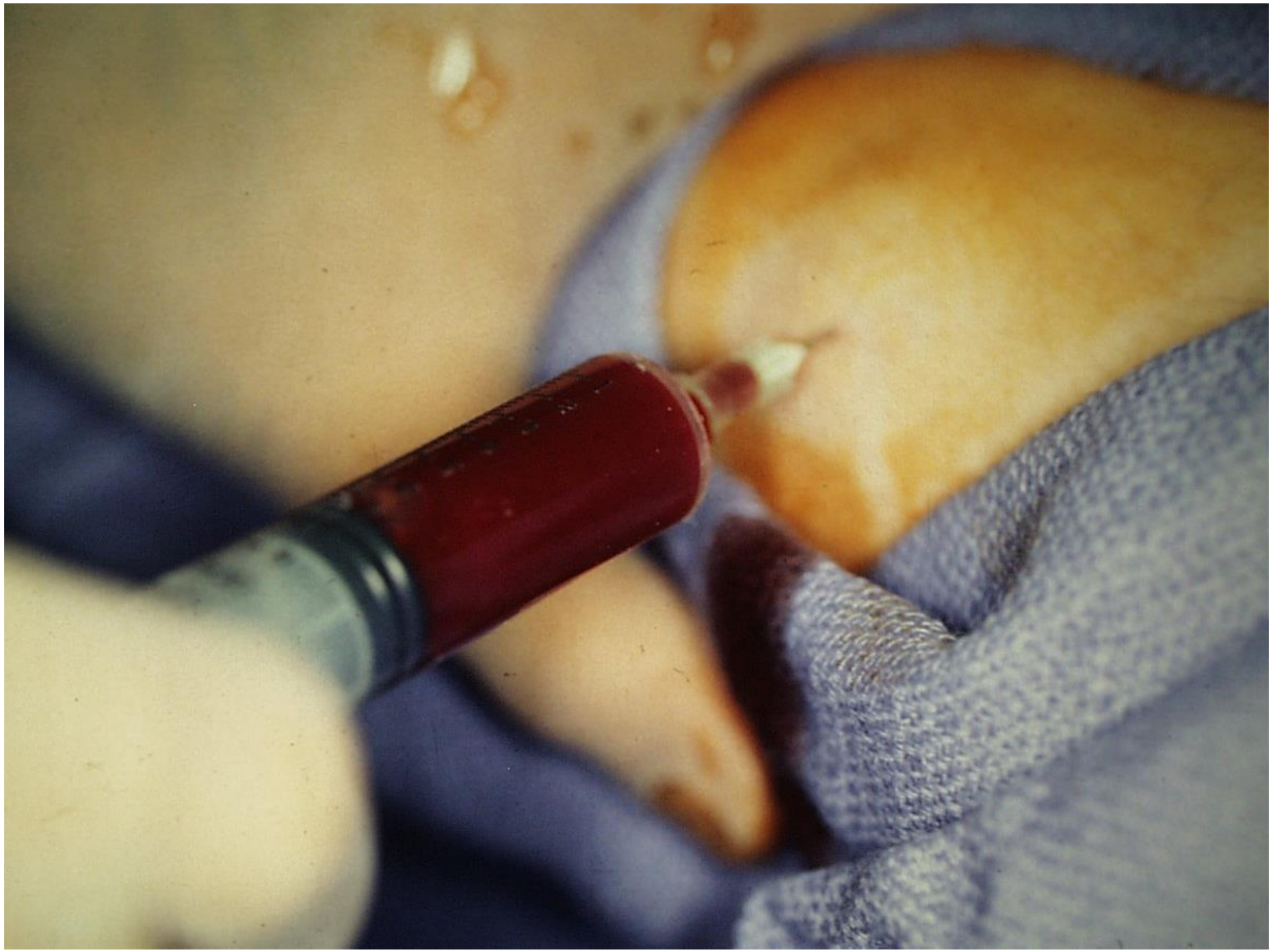
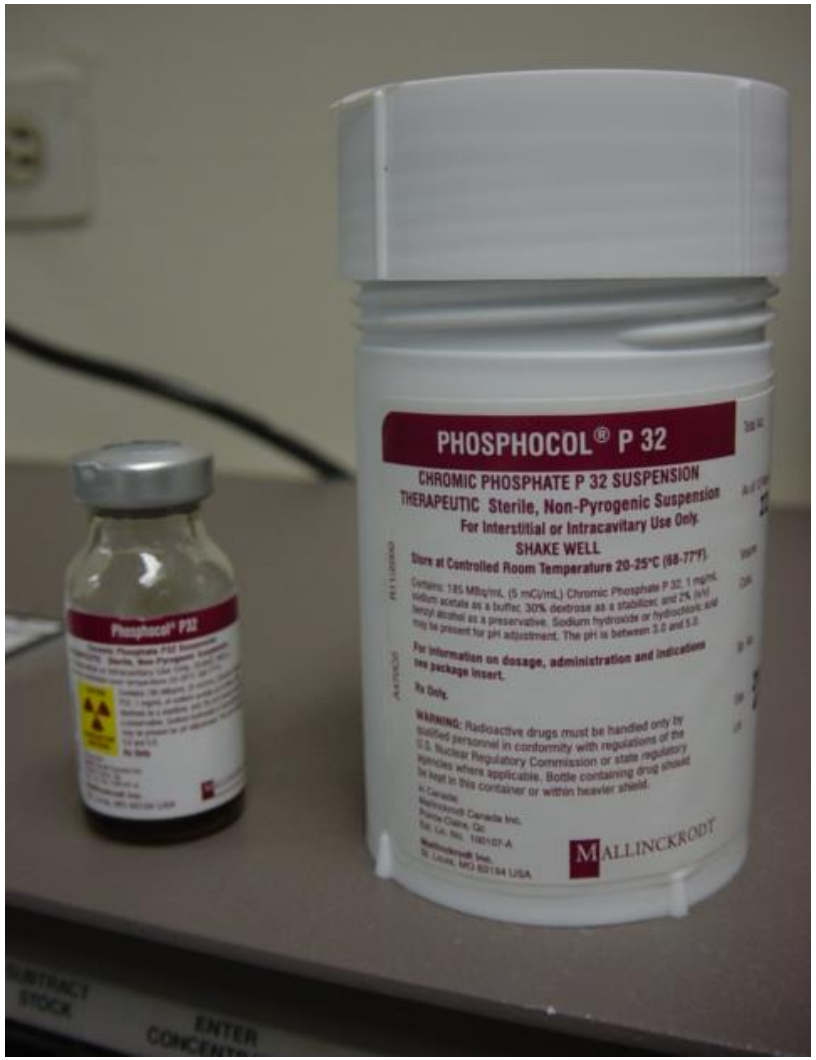
Synovitis

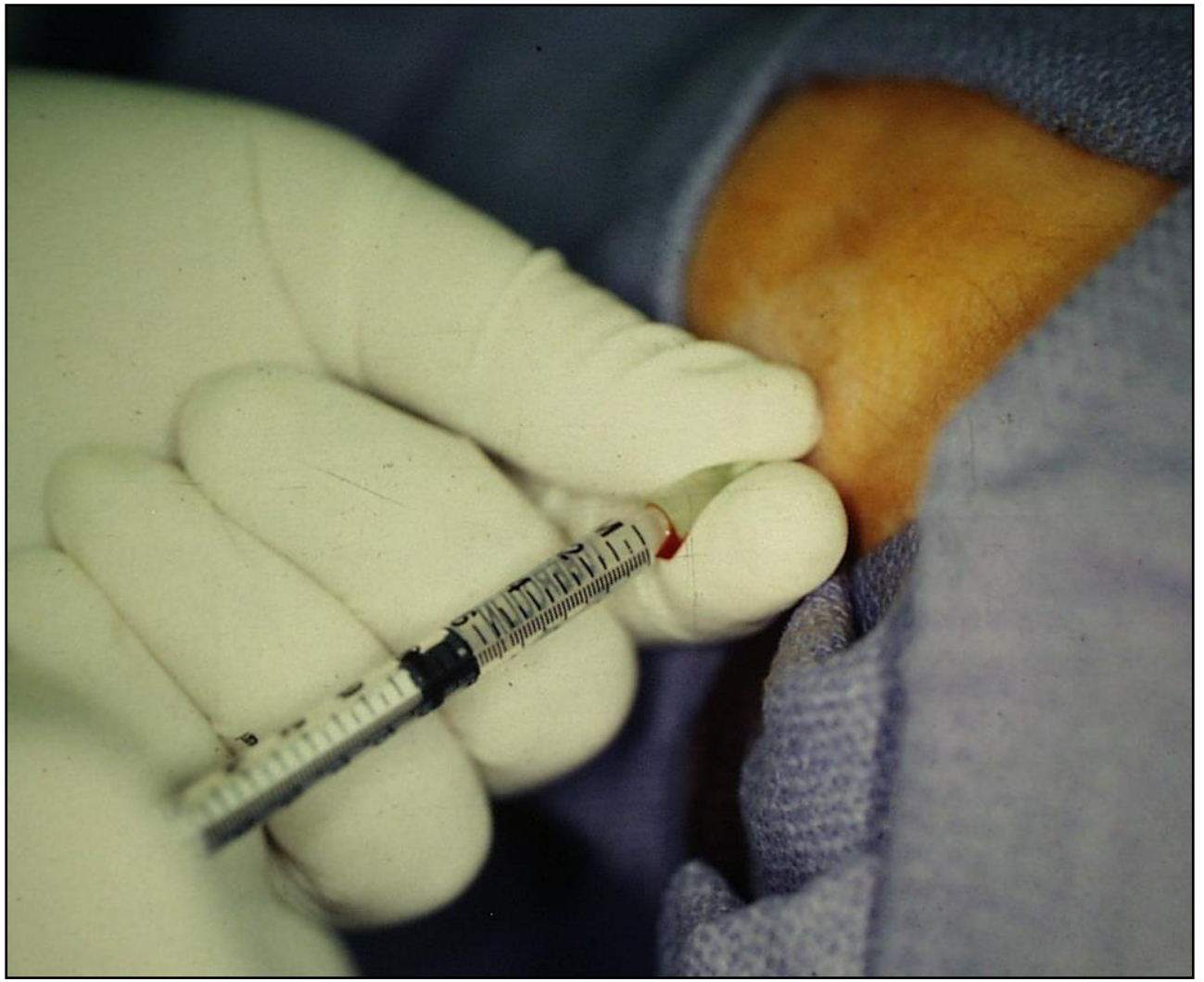
Chronic



Synovitis

Chronic





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Synovitis

Chronic

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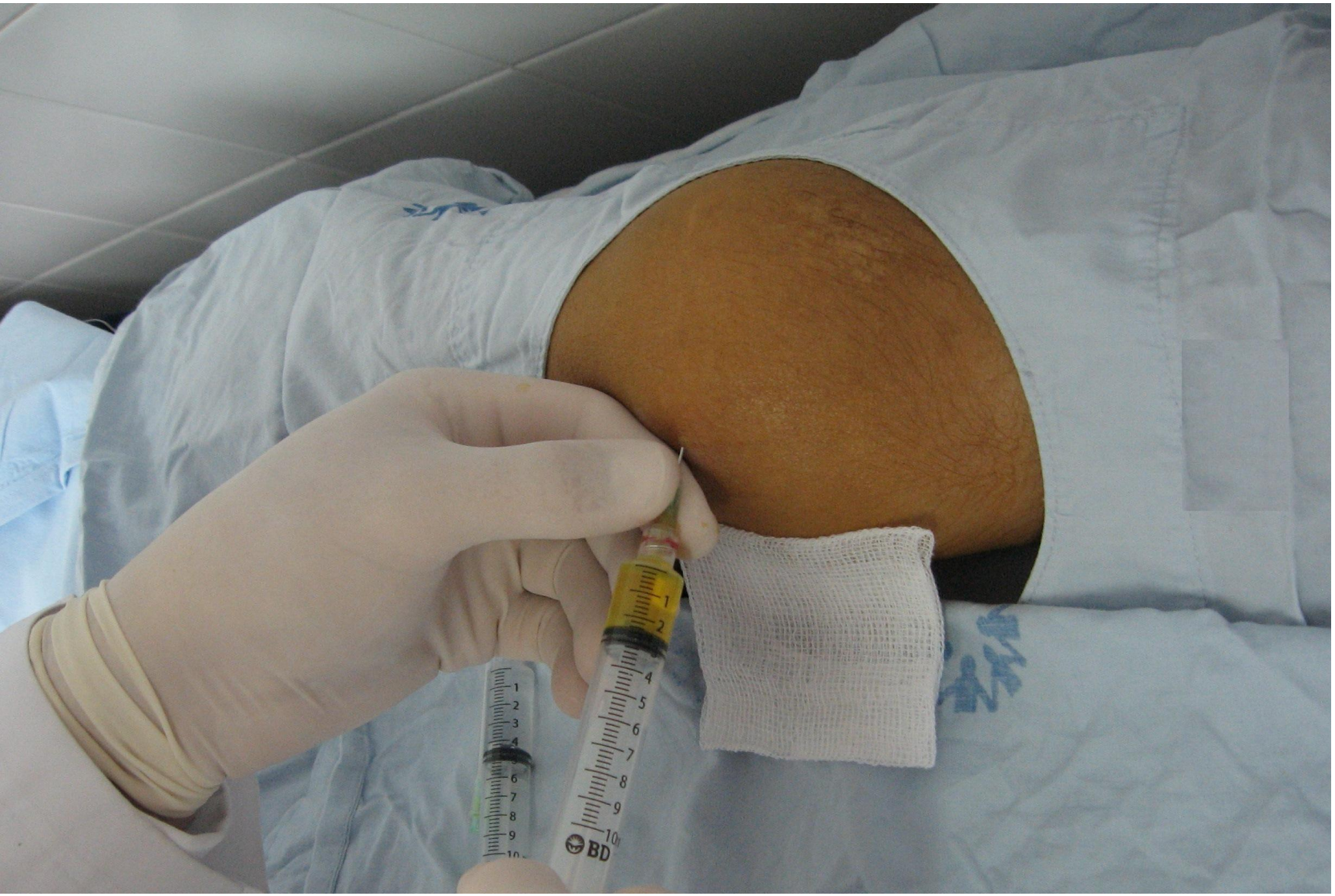
Synovitis

Chronic



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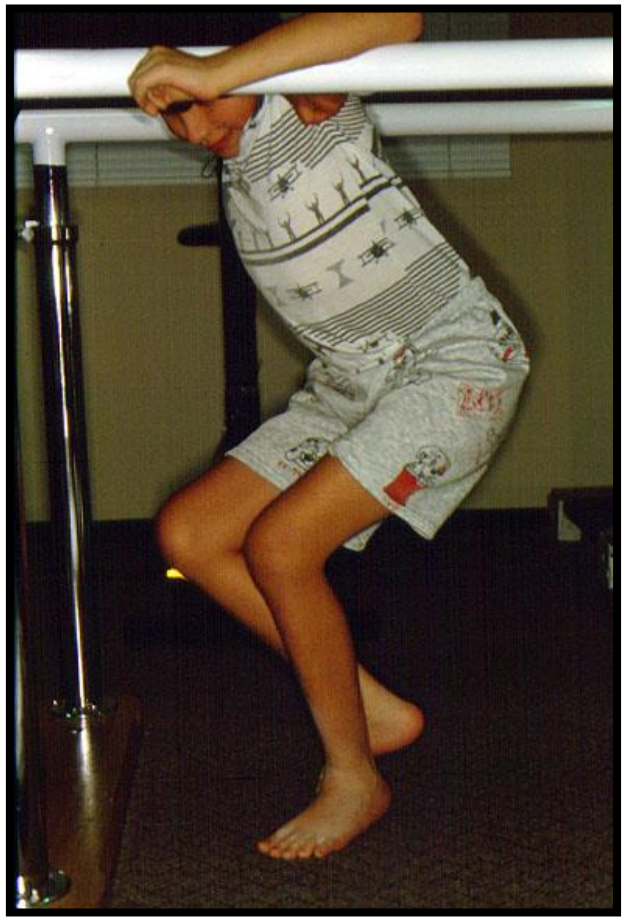
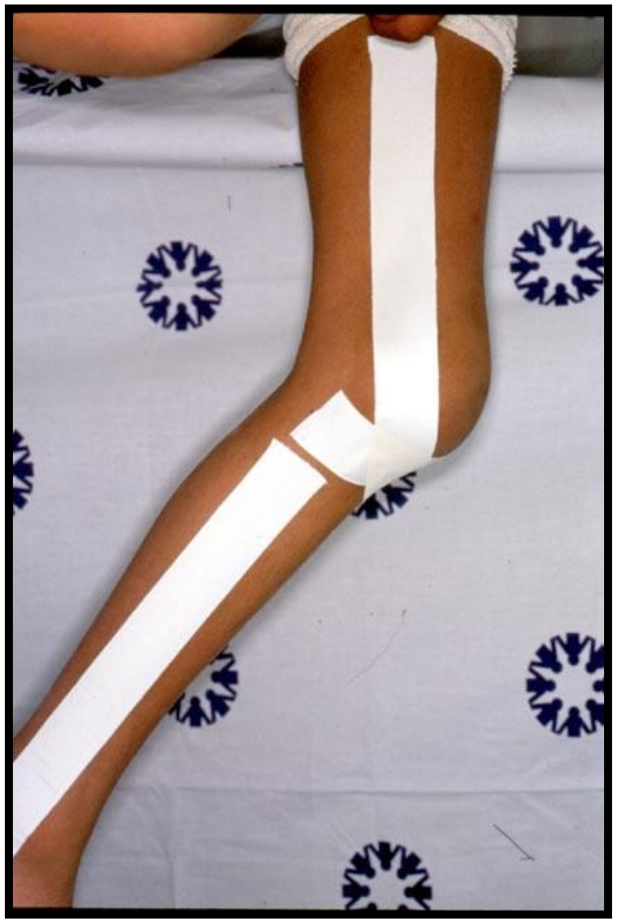
Residual Flexion Contracture

Post Synovectomy





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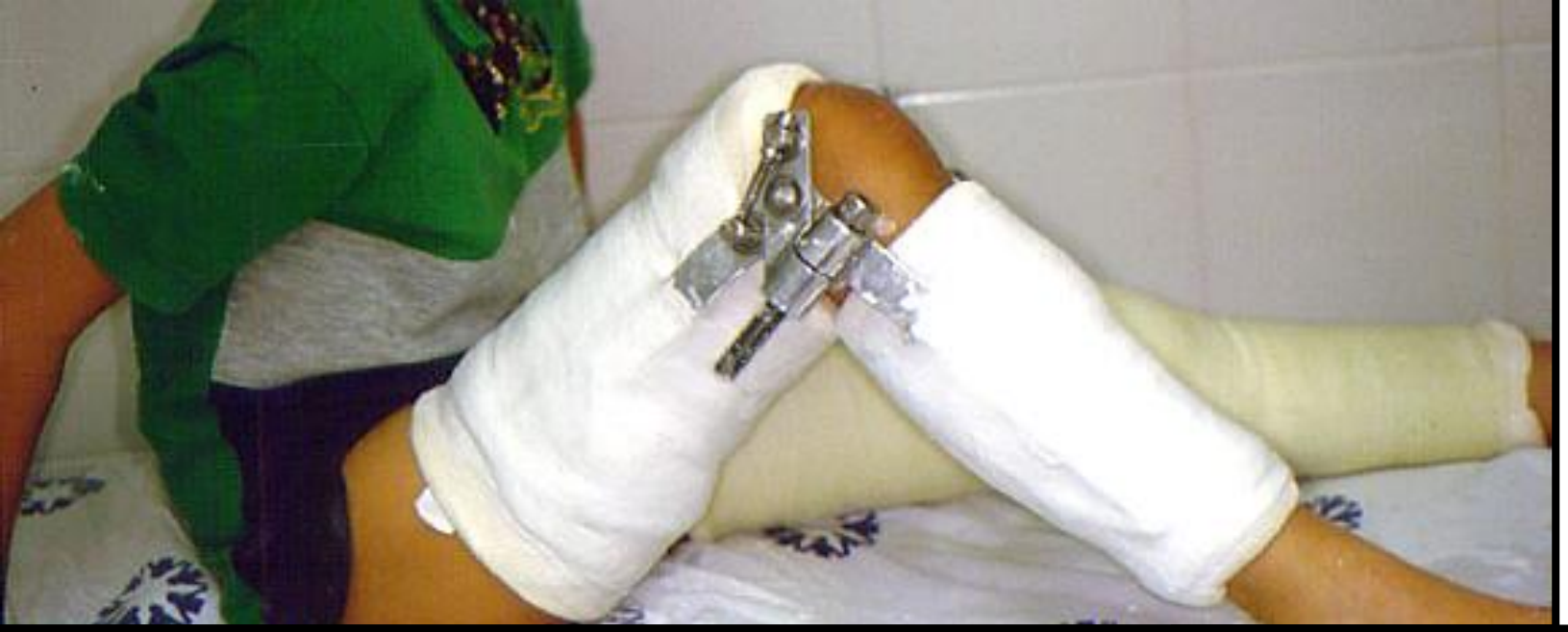
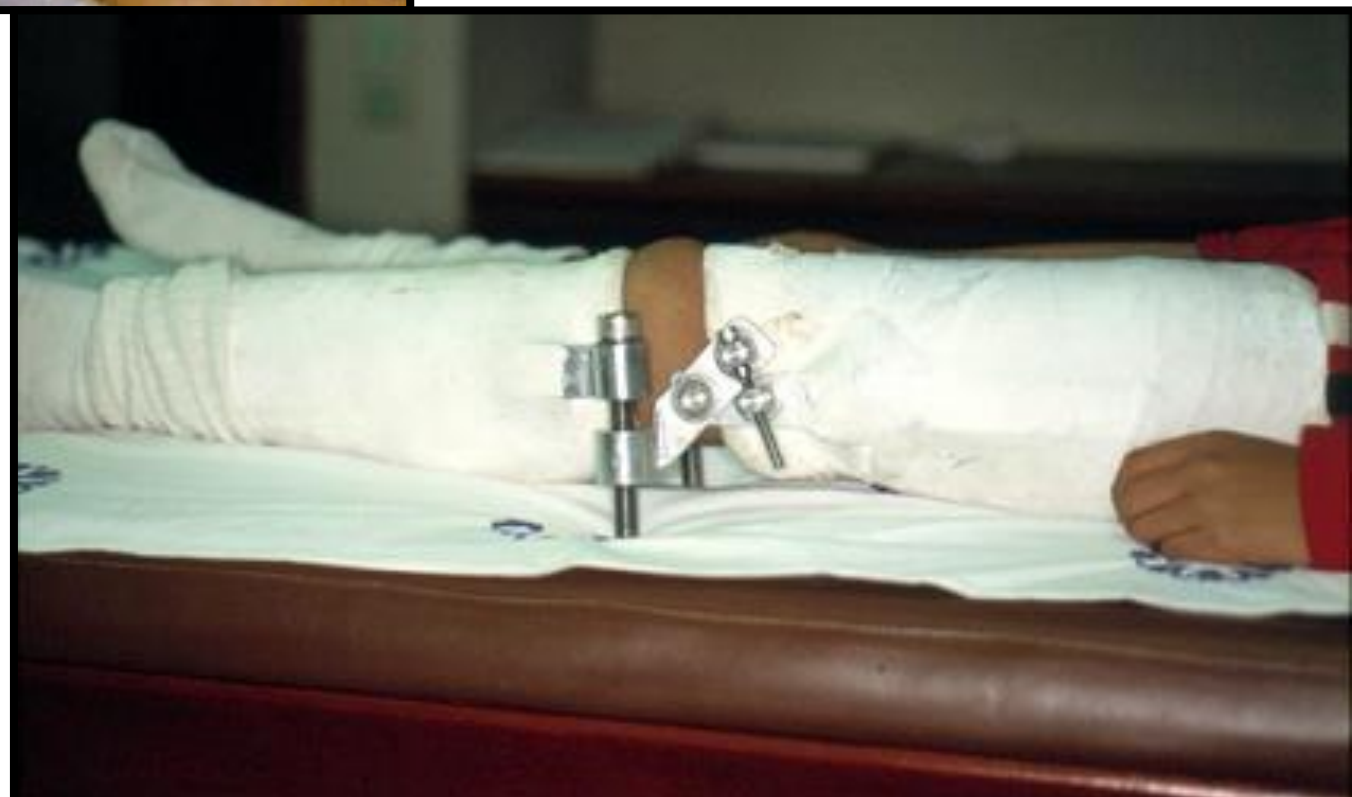


