NORDIC BIOSCIENCE

NITs of the ECM and weight loss

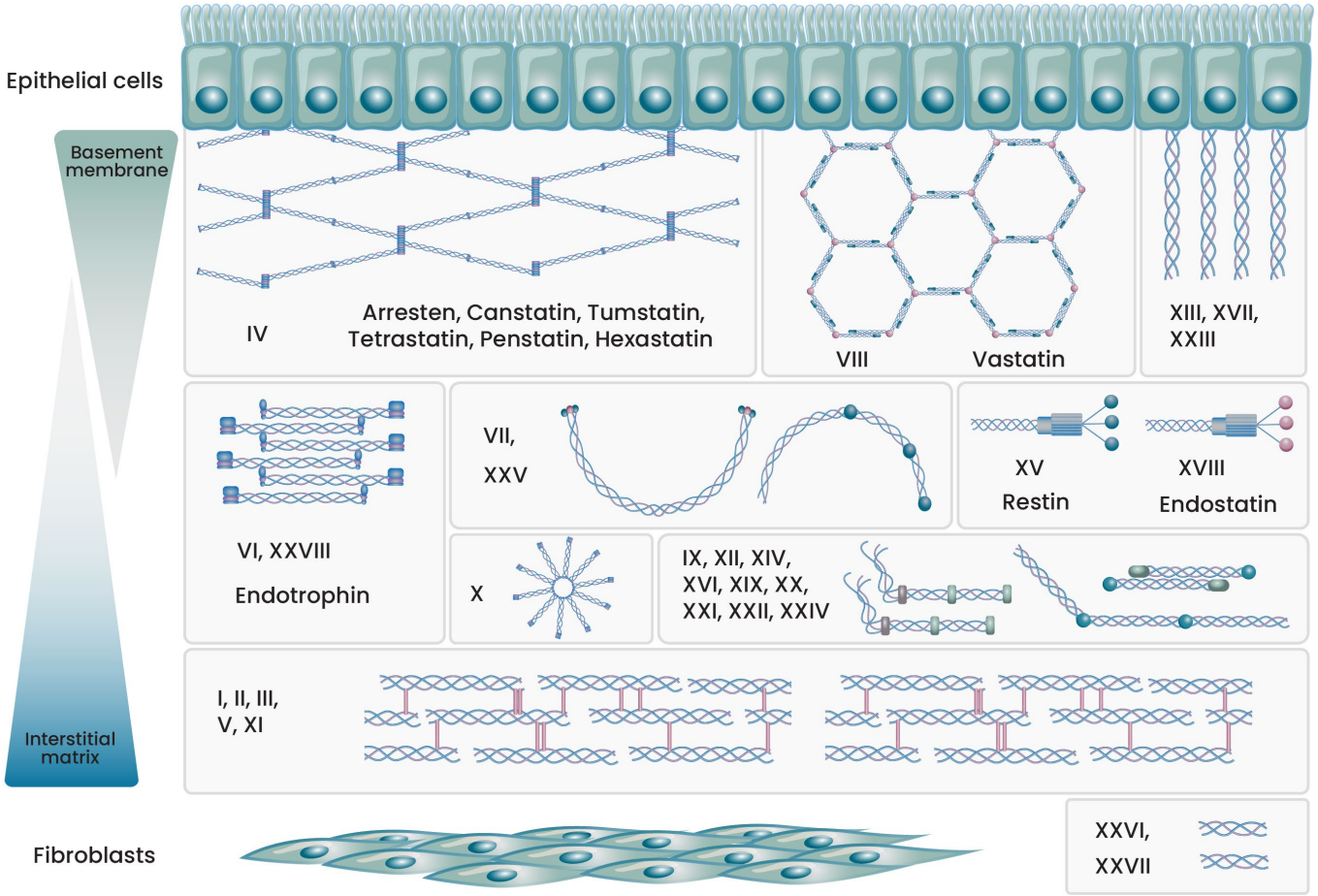
Morten A. Karsdal, MsC, PhD, mMBA

Head of R&D, CEO, Nordic Bioscience

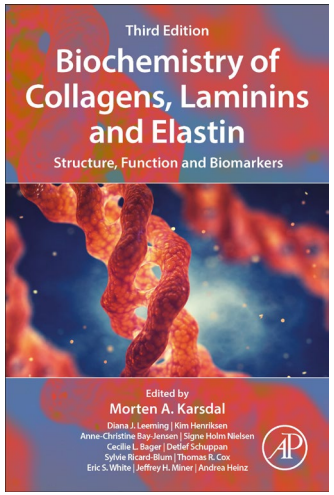
1. Is the ECM important and the prevalance of ECM diseases
2. Unicorn Biomarkers – thoughts on RLSE and biomarker development
3. Biomarkers and weight loss

Collagen is not just collagen & the regenerative ECM is NOT the fibrogenesis ECM – Biomarkers and weight loss

The 28 (46) collagens, laminins and elastins



+30 years of ECM experience



3rd edition

the extracellular matrix pharmacology congress

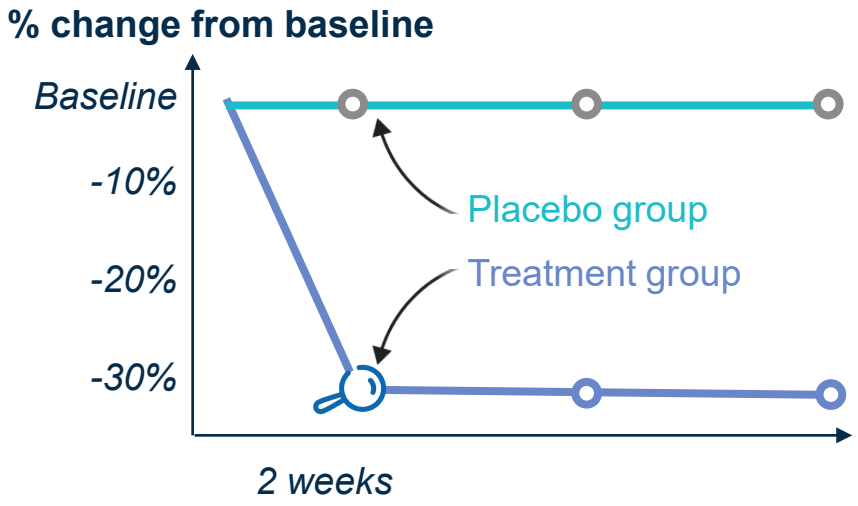
Why work with Biomarkers?

Insights from biomarkers unlock an earlier value inflection point