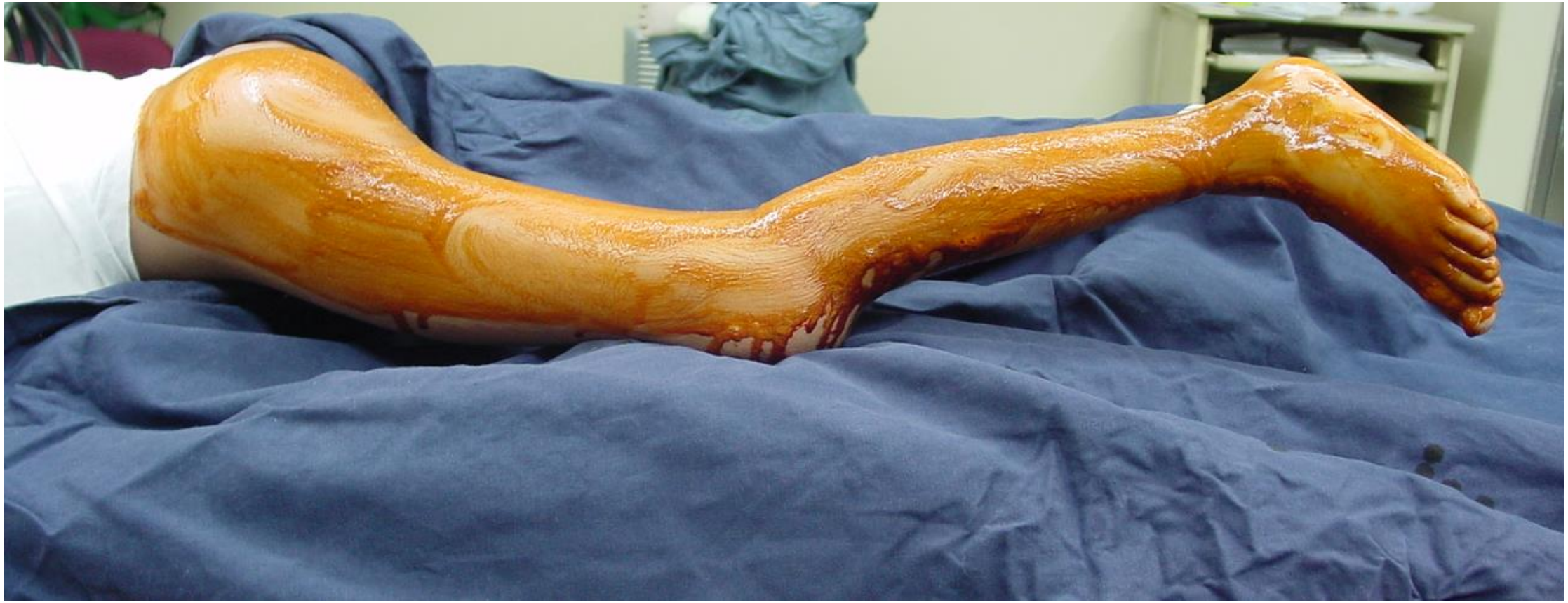
Serial casting and wedges

De-subluxation & extension hinges



Residual Flexion Contracture

Post de-subluxation & extension hinges



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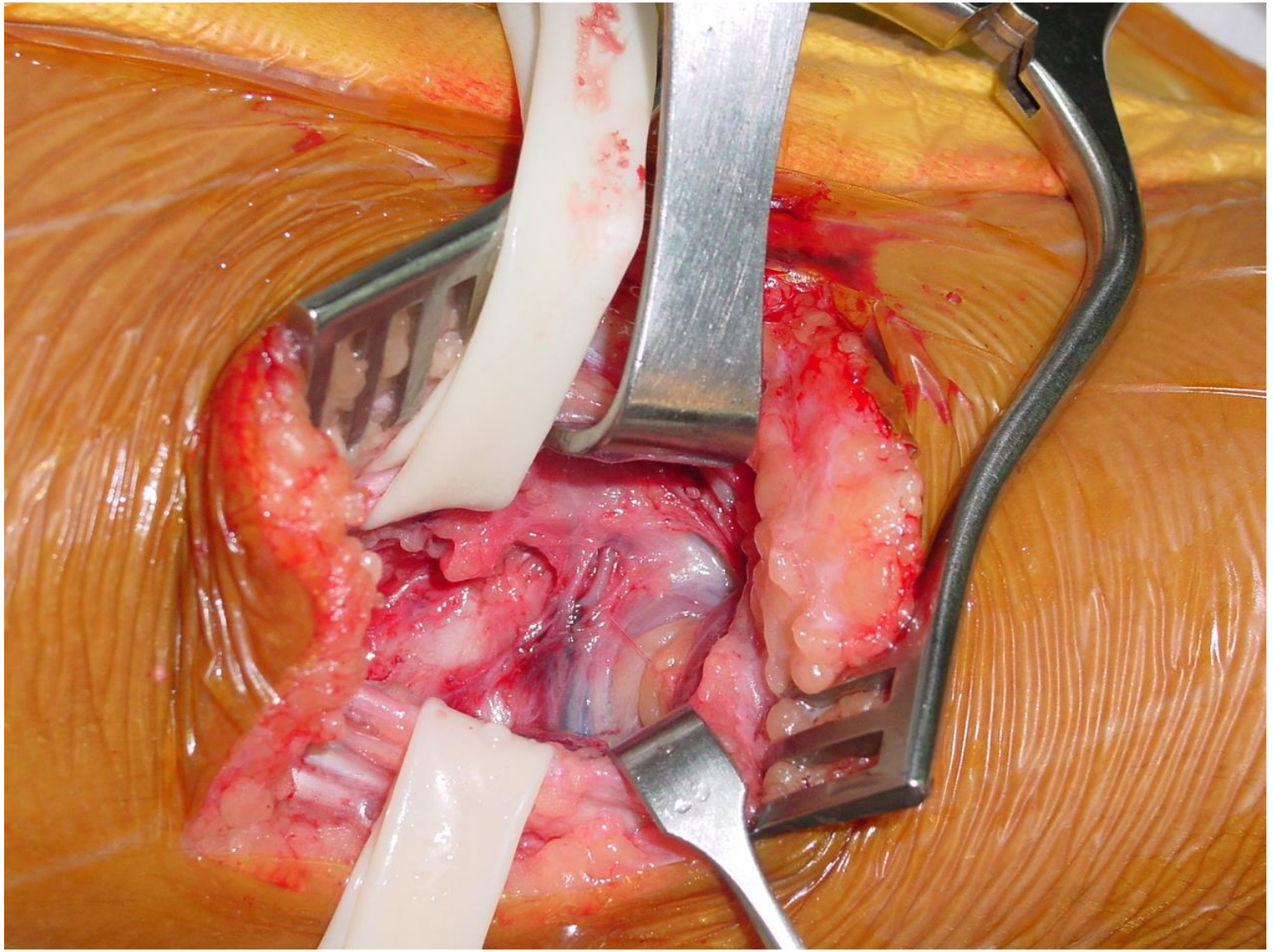
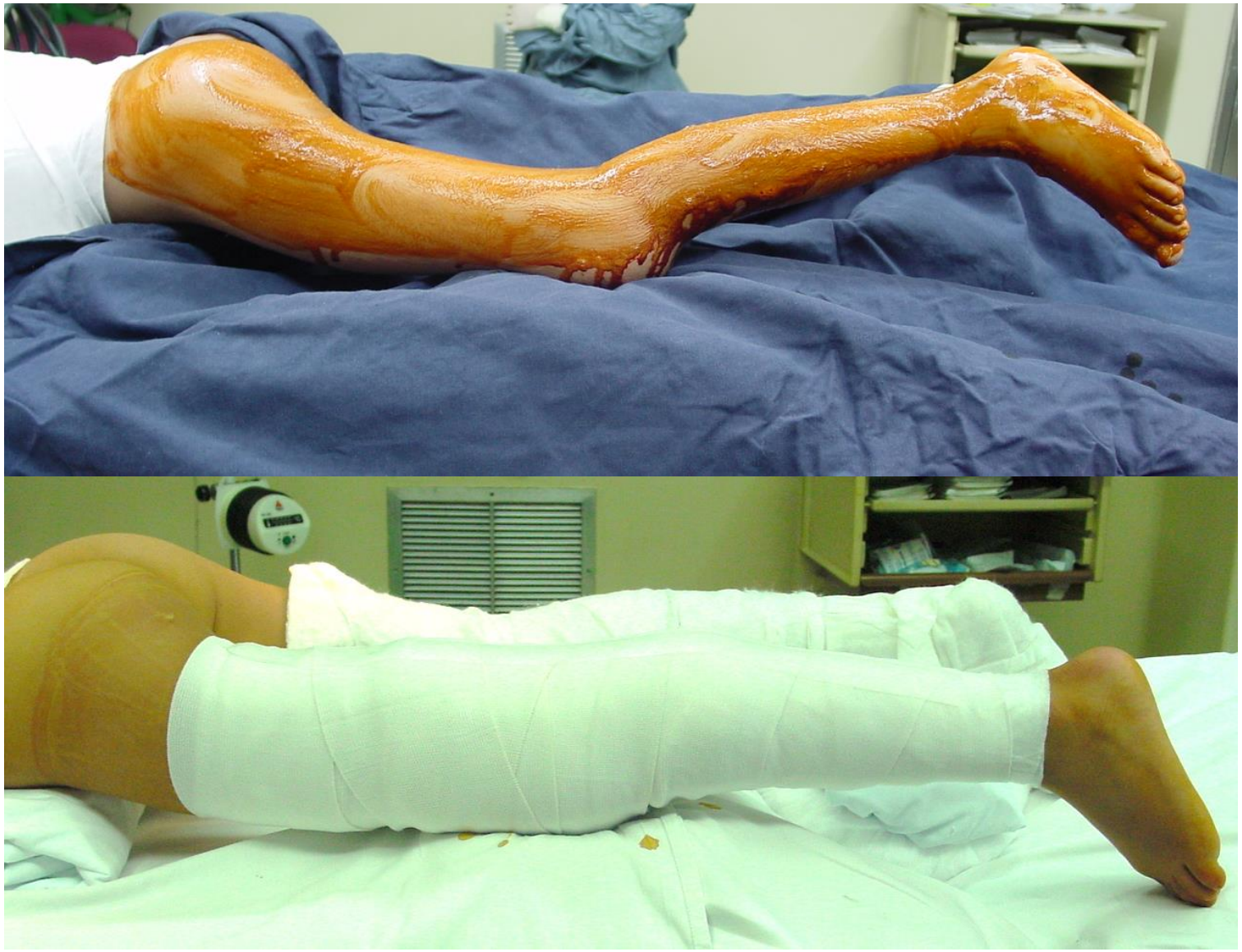
Residual Flexion Contracture

Posterior capsular release + gastrocnemius



Residual Flexion Contracture

Posterior capsular release + gastrocnemius



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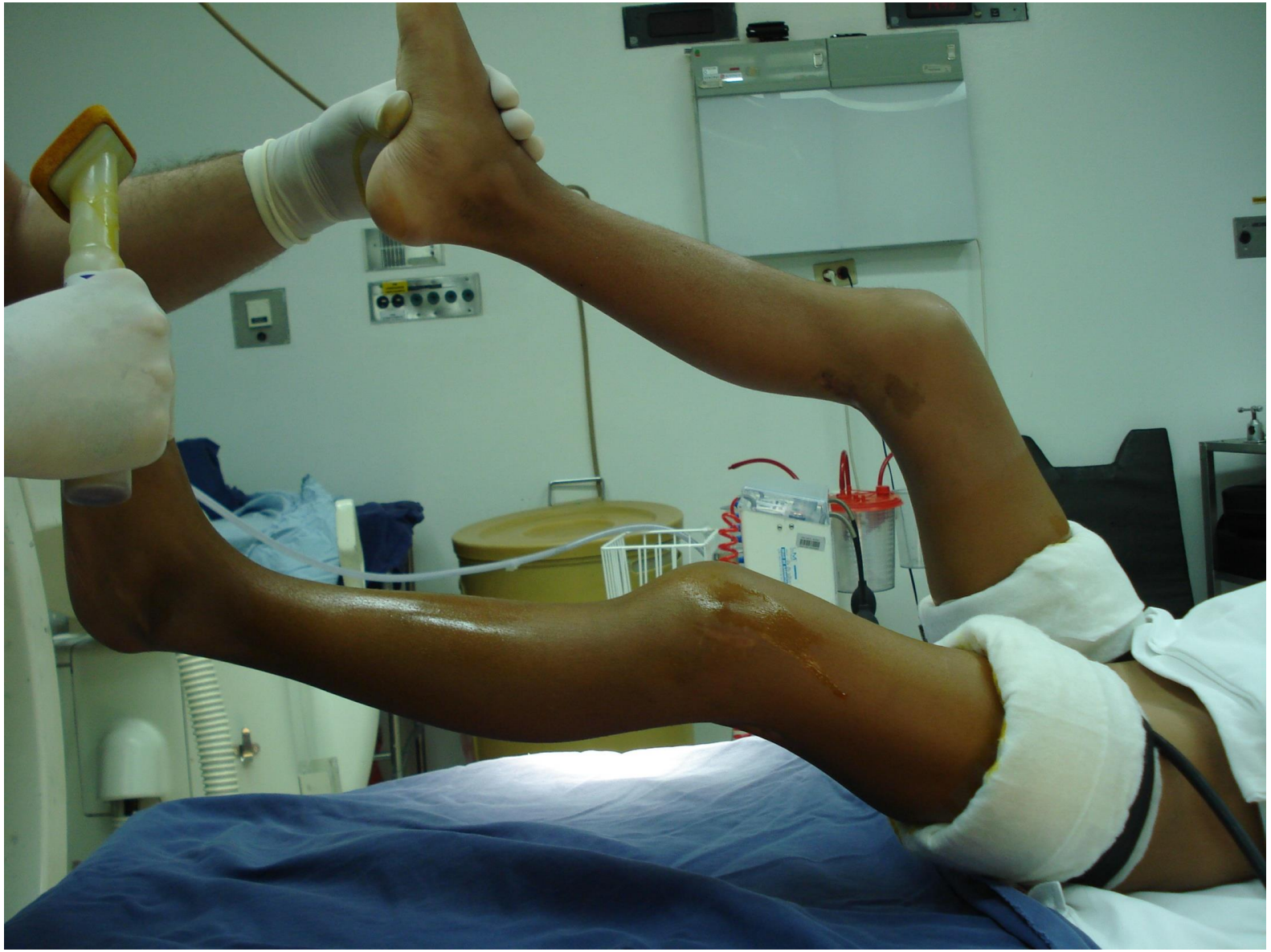
Residual Flexion Contracture

24 y ♂ - Post-posterior release



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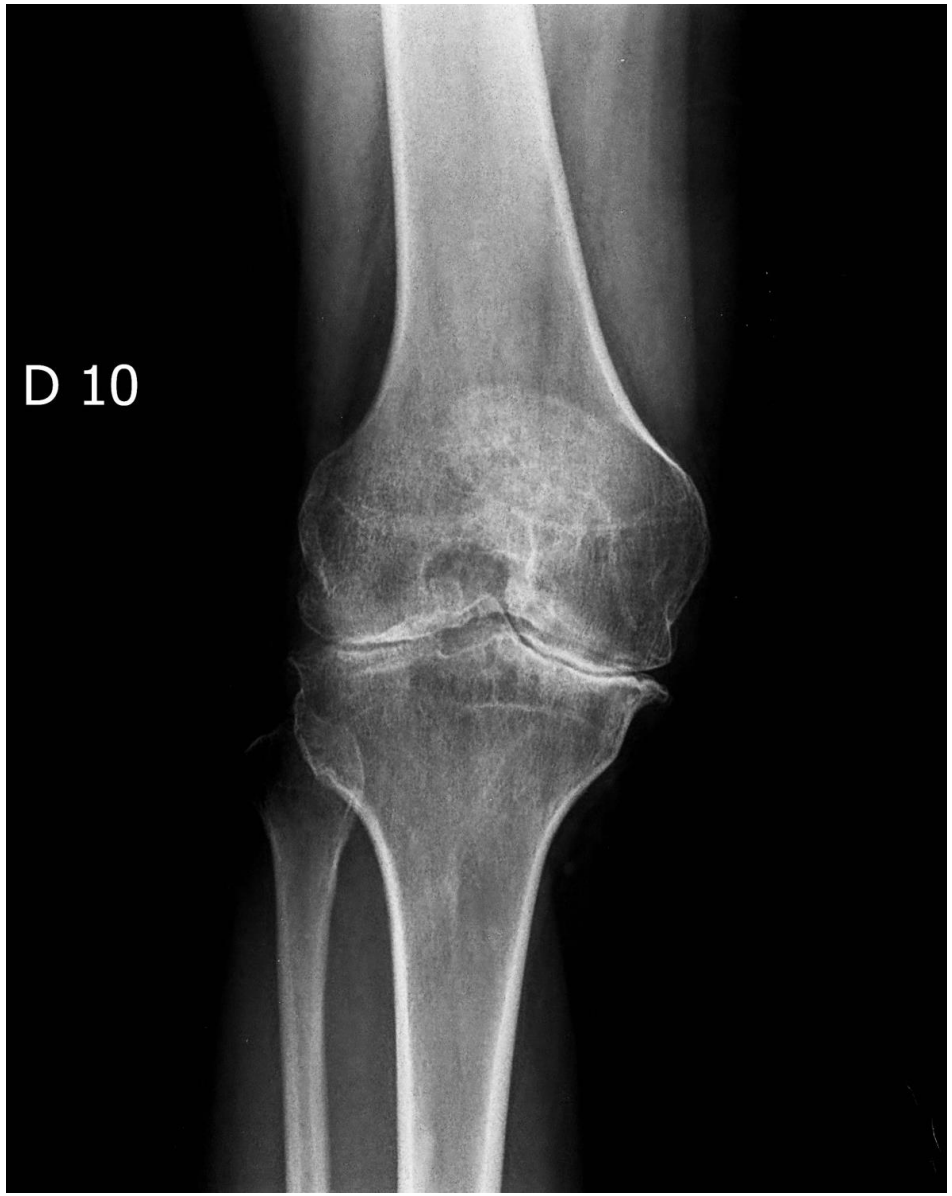
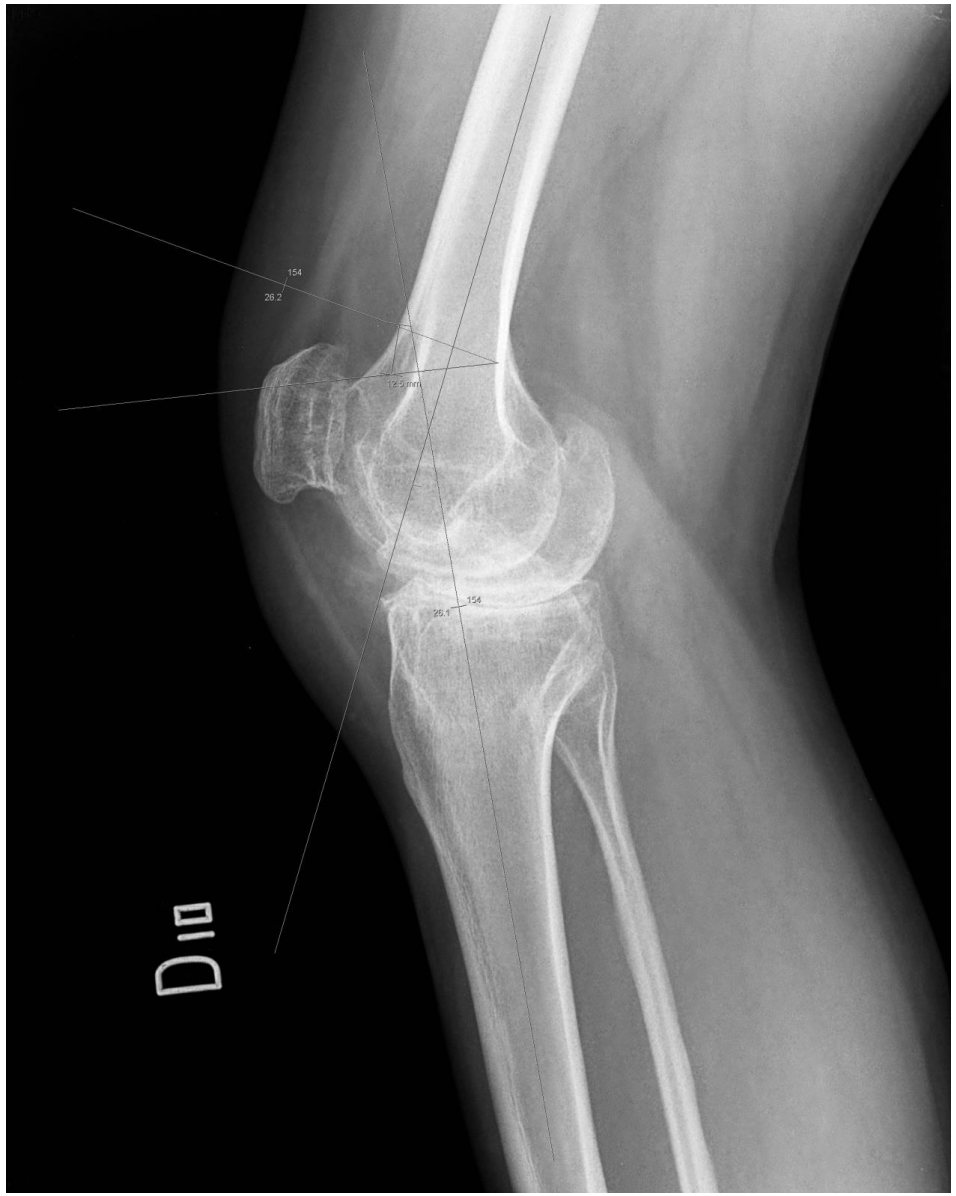
Post-posterior release





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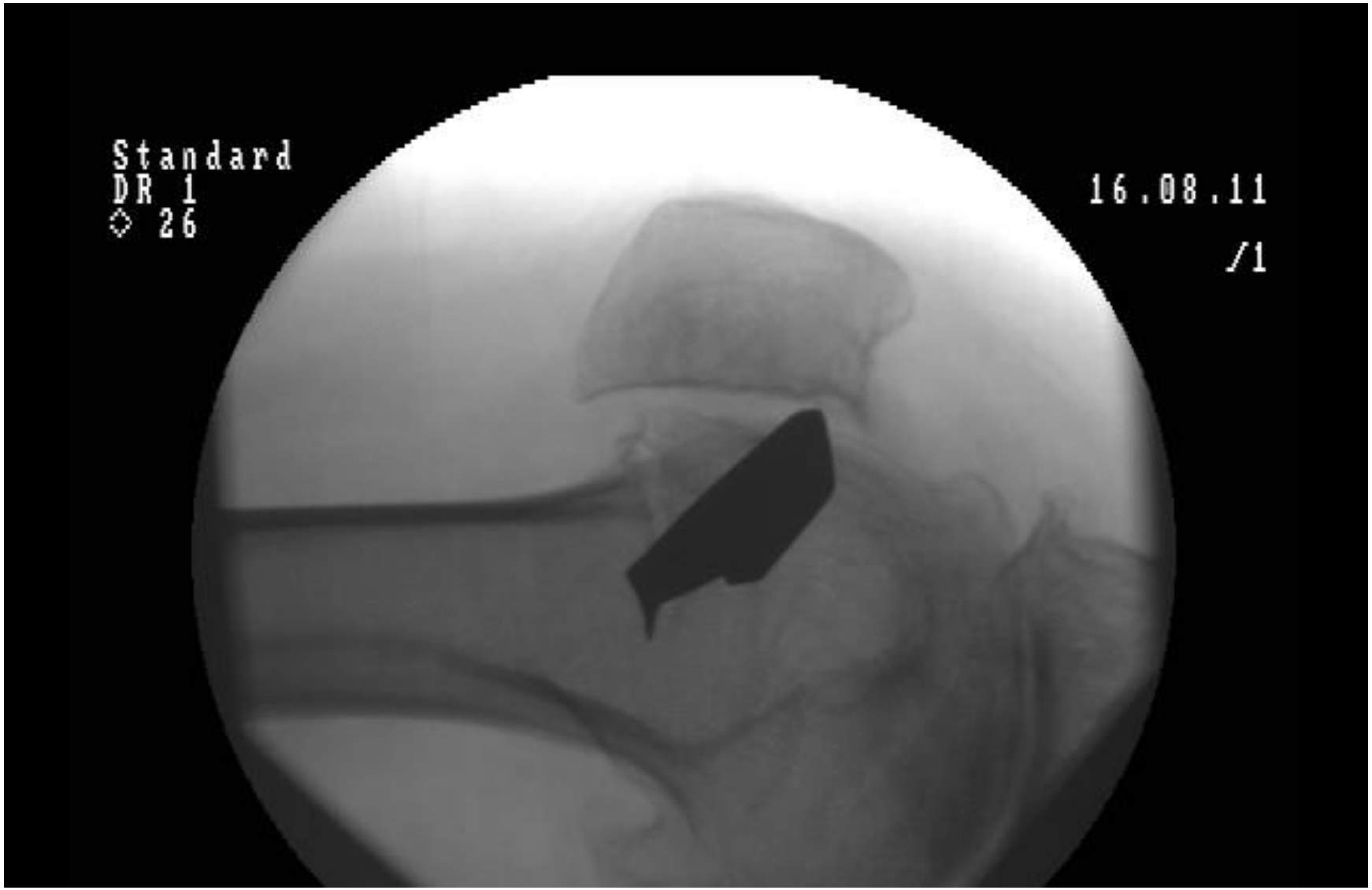

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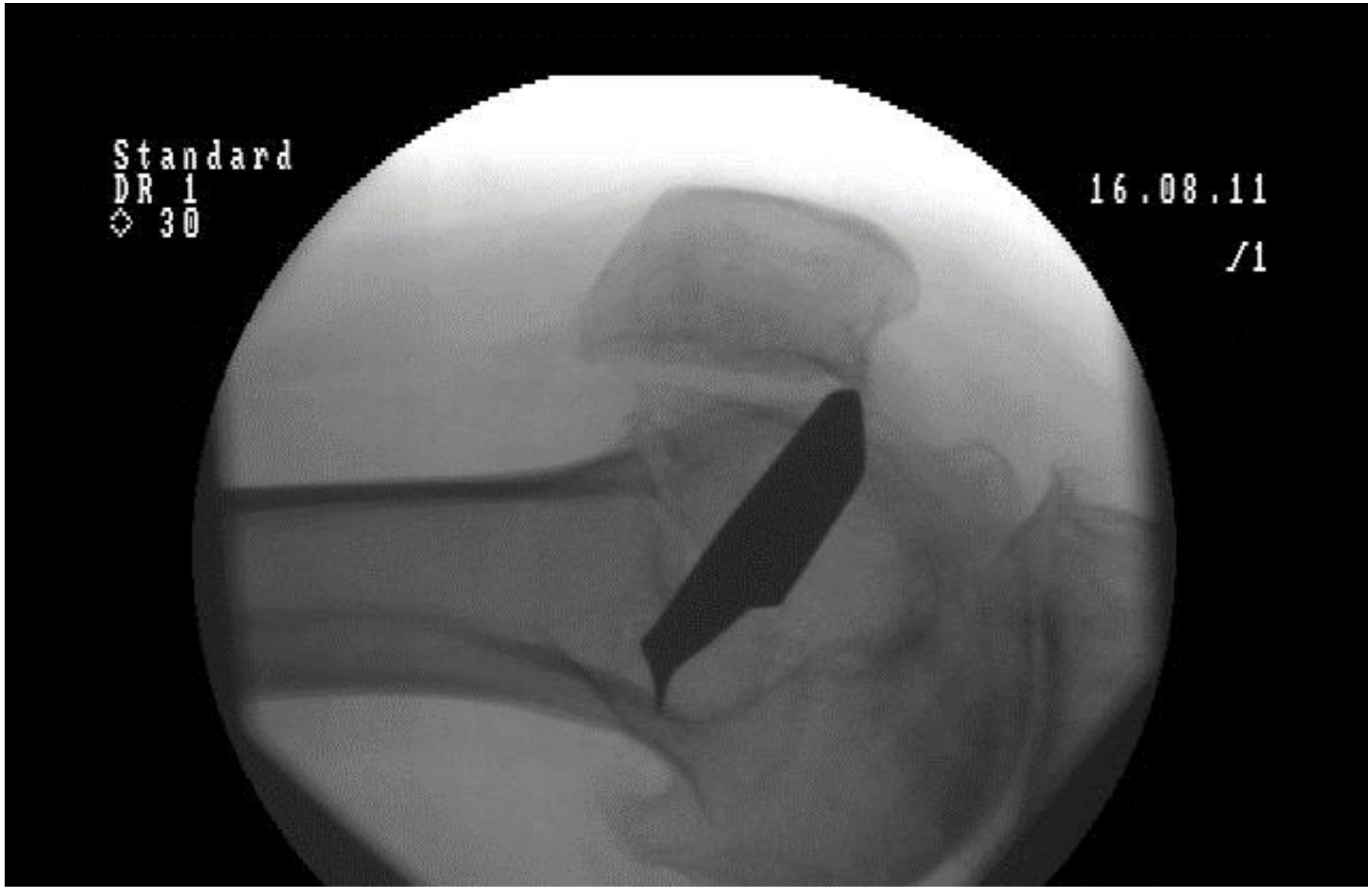

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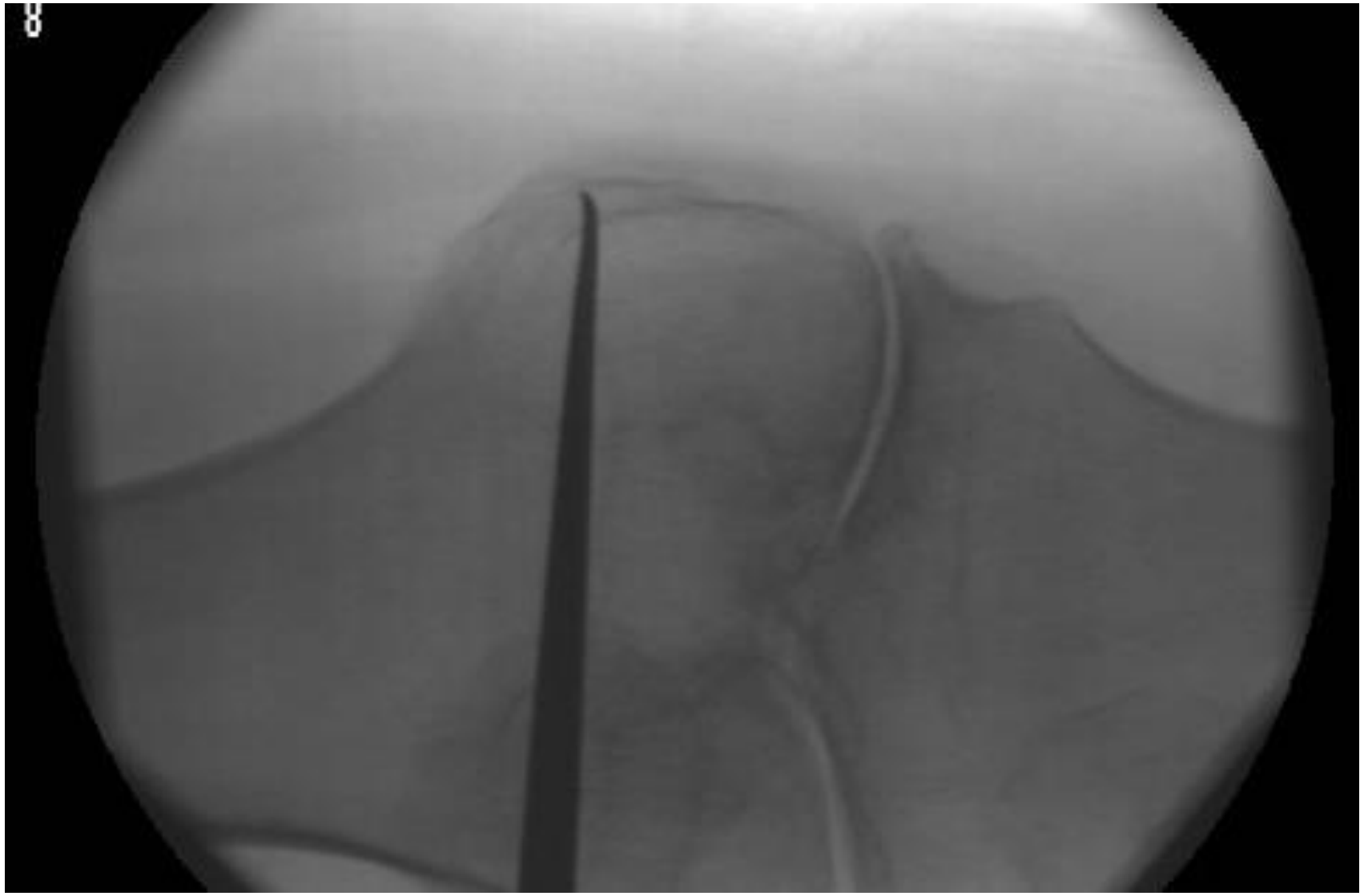

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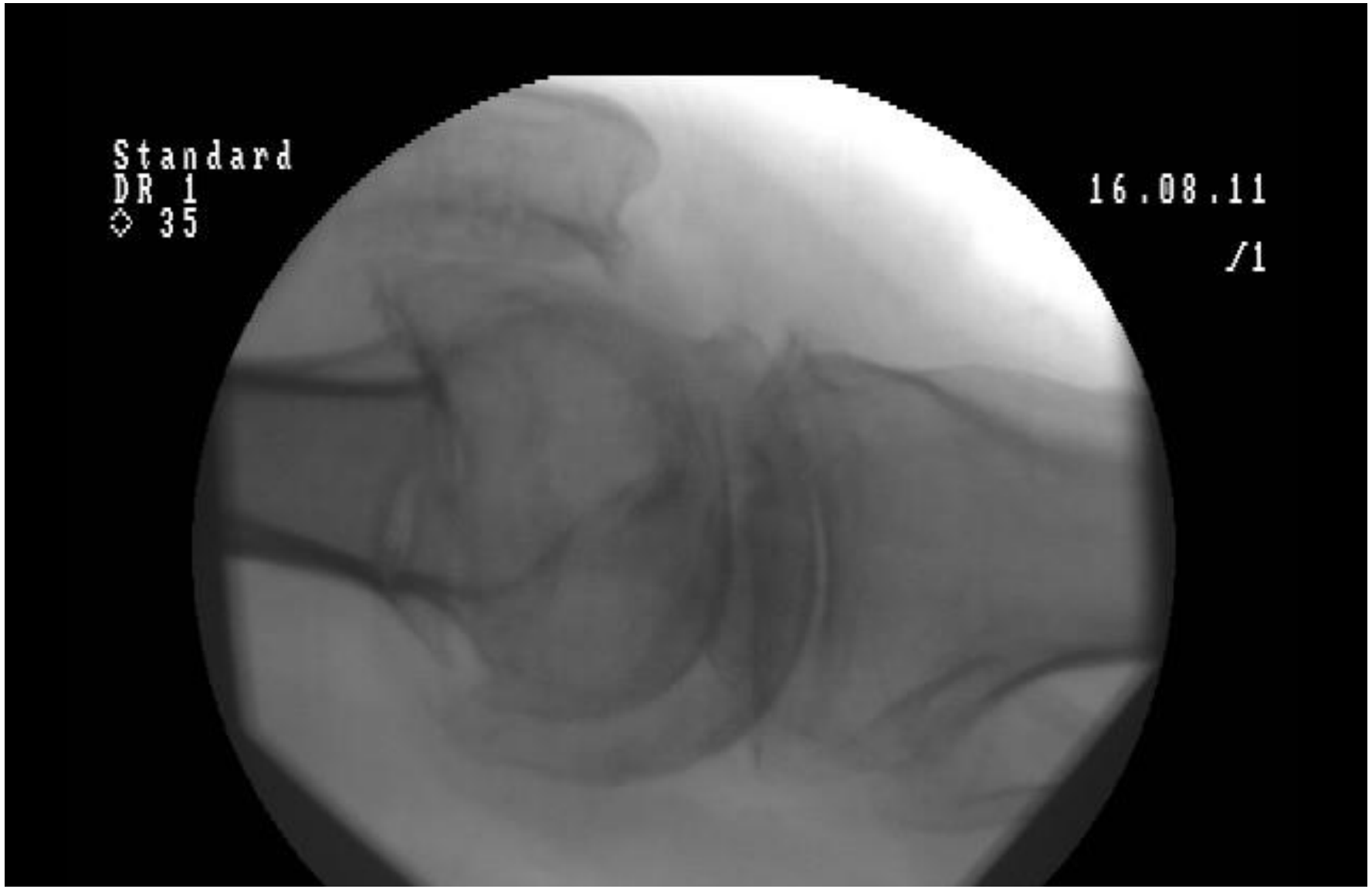

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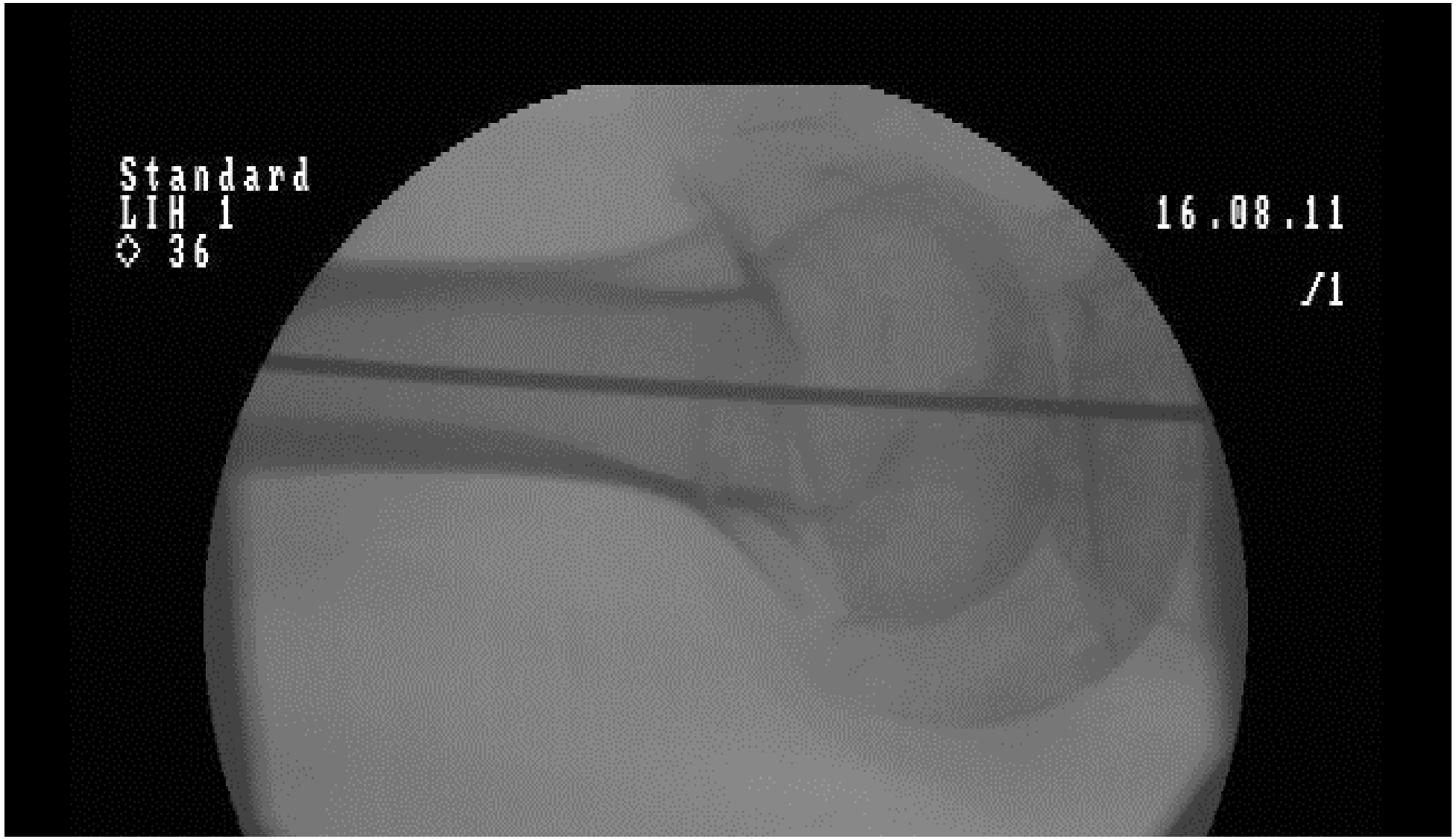

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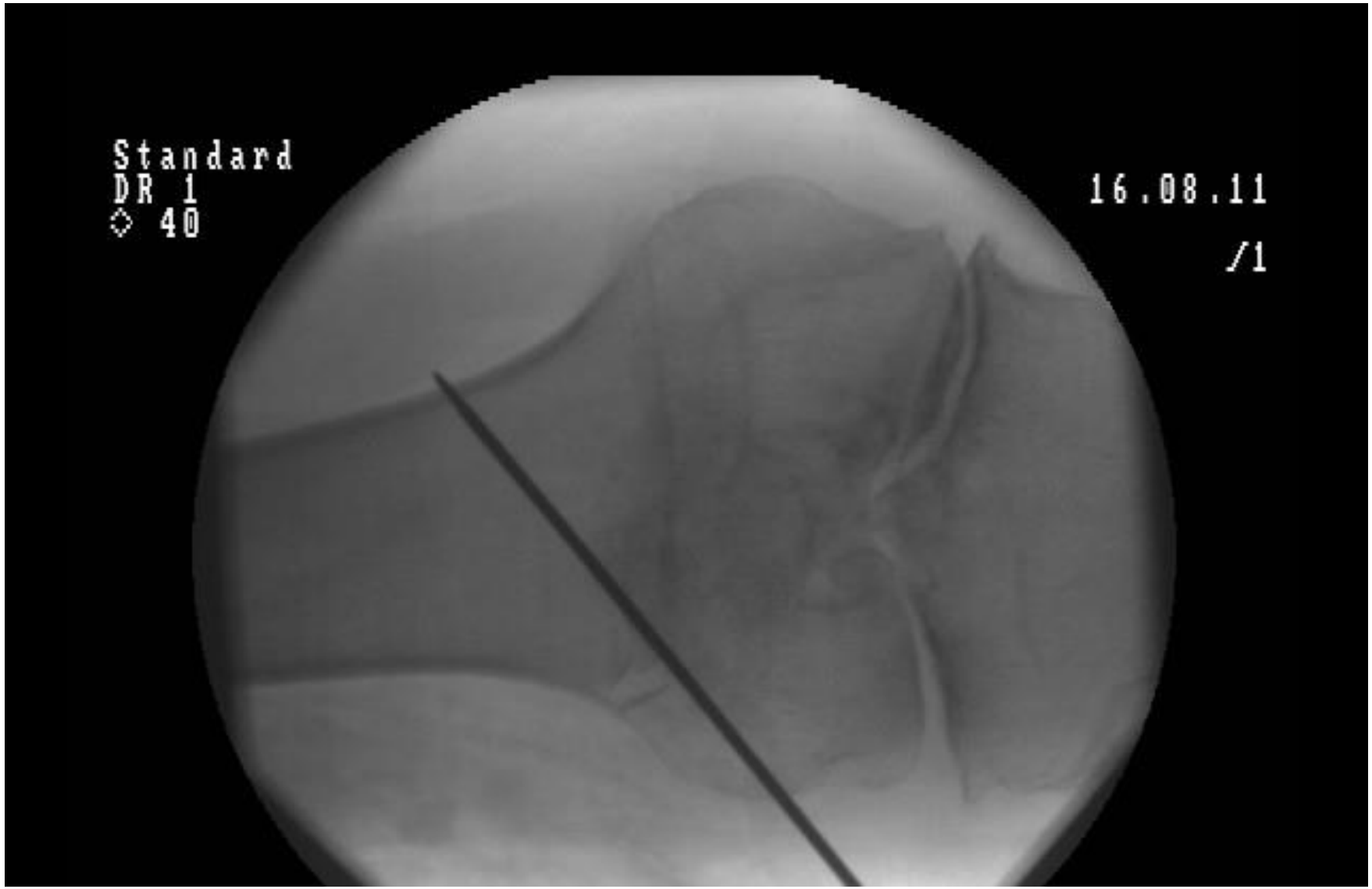

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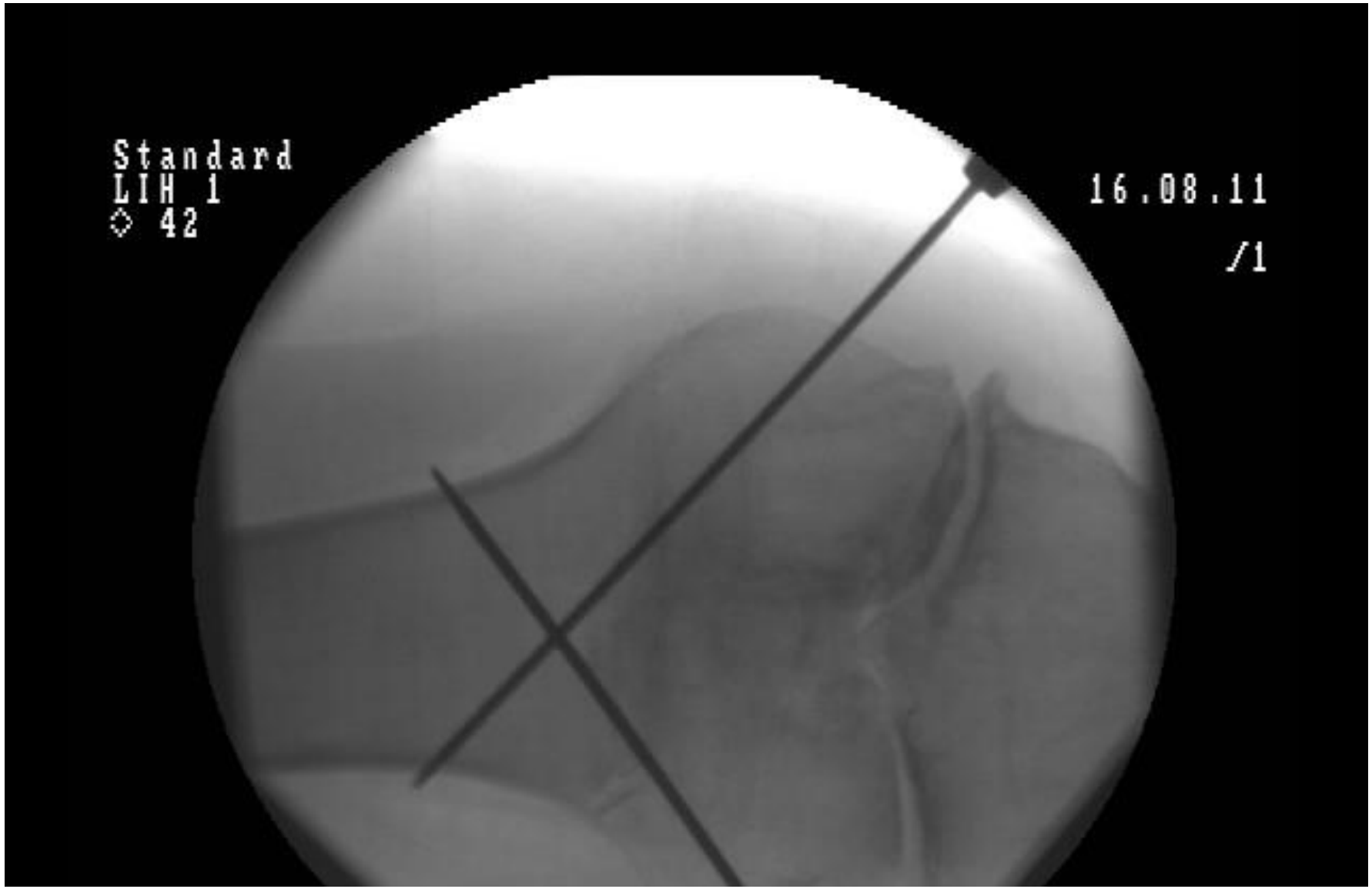

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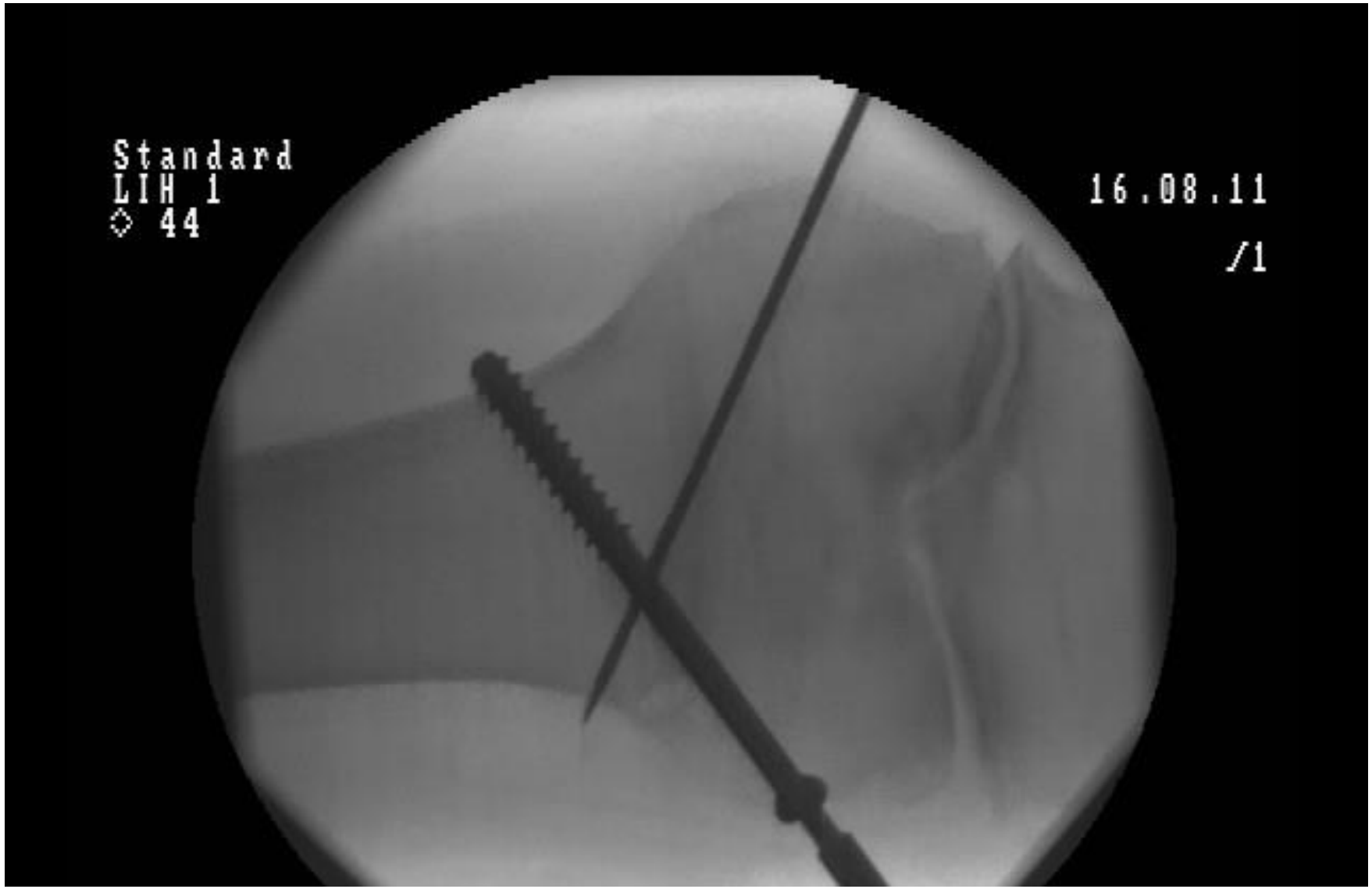

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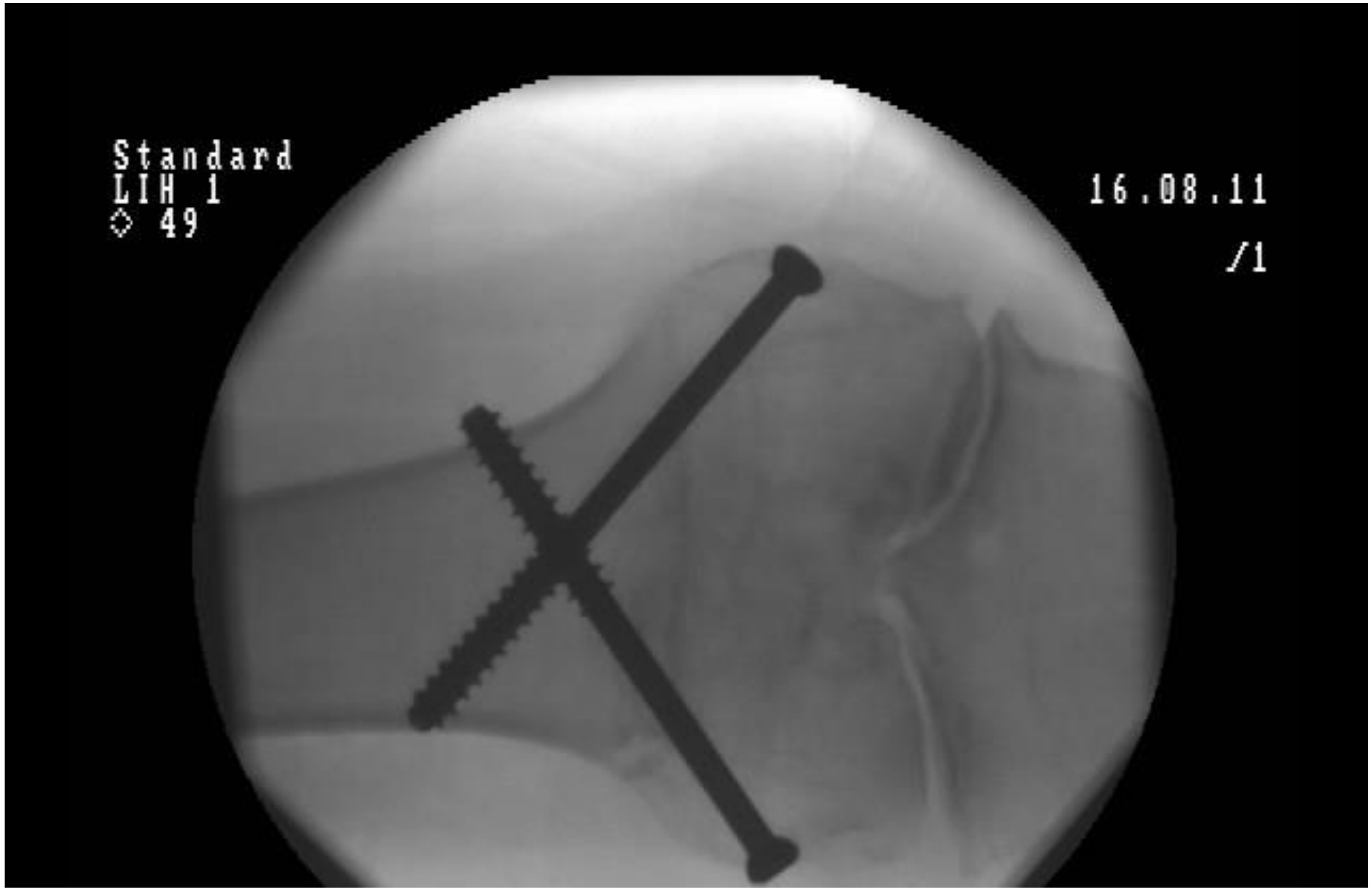

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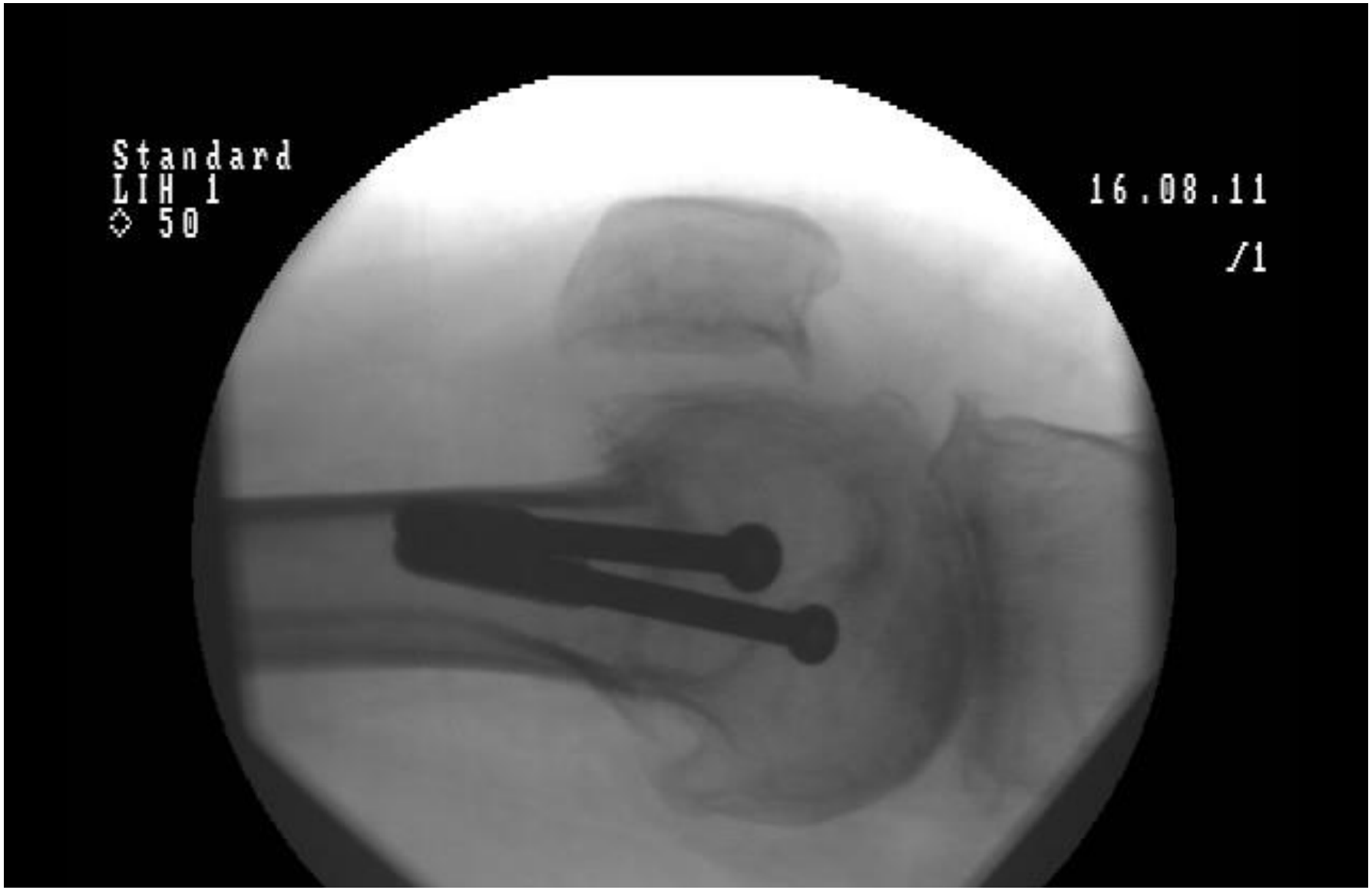

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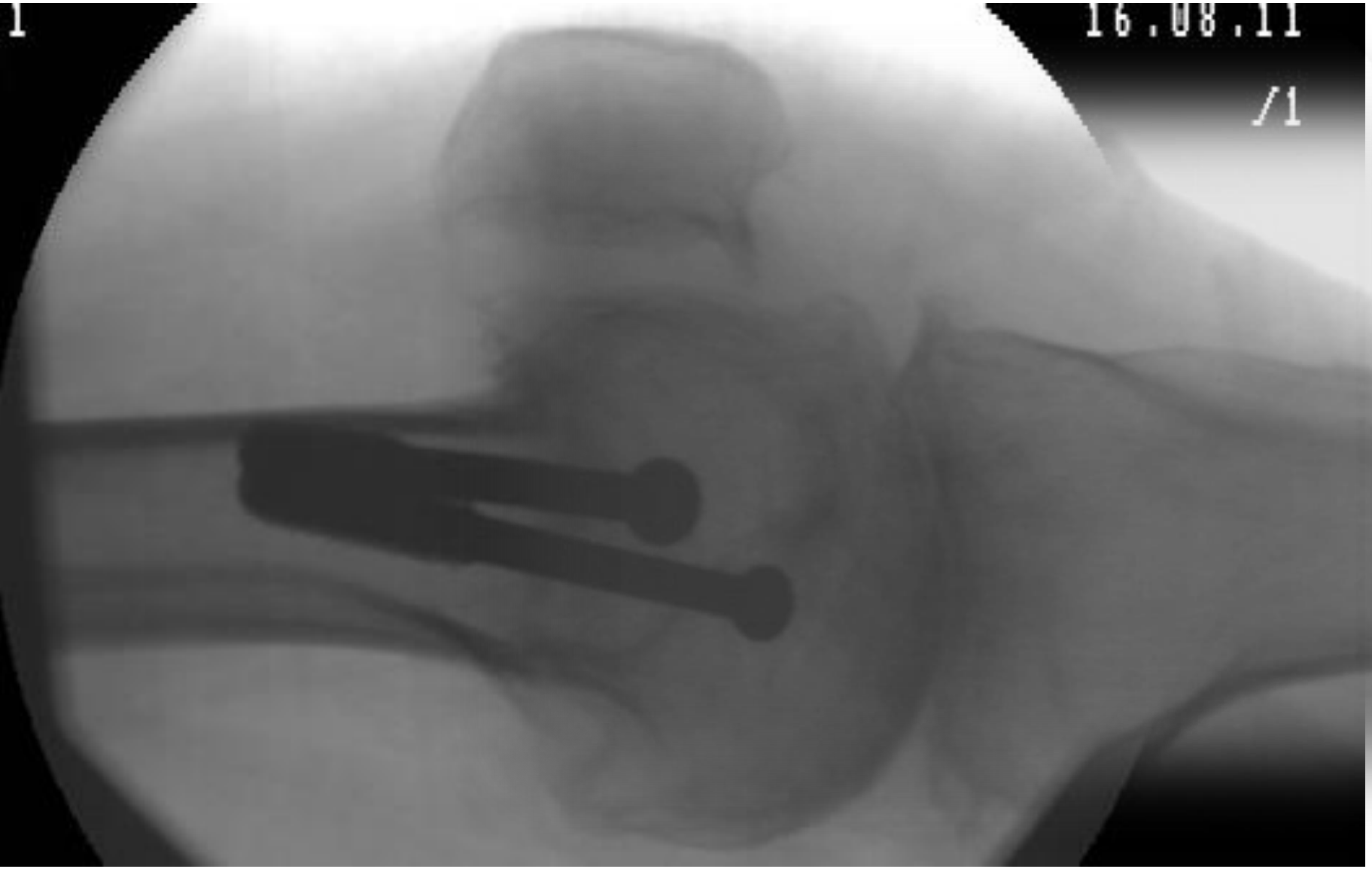

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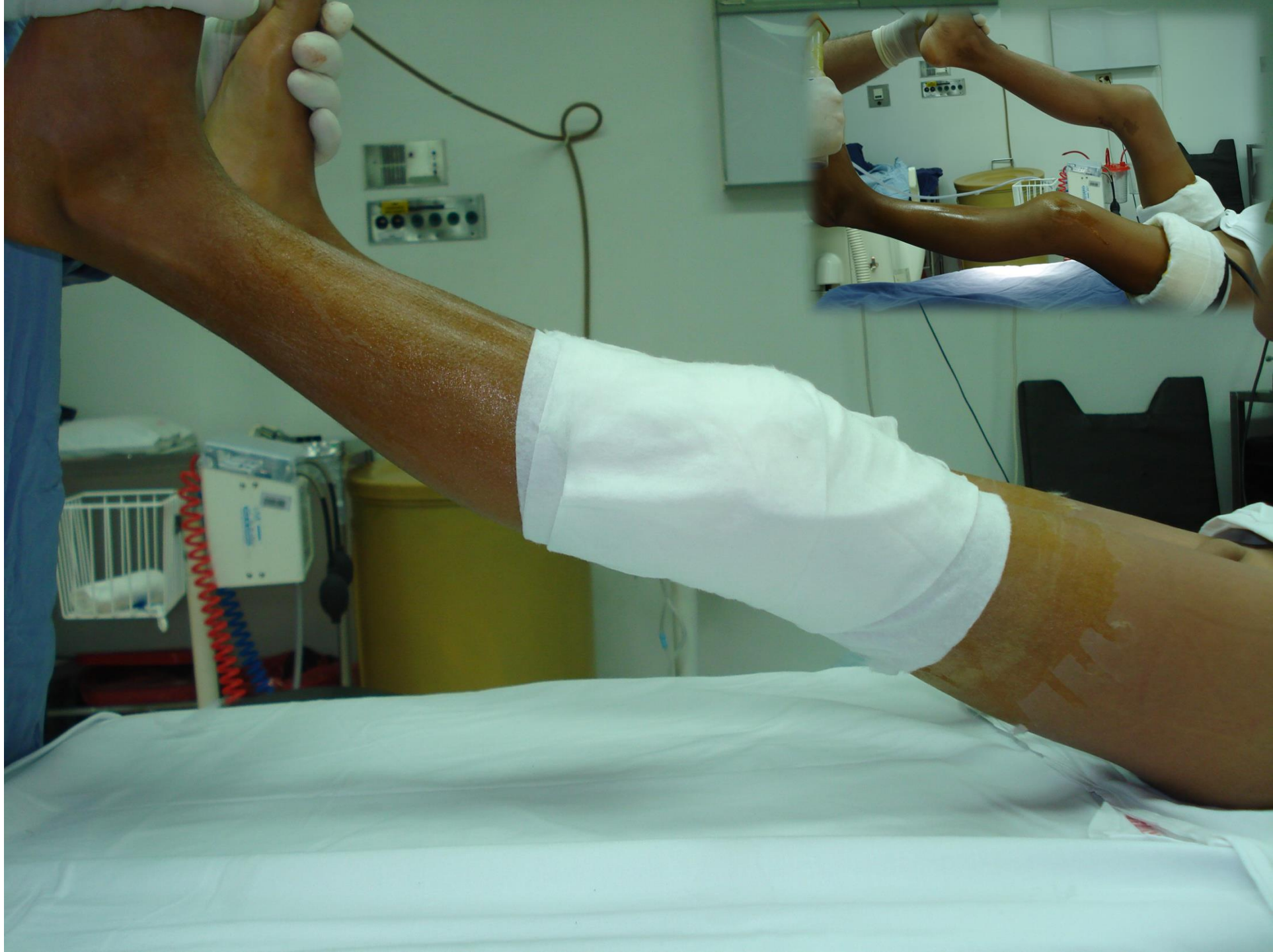

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Synovitis & Flexion Contractures

Recommendation 10.7.3:

• For patients with hemophilia in the postoperative period following orthopedic surgery, the WFH recommends gradual rehabilitation by a physical therapist experienced in hemophilia management.

Srivastava A, Santagostino E, Dougall A, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020: 26(Suppl 6): 1-158. https://doi.org/10.1111/hae.14046

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Synovitis & Flexion contractures

Synovectomy

Cast & wedges or hinges

Posterior Release

Osteotomies

THANK YOU

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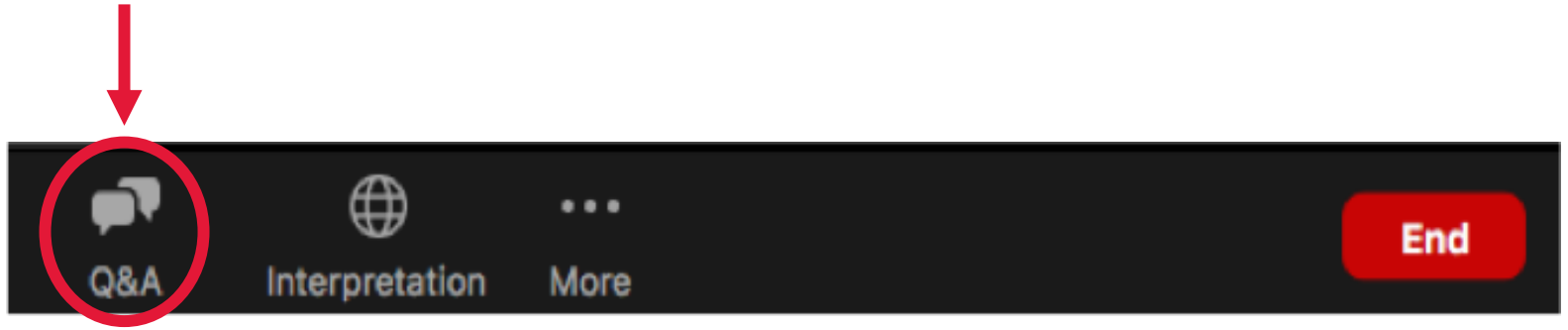
QUESTION & ANSWER

Please submit your questions in the Q&A box



Cardiovascular comorbidities – Hypertension & renal disease

Robert Klamroth, MD
Head of the Department and Director of Comprehensive Care
Germany

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Employee	None
Paid Instructor	None
Speaker bureau	Bayer, Biomarin, Biotest, CSL Behring, Grifols, Novo Nordisk, Octapharma, Pfizer, Roche, Sanofi, Sobi, Takeda,
Other	None

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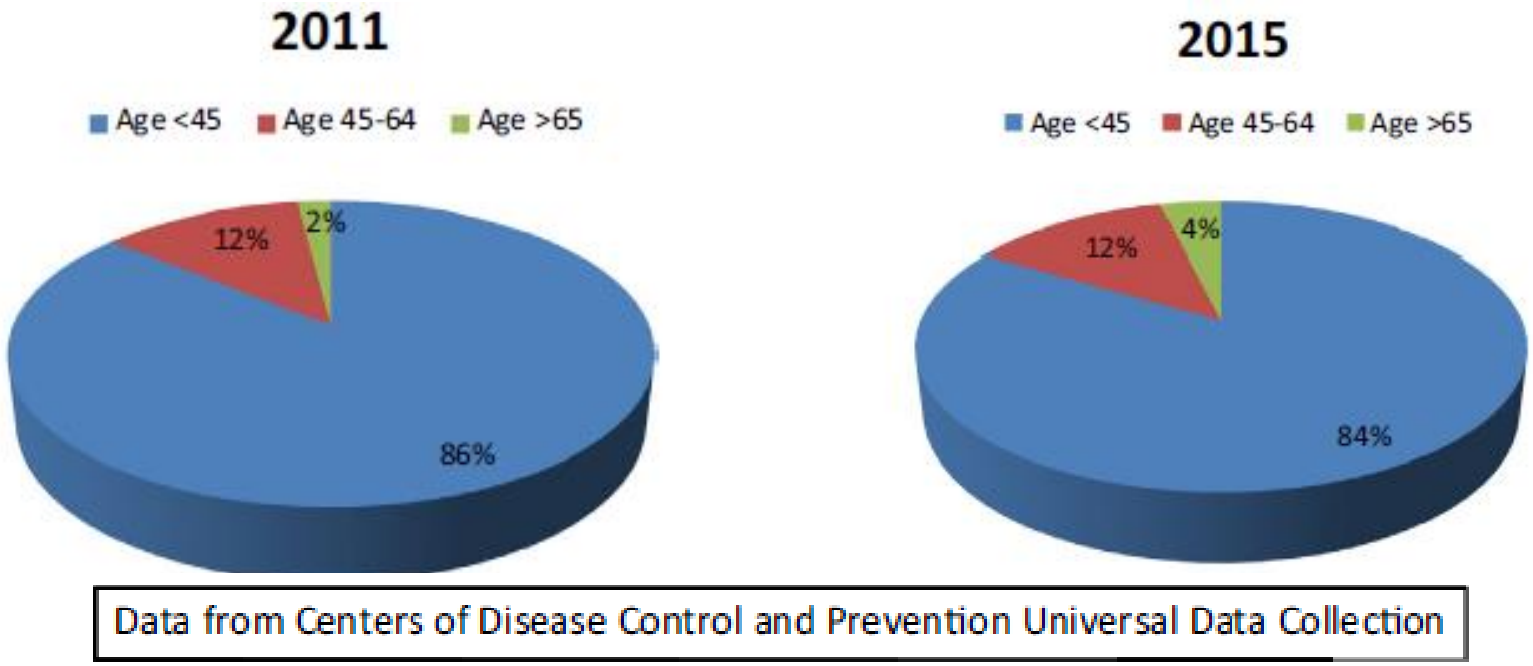
Number of persons > 65 yrs with Haemophilia

PWH = ~ 400.000 worldwide



The population of elderly PWH is growing

Angelini et al Semin. Hematol 2016; 53: 35

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Co-morbidities in patients with haemophilia

Improved life expectancy of haemophilia patients due to:
Advances in haemophilia care and HIV /Hep C
Factor replacement therapy

More older patients with haemophilia
Cancer and cardiovascular disorders increasing

Disorders in the ageing haemophilia population
New challenge for physicians involved in haemophilia
Better knowledge and optimal management

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Renal disease

A higher incidence of renal disease has been reported in people with hemophilia, compared with the general population.

Risk factors for renal disease are

- Older age
- Hypertension
- Diabetes
- HIV infection and combined antiretroviral therapy
- Use of NSAIDs

No correlation was observed with hematuria[1]

1. Holme et al. Haemophilia 2016, 22: 248-255;

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Renal disease

Very few patients with hemophilia require renal replacement therapy

The choice between peritoneal dialysis and hemodialysis depends on patient-specific factors

Hemodialysis requires anticoagulation to avoid clotting of the filter

An individual approach to anticoagulation and factor replacement during hemodialysis is recommended

Personal experience with two patients with severe hemophilia on hemodialysis who required no additional anticoagulation and no additional clotting factor concentrate

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Srivastava A, et al. Haemophilia. 2020; 26: 1-158

Renal disease - Recommendations

Regular monitoring of renal function in older PwH

Screening for risk factors for renal disease

Supervising treatment of

- Hypertension
- Diabetes
- Use of NASIDs

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Srivastava A, et al. Haemophilia. 2020; 26: 1-158

Patient Case: Hypertension

Severe Hemophilia A
52 years old, 82 kg BW
Intron 22 inversion
HIV negative, HCV positive

History of inhibitor development
ITI with partial success
Reduced half-life of factor VIII

Daily injections of 1000 IU factor VIII
No joint bleeds

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Patient Case: Hypertension

Comorbiditiy: Arterial hypertension
Antihypertensive medication since the age of 40

Died without any obvious cause
Autopsy: intracerebral haemorrhage (ICH)

Lots of unused antihypertensive drugs in his apartment

Intracerebral haemorrhage in haemophilia

1977 -1999 ICH in the United Kingdom[1]
Severe Haemophilia: Standard mortality ratio 39,29
Moderate/Mild: Standard mortality ratio 9.29

Prophylaxis seems to be able to reduce ICH
in patients with severe haemophilia[2]

Hypertension is a major risk factor for ICH in all patients

[1] Darby SC et al. Blood, 2007. 110(3):815-25
[2] Ljung RC Br J Haematol, 2008. 140(4):378-84

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Hypertension

Hypertension is a CV risk factor which has repeatedly been reported among PWH since long time:

- An increased incidence of HT (33%) was reported back in 1980 in a retrospective analysis of 233 PWH[1]
- After age adjustment, Dutch PWH were twice as often treated with antihypertensives vs. the general population[2](1990)
- In Canadian mild haemophiliacs, 29% were hypertensive with respect to 18% of age-matched control subjects[3](2008)
- Hypertension was found more common in Italian PWH vs age-matched peers[4] (2009)

1. White G et al South. Med. J. 1980; 73:155 2.,Rosendaal et al Br J Haematol. 1990; 75:125, 3. Walsh et al JTH 2008; 6:755, 4. Siboni et al JTH 2009; 7:780

Increased prevalence of hypertension in haemophilia patients

Dietje E. Fransen van de Putte[1]; Kathelijn Fischer[1,2]; Michael Makris[3]; R. Campbell Tait[4]; Peter W. Collins[5]; Karina Meijer[6]; Goris Roosendaal[1]; Pratima Chowdary[7]; Roger E. G. Schutgens[1]; Eveline P. Mauser-Bunschoten[1]

Thromb Haemost 2012; 108: 750–755

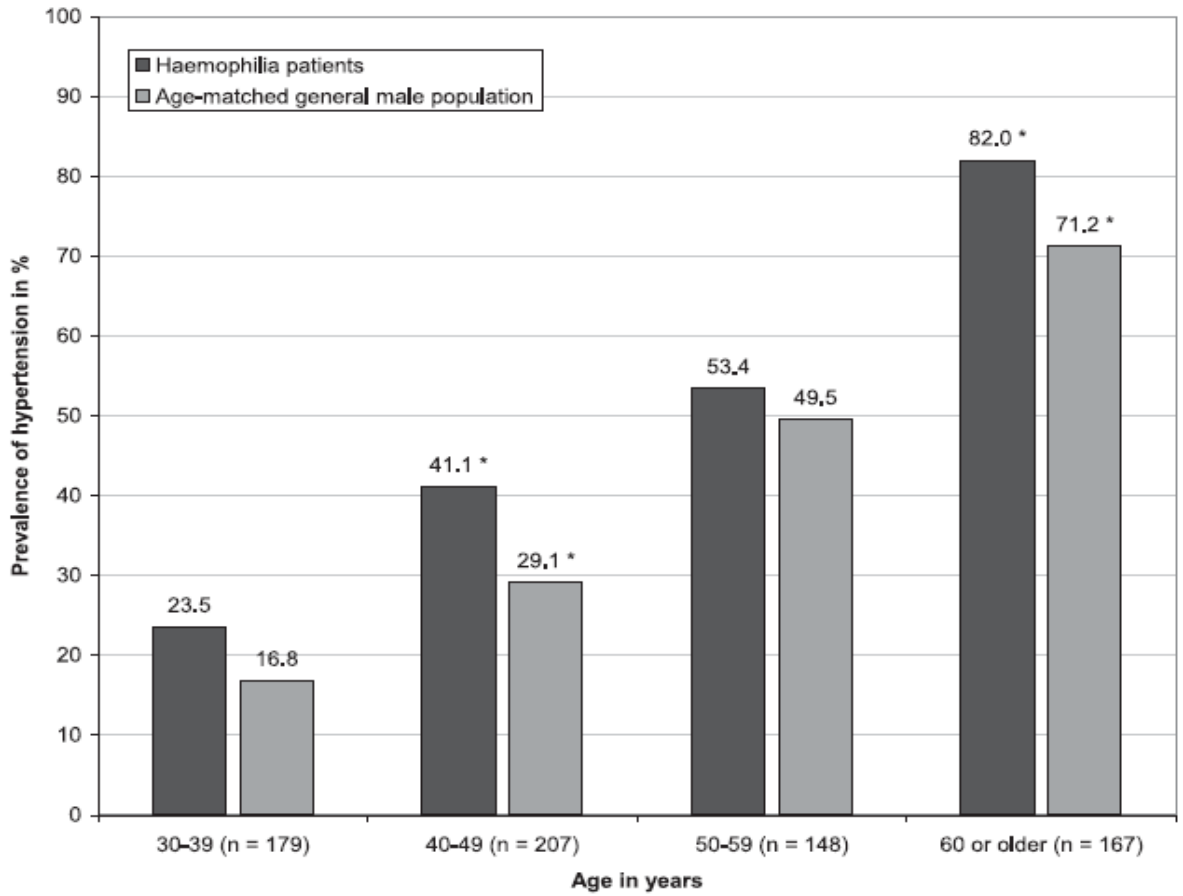

Figure 1: Prevalence of hypertension in 701 haemophilia patients according to age and comparison with the general age-matched male population. * indicates a statistically significant difference between haemophilia patients and the general age-matched male population.

Overall: 49 % vs. 40%

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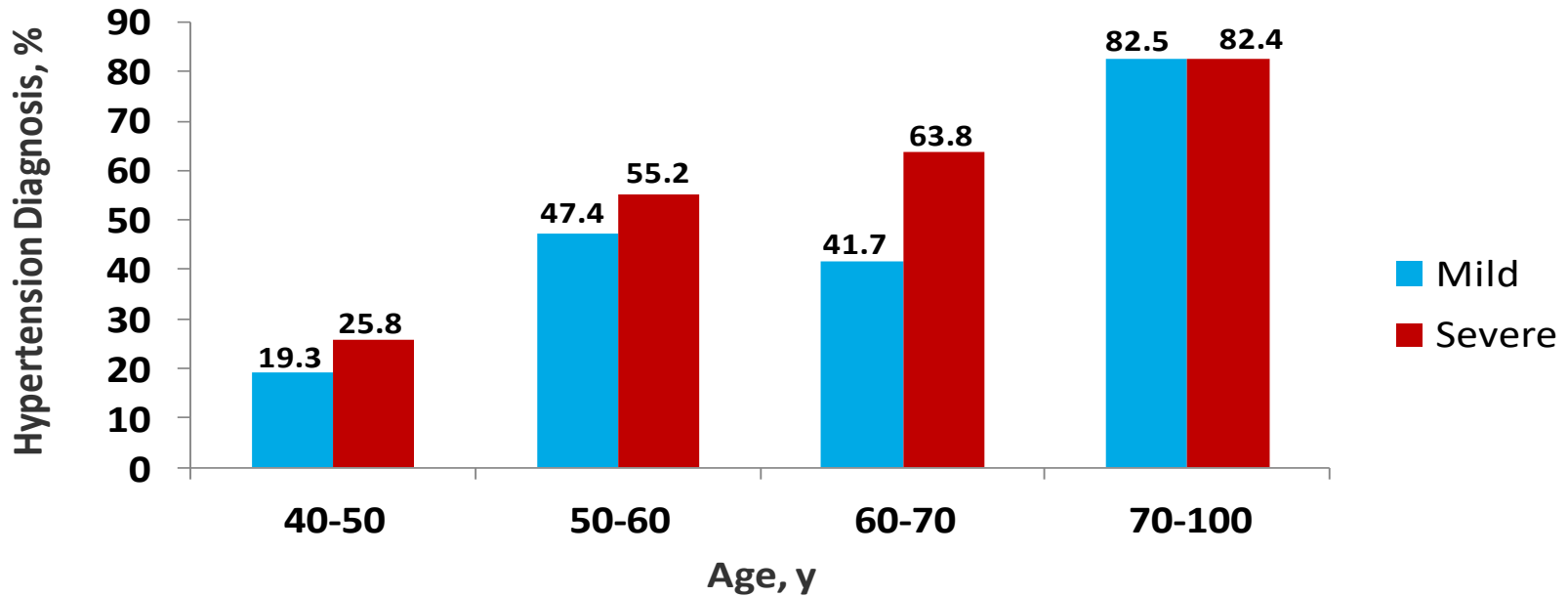
The H3 Study results
Cross-sectional study in Europe

532 pts (59% severe HA) > 40 yrs, 61% OD, 45.2% with known diagnosis of hypertension, 94% treated for hypertension

Additional 6.7% with no diagnosis of hypertension had blood pressure >140/90 => 50.7%

Slightly higher rates in the 3 younger age categories (40–70 y) in severe hemophilia compared with mild hemophilia



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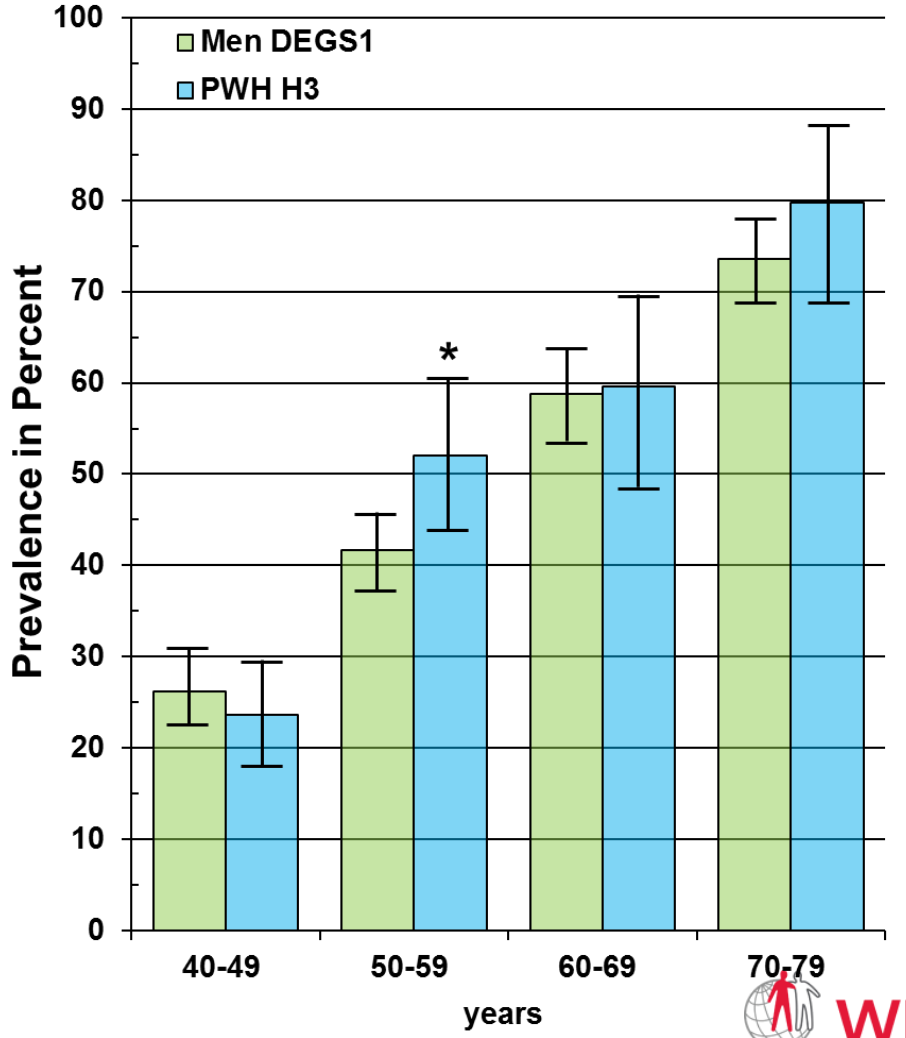
Comparison of the prevalence of hypertension

Hypertension was significantly more prevalent in PWH from the H3 Study aged 50-59 years than in men from the general population from the DEGS1 Study:

40-49 yrs. p=0.48
50-59 yrs. *p=0.03
60-69 yrs. p=0.90
70-79 yrs. p=0.29



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Holme et al. Haemophilia 2016, 22: 248-255; Neuhauser et al. Bundesgesundheitsbl 2013, 56: 795-801

Conclusions: Hypertension

Hypertension is a risk factor for intracerebral bleeding and for atherosclerosis!

Measuring the blood pressure is easy!

Treatment of hypertension is important in patients with haemophilia

Recommendation WFH

Recommendation 9.9.3:

• For all patients with hemophilia, the WFH recommends regular blood pressure measurements as part of their standard care.

• REMARK: This recommendation is based on data indicating a higher prevalence of arterial hypertension among patients with hemophilia irrespective of age as compared with males in the general population.

Srivastava A, et al. Haemophilia. 2020; 26: 1-158

Recommendation WFH

Recommendation 9.9.4:

- For patients with hemophilia, the WFH recommends the same management of arterial hypertension as that applied in the general population.

- REMARK: Patients with hemophilia diagnosed with hypertension may be treated in a hemophilia treatment centre or referred to primary care providers depending on the local healthcare system and practices.

Srivastava A, et al. Haemophilia. 2020; 26: 1-158

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Cardiovascular comorbidities – Atrial fibrillation and anticoagulation

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Center for Benign Haematology, Thrombosis and Haemostasis
Van Creveldkliniek University Medical Center
Utrecht, The Netherlands

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Consultant	
Employee	
Paid Instructor	
Speaker bureau	
Other	

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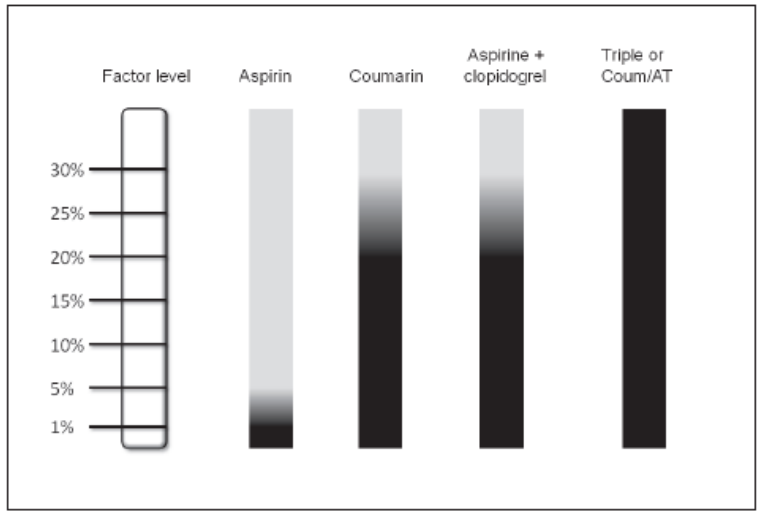
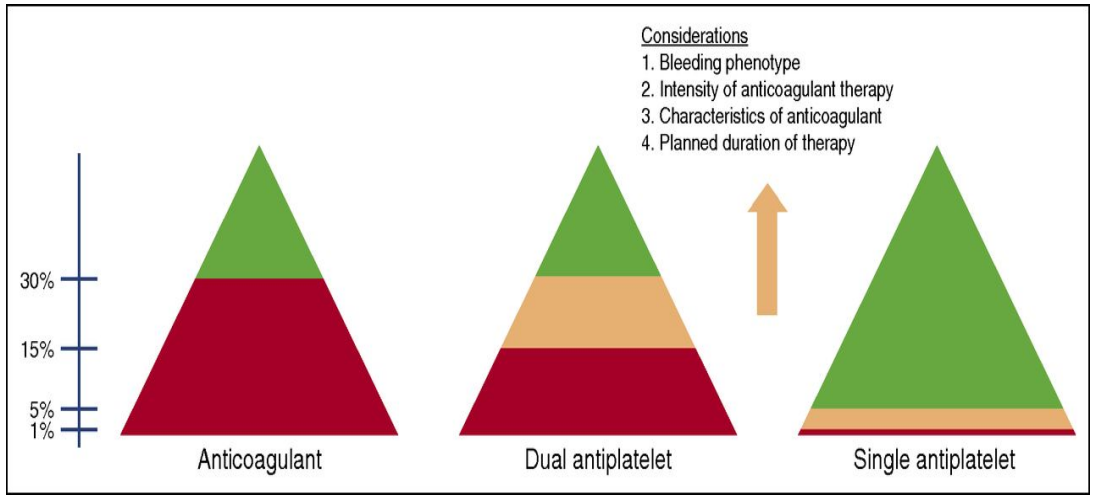
Can we anticoagulate a PWH?



Schutgens et al, Haemostaseologie 2013



Martin et al, Blood 2016

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Haemophilia
The Official Journal of the World Federation of Hemophilia, European Association for Haemophilia and Allied Disorders and the Hemostasis & Thrombosis Research Society

Letter to the Editor | Full Access

Management of atrial fibrillation in people with haemophilia – a consensus view by the ADVANCE Working Group

R. E. G. Schutgens, R. Klamroth, I. Pabinger, G. Dolan, on behalf ofthe ADVANCE working group

First published: 09 October 2014 | https://doi.org/10.1111/hae.12525 | Citations: 8

Table 2. Suggested minimum trough levels of FVIII/FIX considered for safe anticoagulation treatment in different treatment settings.

Setting	Mean value (IU mL^{-1})	Range
Antiplatelet monotherapy	0.035	0.01–0.1
Vitamin K antagonists	0.24	0.1–0.5
Dual antiplatelet therapy	0.14	0.04–0.3
New oral anticoagulants	0.23	0.1–0.5
Cardioversion with concomitant therapeutic doses of heparin	0.40	0.1–0.8
During transoesophageal echocardiography	0.30	0.01–0.8

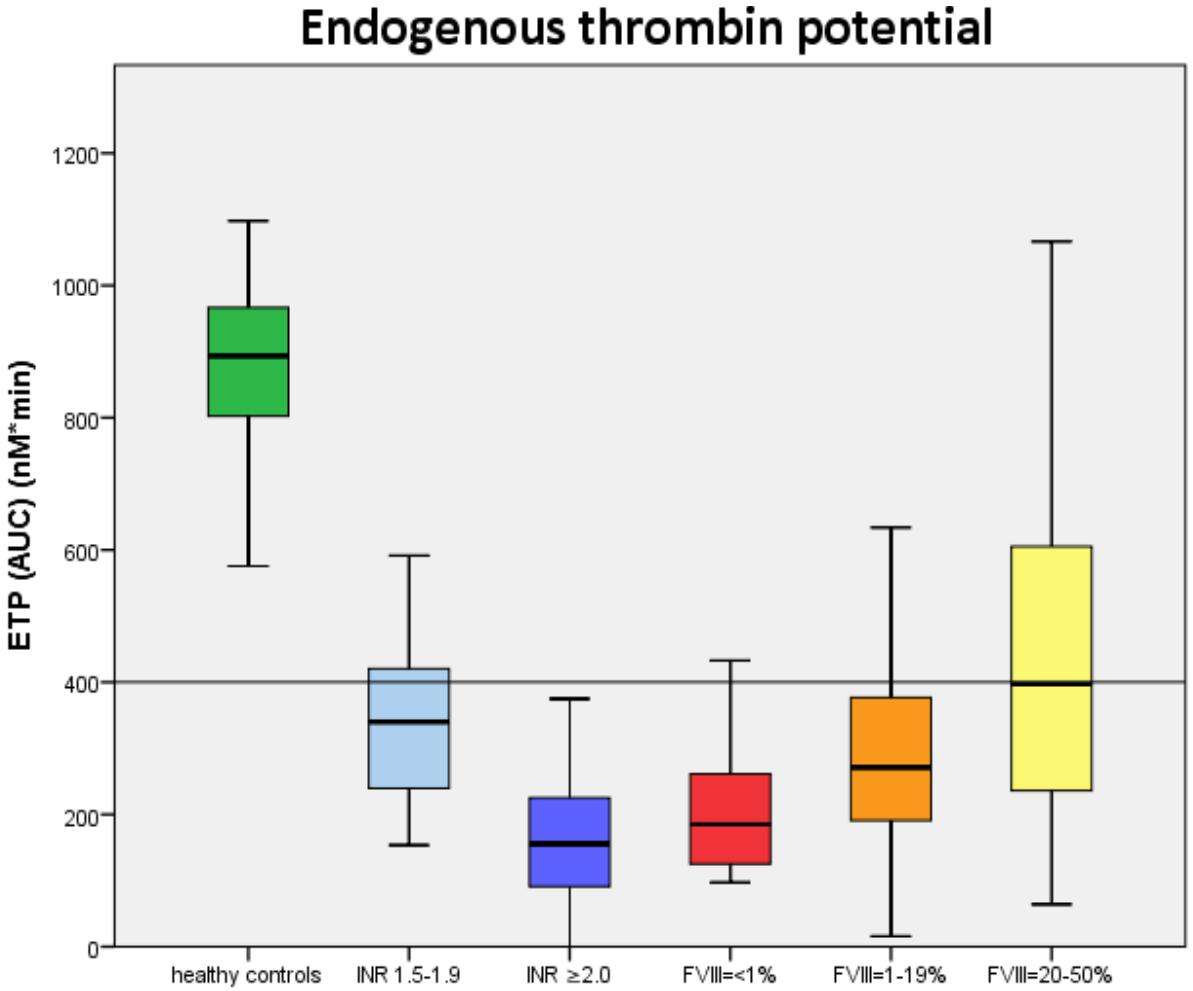
Journal of Thrombosis and Haemostasis, **15**: 868–875 DOI: 10.1111/jth.13674

ORIGINAL ARTICLE

Comparing thrombin generation in patients with hemophilia A and patients on vitamin K antagonists

M. L. Y. DE KONING,* K. FISCHER,* B. DE LAAT,† A. HUISMAN,‡ M. NINIVAGGI† and R. E. G. SCHUTGENS*

*Van Creveldkliniek, University Medical Center Utrecht, Utrecht; †Synapse, Maastricht; and ‡Department of Clinical Chemistry and Hematology, University Medical Center Utrecht, Utrecht, the Netherlands



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De Koning et al, JTH 2017

Clinical data on anticoagulation in PWH

Long-Term Antithrombotic Treatments Prescribed for Cardiovascular Diseases in Patients with Hemophilia: Results from the French Registry

Benoît Guillet‡ *, Guillaume Cayla‡ *, Aurélien Lebreton , Nathalie Trillot, Bénédicte Wibaut, Céline Falaise, Sabine Castet, Philippe Gautier, Ségolène Claeyssens, Jean-François Schved

CC BY-NC-ND 4.0 · Thromb Haemost 2021; 121(03): 287-296
DOI: 10.1055/s-0040-1718410

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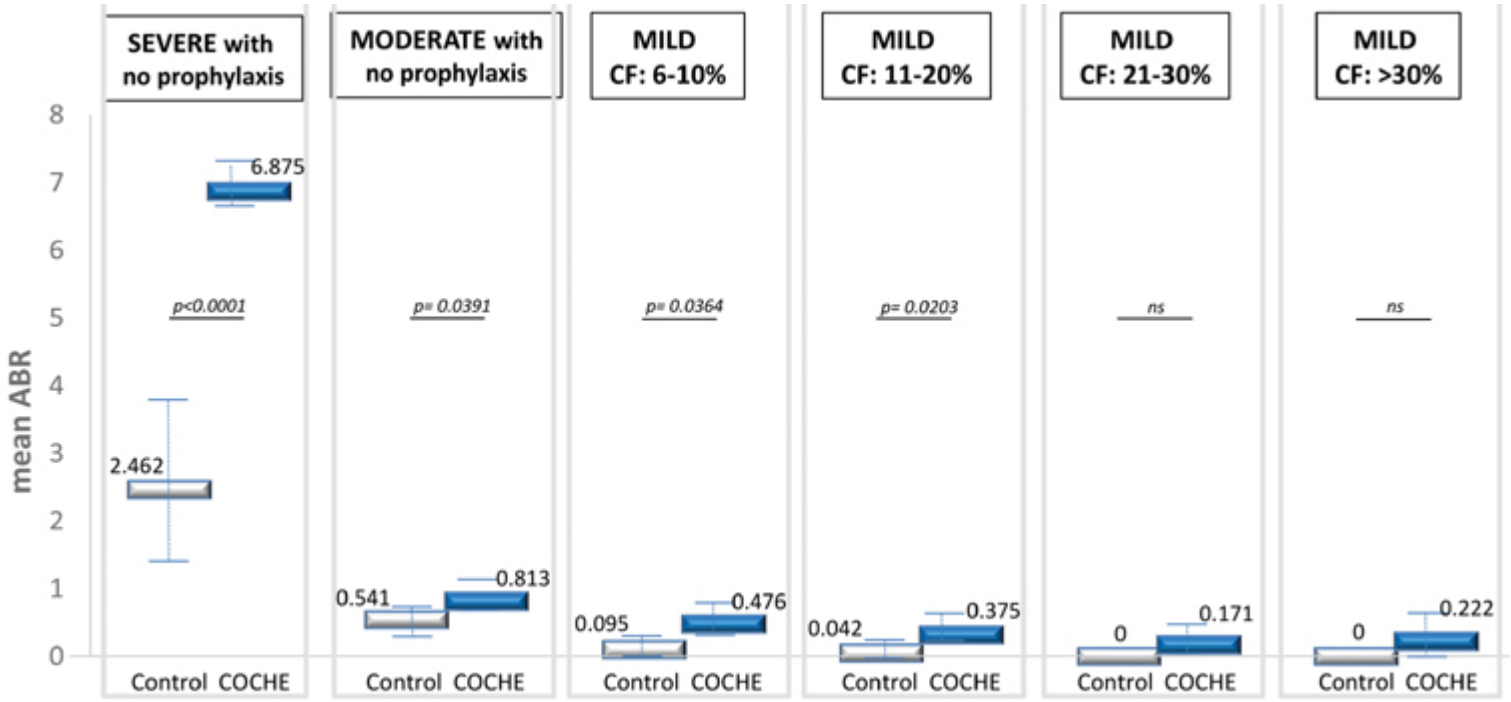

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Supplementary Table S4 Summary of risk factors for major bleeding in antithrombotic-treated patients with hemophilia

Risk factor for major bleedings	Comments
Severity of hemophilia	Mean ABR is directly correlated with basal clotting factor levels up to 20%
Clotting factor treatment	Prophylaxis in severe and moderate hemophilia attenuates mean ABR compared with controls
Type of antithrombotic treatment	Mean ABR is for DPT > DAPT > SAPT (with insignificantly, DAPT ≥ AC ≥ SAP). Antiplatelet drugs can promote GIB
HAS-BLED score ≥ 3	Other patient-related parameters than hemophilia can promote bleeding (e.g., arterial hypertension, age > 65 years old or liver disease)

Abbreviations: ABR, annualized bleeding rate; AC, anticoagulant drug alone; DAPT, dual antiplatelet therapy; DPT, dual pathway therapy; GIB, gastrointestinal bleeding; HAS-BLED, hypertension, abnormal liver or renal function, stroke, bleeding history, labile INR, elderly (> 65 years old) and drugs/alcohol/tobacco use; SAPT, single antiplatelet therapy.

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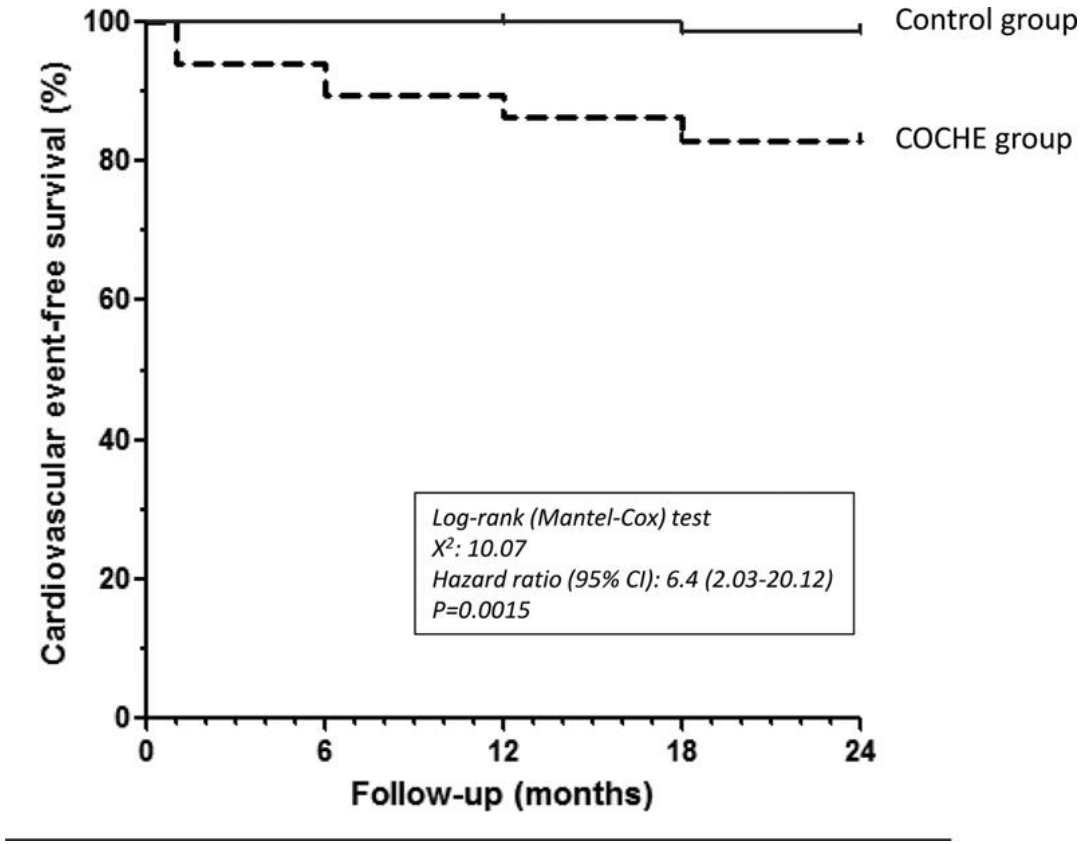

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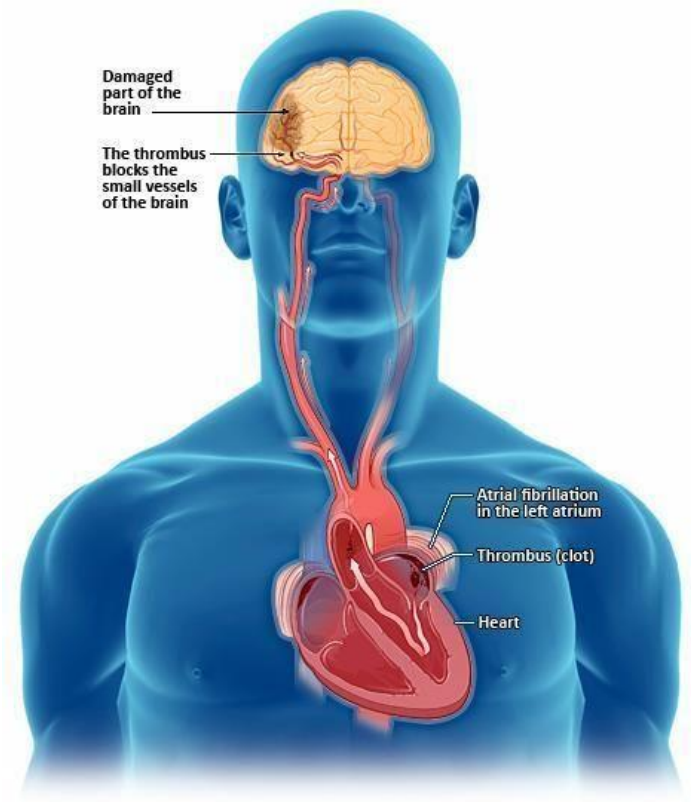
Atrial fibrillation = stroke prevention!



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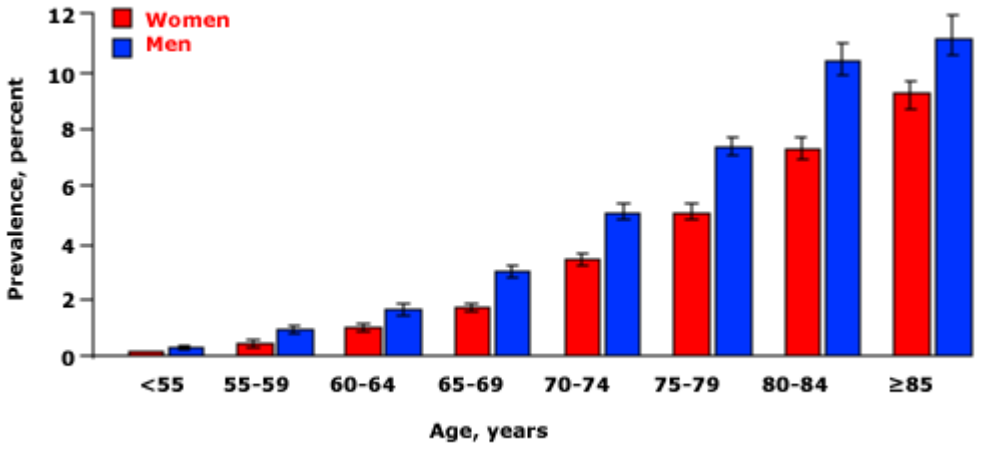
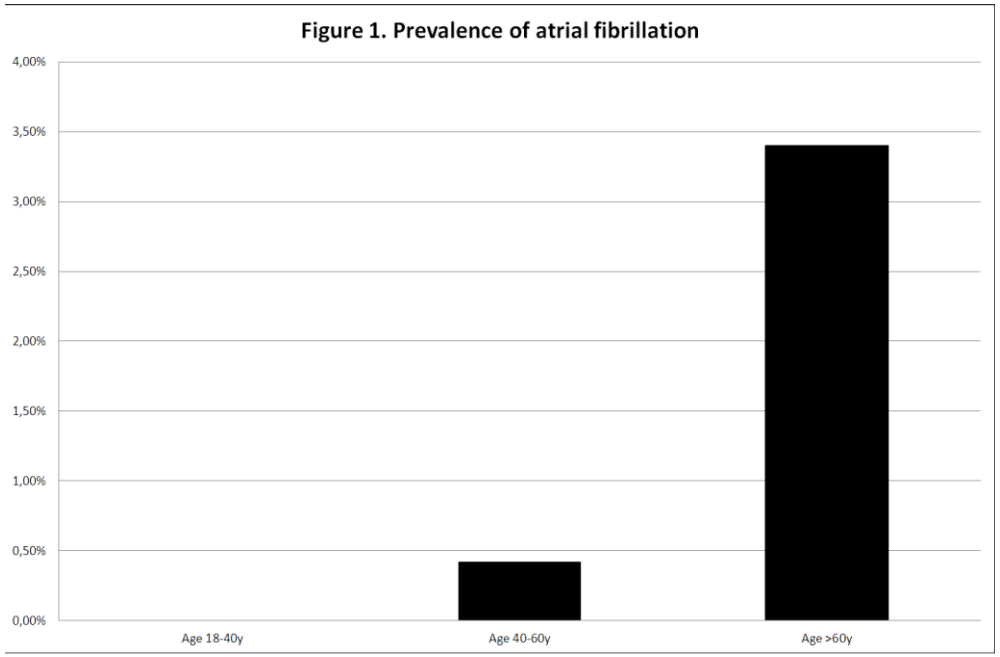
Prevalence

general population 1.0%



Go et al., JAMA 2001;285:2370

haemophilia population 0.84%



Schutgens et al, Haemophilia 2014;20(5):682-6

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Managing atrial fibrillation

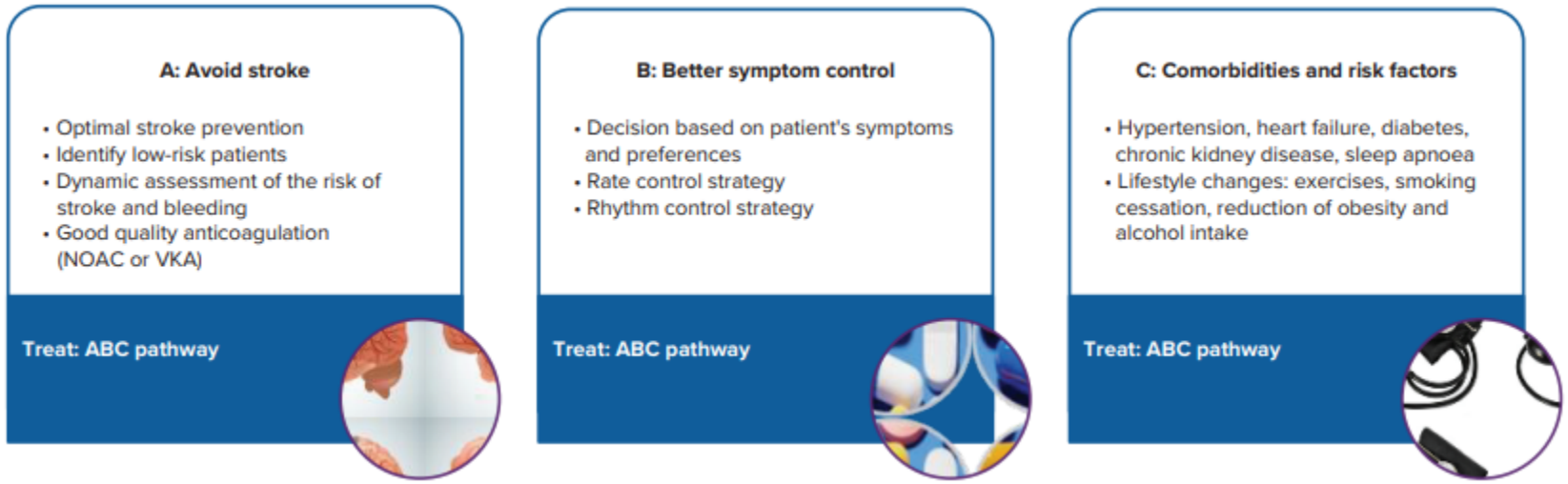
- General population:

Review > Arrhythm Electrophysiol Rev. 2021 Jul;10(2):65-67. doi: 10.15420/aer.2021.07.

The 2020 ESC Guidelines on the Diagnosis and Management of Atrial Fibrillation

Agnieszka Kotalczyk [1 2], Gregory Yh Lip [1 2 3], Hugh Calkins [4]

AF Better Care (ABC) pathway



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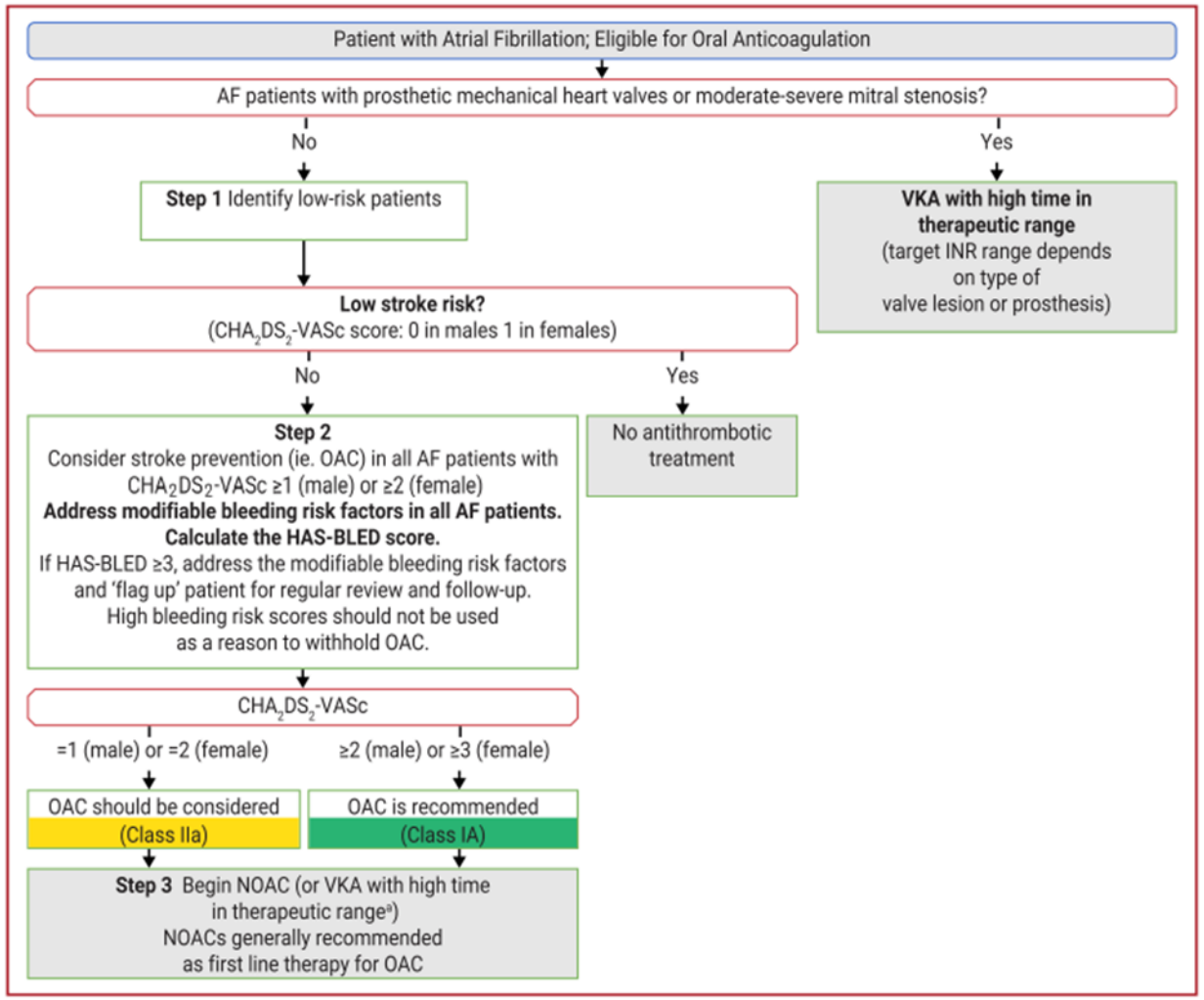
Managing atrial fibrillation

General population: 2020 ESC guideline



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Managing atrial fibrillation

RISK FACTORS	SCORE
Congestive heart failure	1
Hypertension	1
Age ≥ 75	2
Age 65-74	1
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease	1
Sex Female	1

CHA_2DS_2-VASc score	Patients (N=7,329)	Thromboembolism rate (95% confidence interval)	Adjusted stroke rate (%/year)
0	1	0 (0–0)	0.0
1	422	0.46 (0.10–1.34)	1.3
2	1,230	0.78 (0.44–1.29)	2.2
3	1,730	1.16 (0.79–1.64)	3.2
4	1,718	1.43 (1.01–1.95)	4.0
5	1,159	2.42 (1.75–3.26)	6.7
6	679	3.54 (2.49–4.87)	9.8
7	294	3.44 (1.94–5.62)	9.6
8	82	2.41 (0.53–6.88)	6.7
9	14	5.47 (0.91–27.0)	15.2

Managing atrial fibrillation

HAS-BLED Criteria	Score
Hypertension	1
Abnormal renal or liver function (1 point each)	1 or 2
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (> 65 years)	1
Drugs or alcohol (1 point each)	1 or 2

Total Score	Bleeds per 100 patient years
0	1.13
1	1.02
2	1.88
3	3.74
4	8.7
5	12.5

Managing atrial fibrillation in haemophilia

CHA_2DS_2-VASc / HAS-BLED / EHRA atrial fibrillation risk score calculator

Please select CHADSVASC and HASBLED risk factors, EHRA score and click copy to clipboard to copy and paste in your electronic files

Chadsvasc risk factors [click on present risk factors]

RISK FACTORS	SCORE
Congestive heart failure	1
Hypertension	1
Age ≥ 75	2
Age 65-74	1
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease	1
Sex Female	1
Your score	2

view results

CHADSVASC clinical risk estimation. Adapted from Lip et al. See Van den Ham et al. below for actual risks in a larger population.

CHA_2DS_2VASc SCORE	PATIENTS (n=7329)	ADJUSTED STROKE RATE (% year)
0	1	0%
1	422	1,3%
2	1230	2,2%
3	1730	3,2%
4	1718	4,0%
5	1159	6,7%
6	679	9,8%
7	294	9,6%
8	82	6,7%
9	14	15,2%

HASBLED clinical characteristic [click on present risk factors]

CLINICAL CHARACTERISTIC	POINTS AWARDED
Hypertension	1
Abnormal liver function	1
Abnormal renal function	1
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (Age >65)	1
Drugs	1
Alcohol	1
Your score	2

view results

HASBLED clinical risk estimation. Adapted from Pisters et al.

HAS BLED SCORE	NUMBER OF PATIENTS	NUMBER OF BLEEDING	BLEEDS PER 100 PATIENT YEARS
0	798	9	1,13
1	1286	13	1,02
2	744	14	1,88
3	187	7	3,74
4	46	4	8,70
5	8	1	12,50
6	2	0	0
7	---	---	---
8	---	---	---
9	---	---	---
Total	2828	36	4.029999999999999

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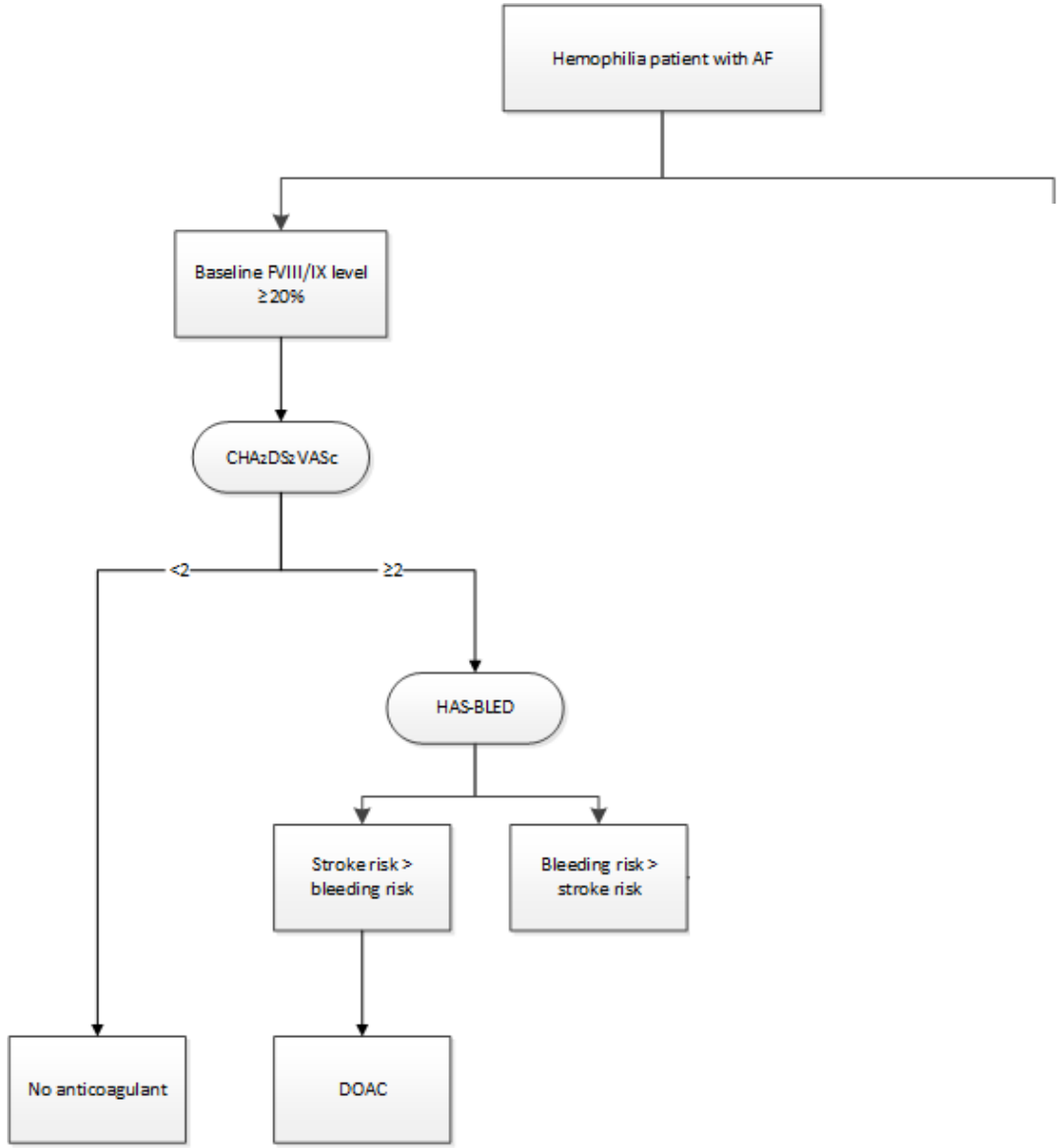

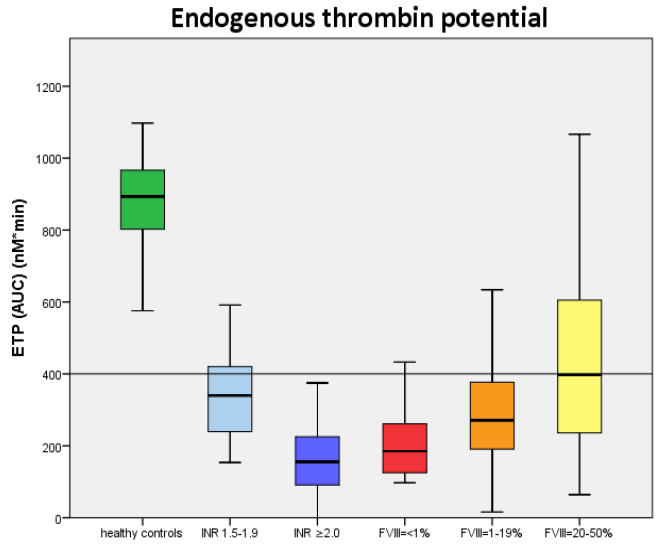

Schutgens et al, adapted from Blood 2016

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Pulmonary vein isolation

Catheter Ablation for Atrial Fibrillation in Patients with Hemophilia or von Willebrand Disease

Paul R. van der Valk[1] Eveline P. Mauser-Bunschoten[1] Jeroen F. van der Heijden[2] Roger E. G. Schutgens[1]

TH Open. 2019 Oct 24;3(4):e335-e339. doi: 10.1055/s-0039-1698756. eCollection 2019 Oct.

Patient	Age	Bleeding disorder	Clotting factor level (IU/mL)	Reason for intervention	CHA_2DS_2 VASC	Duration (y)	Prior therapy	On chronic anticoagulation before PVI
1	70	HA	FVIII 0.35	AF: dyspnea and fatigue	3	5	CV, ECV	VKA
2	72	HA	FVIII < 0.01	pAF: with severe fatigue	1	7	BB	No
3	59	HA	FVIII 0.23	pAF: bradycardia with decreased ejection fraction	0	4	ECV, flecainide	No
4	50	HA	FVIII < 0.01	pAF: frequent tachycardia	0	5	CV, flecainide, BB	No
5	55	HA	FVIII 0.06	pAF: persistent paroxysm under medication	0	5	Flecainide, BB	No
6	67	VWD	vWF RCo 19% FVIII 0.50	AF: dyspnea and fatigue	2	7	VATS Maze; ECV	No

Abbreviations: AF, atrial fibrillation; BB, beta-blocker; CV, chemical cardioversion; ECV, electric cardioversion; HA, hemophilia A; pAF, paroxysmal atrial fibrillation; RCo, ristocetin cofactor (IU/dL); VWD, von Willebrand disease; vWF, von Willebrand factor; VATS Maze: video assisted thoracoscopic surgery.

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Intervention		Patient	Outcome	AC before	AC after procedure	Stopped VKA/DOAC	Periprocedural groin bleeding
1	PVI	1	SR, later pAF	VKA	3 mo VKA (LMWH[b])	No: recurrent pAF	Day 5: Hb drop 3.22 g/dL
2	PVI (redo)	1	SR	Dabigatran[a]	Dabigatran[a]	No	No
3	PVI	2	SR, later pAF	No	1 mo VKA (LMWH[b])	Yes, as planned after 1 mo	Day 3: Hb drop 4.83 g/dL
4	PVI (redo)	2	SR under sotalol	No	1 mo VKA (LMWH[b]), 2 mo ASA	Yes, as planned after 1 mo	Postprocedure oozing during 4 h
5	PVI	3	SR	Dabigatran[a]	6 mo dabigatran[a]	Yes, after 6 mo	No
6	PVI	4	SR	No	6 wk VKA (LMWH[b])	Yes	No
7	PVI	5	SR	No	6 wk dabiagtran[a]	Yes	No
8	PVI	6	SR	No	6 wk dabigatran[a]	Yes	No

Abbreviations: AC, anticoagulation; ASA, 38 mg acetylsalicylic acid; Hb, hemoglobin: 3.22 g/dL = 2.0 mmol/L; 4.83 g/dL = 3.0 mmol/L; pAF, paroxysmal atrial fibrillation; PVI, pulmonary vein isolation; SR, sinus rhythm; VKA, vitamin K antagonist: target INR 2.0–3.0.
[a]110 mg BID 4 weeks before PVI, last dose 24 h before intervention.
[b]Therapeutic LMWH until therapeutic INR.

Left atrial appendix closure

Letter to the Editors-in-Chief

Left atrial appendage occlusion for management of atrial fibrillation in persons with hemophilia

Ming Y. Lim, Mouhamed Yazan Abou-Ismail

Thrombosis Research
Volume 206, October 2021, Pages 9-13

- Male 76y,
- Mild hemophilia A (9%)
- CHADSVASC 7
- HAS-BLED 5

Chadsvasc risk factors [click on present risk factors]

RISK FACTORS	SCORE
Congestive heart failure	1
Hypertension	1
Age ≥ 75	2
Age 65-74	1
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease	1
Sex Female	1
Your score	7

view results

CHADSVASC clinical risk estimation. Adapted from Lip et al. See Van den Ham et al. below for actual risks in a larger population.

CHA_2DS_2VASc SCORE	PATIENTS (n=7329)	ADJUSTED STROKE RATE (% year)
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4	1718	4,0%
5	1159	6,7%
6	679	9,8%
7	294	9,6%
8	82	6,7%
9	14	15,2%

HASBLED clinical characteristic [click on present risk factors]

CLINICAL CHARACTERISTIC	POINTS AWARDED
Hypertension	1
Abnormal liver function	1
Abnormal renal function	1
Stroke	1
Bleeding	1
Labile INRs	1
Elderly (Age >65)	1
Drugs	1
Alcohol	1
Your score	5

HASBLED clinical risk estimation. Adapted from Pisters et al.

HAS BLED SCORE	NUMBER OF PATIENTS	NUMBER OF BLEEDING	BLEEDS PER 100 PATIENT YEARS
0	798	9	1,13
1	1286	13	1,02
2	744	14	1,88
3	187	7	3,74
4	46	4	8,70
5	8	1	12,50
6	2	0	0
7	---	---	---
8	---	---	---
9	---	---	---
Total	3069	48	28.97

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Lim et al, Thromb Res 2021

Left atrial appendix closure

FVIII/IX %	CHADSVASC	procedure	Antithrombotic therapy	Trough during antithrombotic therapy	Longterm anticoagulation
9	7	Factor replacement >100%	Warfarin 6w	>30%	ASA
8	6	Factor replacement >100%	DAPT	>30%	Clopidogrel
NR	3	Factor replacement	DAPT	NR	None
<1	3	Factor replacement >80%	Clopidogrel	>5%	None, epistaxis
<1	3	Factor replacement >80%	Clopidogrel	>5%	NR
<1	3	Factor replacement >60%	Clopidogrel	NR	None, epistaxis
<1	5	Factor replacement	Clopidogrel	NR	None
1-5	4	Factor replacement >50%	DAPT	NR	None
15	3	Factor replacement >80%	Warfarin	>30%	None

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Lim et al, Thromb Res 2021

Conclusions

- Atrial fibrillation is an emerging issue in PWH
- Anticoagulation in PWH: feasible but individual approach

THANK YOU

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Cardiovascular comorbidities – Ischaemic Cardiovascular Disease in PWH

Gerry Dolan, MD

Haemophilia Centre Director,
St Thomas' Hospital, London

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Grant / Research Support	No relevant conflicts of interest to declare
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Employee	No relevant conflicts of interest to declare
Paid Instructor	No relevant conflicts of interest to declare
Speaker bureau	Pfizer, Bayer, Baxter, Novo Nordisk, Biotest, Grifols
Other	

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Key questions

- Is cardiovascular disease a problem in persons with hemophilia (PWH)?
- Are the classical CVD risk factors the same in PWH?
- How should coronary heart disease be managed in PWH?

Cardiovascular Disease (CVD) in PWH

- PWH now have life expectancy approaching normal.

- Past cohort studies suggest PWH have a lower mortality rate from ischemic heart disease

	year	n	SMR	95% CI
Netherlands	1973-1986	717	0.2	0-1.1
Greece	1972-1993	531	0.25	0-1.4
Netherlands	1986-1992	919	0.2	0-1.1
Netherlands	1992-2001	2950	0.5	0.2-1.1
UK [HIV excluded]	1977-2000	6018	0.62	0.51-0.76

- Carriers of hemophilia have 36% reduction in fatal ischemic heart disease

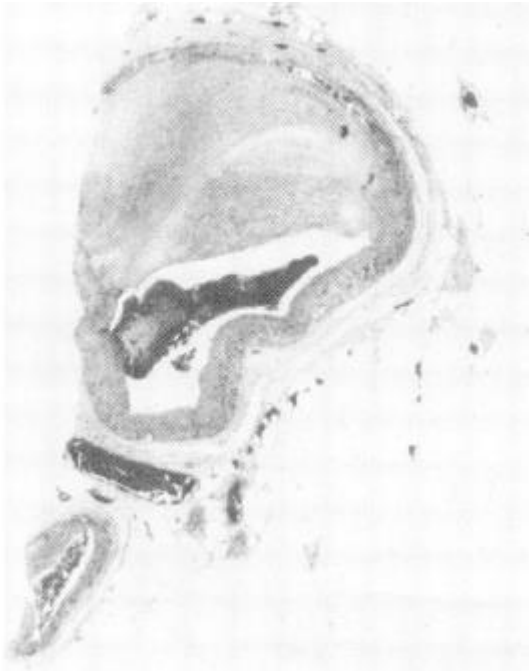
Sramek et al. Lancet 2003

Fatal MI in Severe Hemophilia A

Br Heart J 1983; **49**: 604–7

Coronary artery disease in severe haemophilia

M SMALL, A S JACK, G D O LOWE, A F MUTCH, C D FORBES, C R M PRENTICE
From University Department of Medicine and the Department of Pathology, Royal Infirmary, Glasgow



- 57 yrs, severe hemophilia A, suffered fatal MI following factor replacement for a hematemesis

- 53 yrs, severe hemophilia A, found to have asymptomatic severe coronary artery atheroma at autopsy

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Review of 42 Cases of CVD in Hemophilia A

- 36 acute MI + 6 CVA
- Age 7 – 79 yrs (mean 44 yrs)
- 16 of 42 less than 40 yrs of age
- 7/36 MI were fatal
- 22/36 MI followed treatment with factor replacement or (a)PCC or rFVIIa

A Girolami et al., Acta Haematologica 2006

Atherosclerosis in PWH

- Intima media thickness (IMT) no different in 59 PWH vs. 142 controls
  Sramek, *Circulation* 2001

- Reduced IMT in 50 PWH (severe and moderate) vs. 50 age-matched controls
  Bilora, *Clin Appl Thromb Hemost* 2006

- Carotid IMT no different in 40 PWH vs. 40 controls
  Sartori, *Hemophilia* 2008

Atherosclerosis and Haemophilia

Autopsy study

- 14 Haemophilia 10 severe, 2 mod, 2 mild.
- 42 age-matched controls.

	Haemophilia	**Controls**
Coronary Stenosis	78.6%	59.5%
Stenosis Score	1.1± 0.9	1.2± 1.2

Foley et al., *J Thromb Haemost*, 2010;8:208-11

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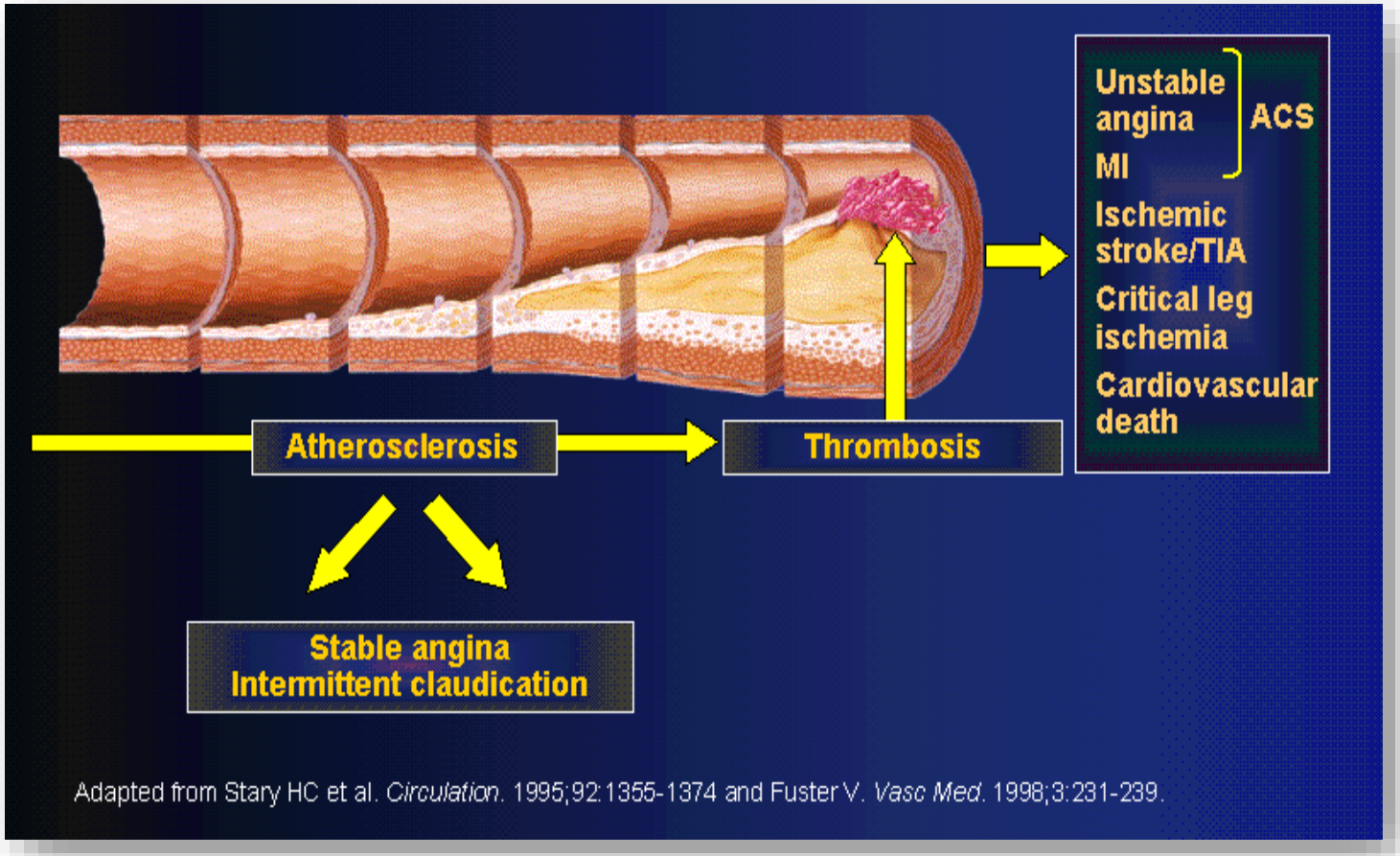
Vascular Disease: A Generalized and Progressive Process



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Summary of evidence

- Cardiovascular risk factors similar or increased in PWH
- Atherosclerosis similar or slightly reduced in PWH
- Clinical IHD and fatal MI possibly reduced in PWH

- Hypothesis:
  Reduced FVIII may not prevent atherosclerosis but may reduce the risk of occlusive thrombosis at the site of a ruptured plaque

Current ESC Guidelines on Management of ACS

European Heart Journal (2008) **29**, 2909–2945
doi:10.1093/eurheartj/ehn416

ESC GUIDELINES

Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation

European Heart Journal (2010) **31**, 2501–2555
doi:10.1093/eurheartj/ehq277

ESC/EACTS GUIDELINES

Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

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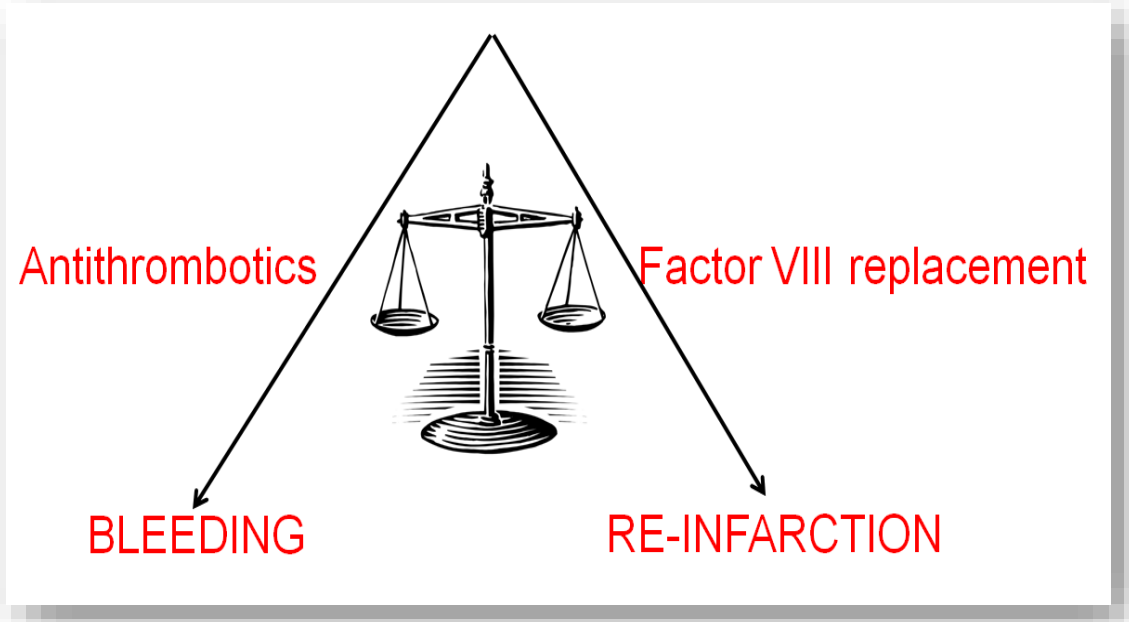
Current ESC Guidelines on Management of ACS

- Acute Coronoary Syndrome (ACS)
  - ‘Time is muscle‘ – earlier intervention saves lives
  - Dual anti-platelet therapy for 12 months

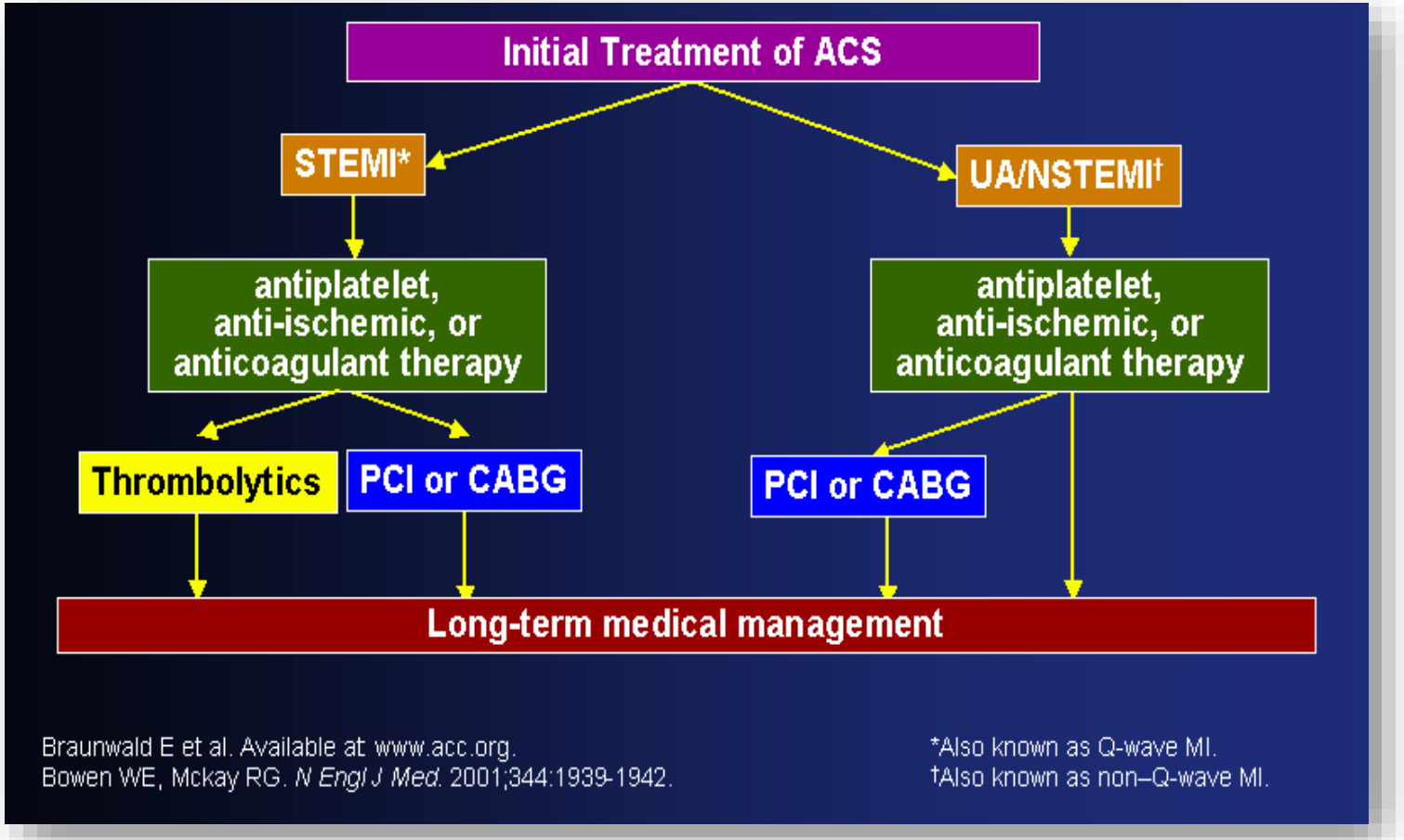
- STEMI
  - Mechanical revascularisation (PCI) > fibrinolysis [especially within 120 mins]

- NonSTE ACS
  - Nitrates, beta-blocker, anticoagulation

ACS in PWH: balancing the risks



Treatment of Acute Coronary Syndrome



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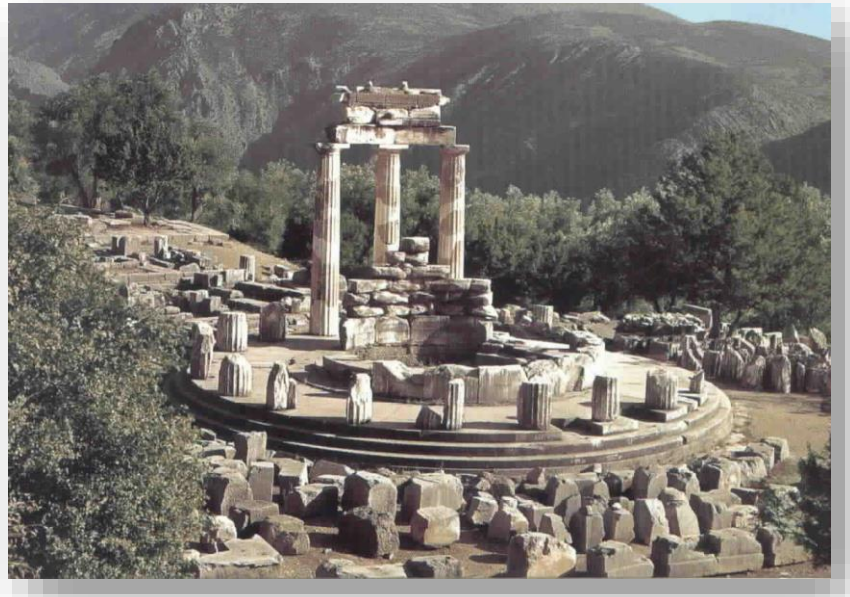
The Delphi Method

- The Delphi Method is a group decision process.
- The Delphi Method uses a panel of experts.
- Expert responses to a series of questionnaires are anonymous.
- Each round of questionnaires results in a median answer.
- The process guides the group towards a consensus.



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Haemophilia
The Official Journal of the World Federation of Hemophilia,
European Association for Haemophilia and Allied Disorders and
the Hemostasis & Thrombosis Research Society

Haemophilia (2013), 19, 833–840

DOI: 10.1111/hae.12189

ORIGINAL ARTICLE *Clinical haemophilia*

Applicability of the European Society of Cardiology guidelines on management of acute coronary syndromes to people with haemophilia – an assessment by the ADVANCE Working Group

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Areas where Agreement Reached Easily

- PWH should wear or carry an alert allowing medical staff to easily identify them as having a bleeding disorder

- A hemophilia expert should be consulted as soon as a PWH presents with an ACS

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Areas where Agreement Reached Easily

- PWH should wear or carry an alert allowing medical staff to easily identify them as having a bleeding disorder
- A hemophilia expert should be consulted as soon as a PWH presents with an ACS
- PWH, even after factor VIII replacement, should be categorised as an ACS patient with high bleeding risk
- In ACS (STEMI or NSTE-ACS) dual anti-platelet therapy should be administered without delay

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STEMI in PWH – PCI vs. Fibrinolysis

- Experts agree that PCI is preferred in PWH, although fibrinolysis should be considered if patient not suitable for PCI or it is not available.

Conclusions

- PWH do suffer from atherosclerosis, and are at risk of ACS (especially following factor or by-passing agent therapy)

- In the event of an ACS in a PWH:
  - A hemophilia expert should be consulted at the earliest opportunity
  - In general, Factor replacement should be given early in order to
  - allow standard ACS treatment strategies to be followed
  - Fibrinolysis or PCI should be delayed until factor replacement therapy has been administered

- Dual anti-platelet therapy should be administered for as short a duration as possible, and should be accompanied by gastro-protection and in most cases prophylaxis factor replacement therapy

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Important Considerations

Much of haemophilia care has been focussed on

- Preventing or treating bleeding
- Manging musculoskeletal disease
- Managing transfusion-transmitted infection

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CVD Risk Factors in PWH

TABLE II. Patient Characteristics Independently Associated With Ischemic and Other Heart Disease Among 3,422 Persons With Hemophilia

Factor[a]	Odds ratio (95% CI)	*P* value
Ischemic heart disease		
Age (per 10-year increase)	2.1 (1.7–2.5)	<0.001
Hypertension	5.4 (2.6–11.0)	<0.001
Diabetes	3.2 (1.3–8.1)	0.01
Hyperlipidemia	3.8 (0.9–15.5)	0.06
Other heart disease		
Age (per 10-year increase)	1.7 (1.5–1.9)	<0.001
Hypertension	3.0 (1.7–5.3)	0.001
HIV infection	2.1 (1.3–3.5)	0.005
Hemophilia B (vs. A)	1.6 (1.0–2.6)	0.05
Diabetes	2.0 (0.9–4.2)	0.08

[a]Factors included in both logistic regression models are age, race (white vs. other), hemophilia type, severity (severe vs. mild/moderate), inhibitor, diabetes, hypertension, hyperlipidemia, and HIV and HCV infection.

Kulkarni et al. Am J *Hematol* 2005;79:36

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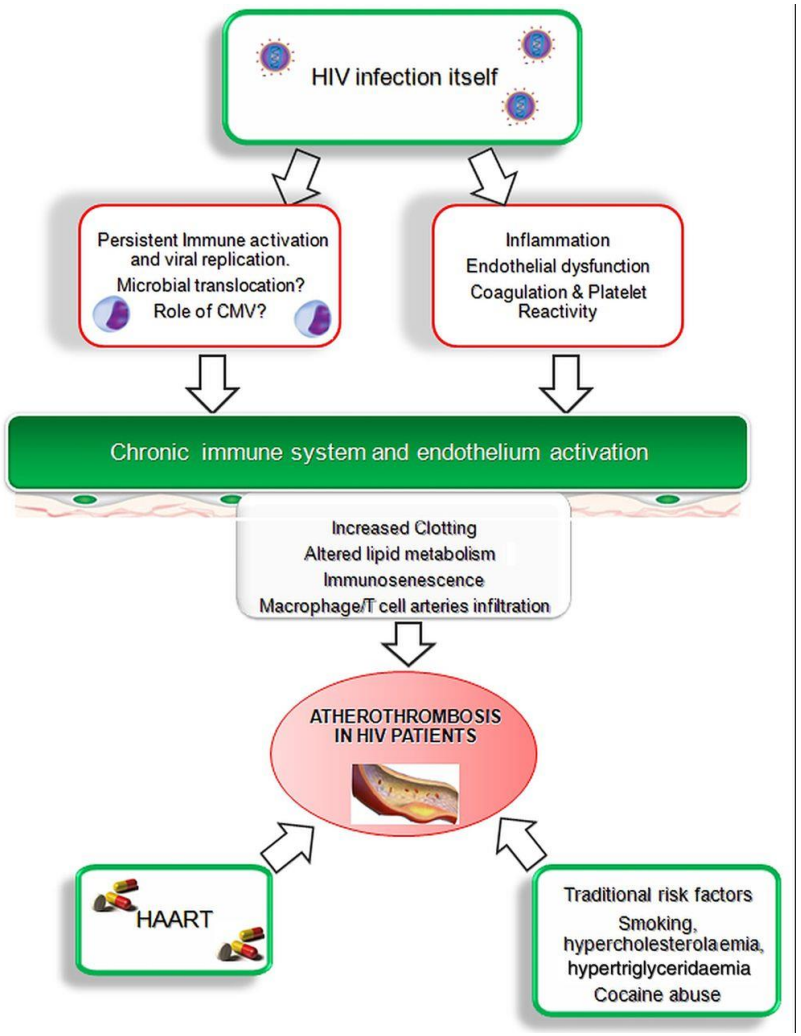
Pathogenesis of Atherothrombosis in HIV Infection



Enrico Cerrato et al. Open Heart 2015;2:e000174

openheart

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- Ignorance or wariness of haemophilia → in many countries

- HTC focus of ALL medical issues
- Many patients do not access primary care and preventative medical programmes

Important Considerations

- Who manages?

    a) Weight management
    b) Exercise strategies
    c) Stopping smoking
    d) Blood pressure management
    e) Diabetes screening
    f) Lipid screening and management

Role of HTC

- Ensure a holistic healthcare programme for PWH

  a) Adapt local comprehensive care to manage these issues.
  b) Work with primary and secondary care systems to ensure delivery of care and communication eg patient passport.

Summary

- The focus on medical morbidity in haemophilia is a success story!
- Improvement in haemophilia therapy → marked reduction in death from haemorrhage.
- Recombinant/Viral inactivation methods → eliminated HIV/HCV.
- Improved antiviral therapy → greatly reduced deaths from TTI.

- Important we are proactive in supporting our patients though later life.

- Adapt Comprehensive Care to address issues such as Ischaemic Heart Disease.

THANK YOU

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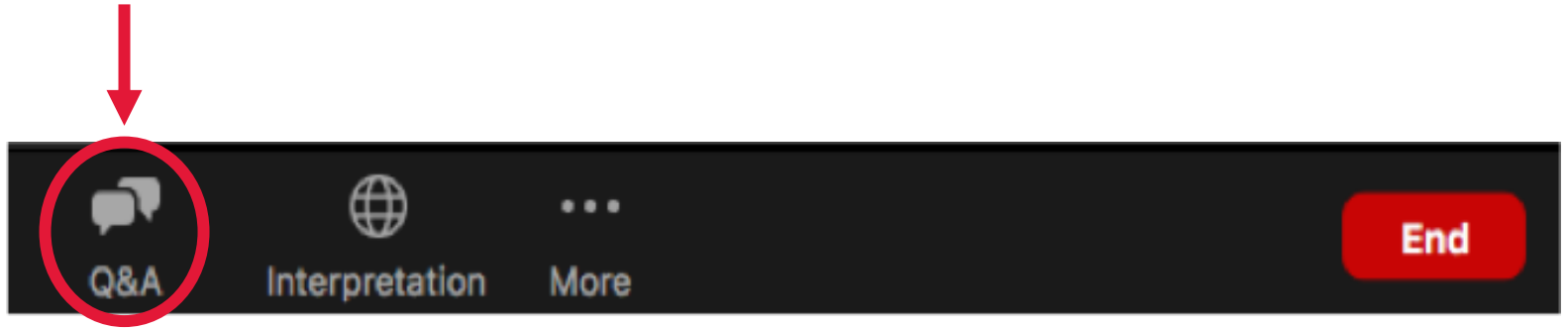
QUESTION & ANSWER

Please submit your questions in the Q&A box



This webinar was part of a series. The last session of this year will be taking place on :

- **Thursday, December 16, 2021 from 8AM to 10AM ET**

Registration will be open soon.

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COMPASSION to ACTION
Together we can

THANK YOU!

¡GRACIAS!

MERCI!

شكرا

СПАСИБО

STAY SAFE!

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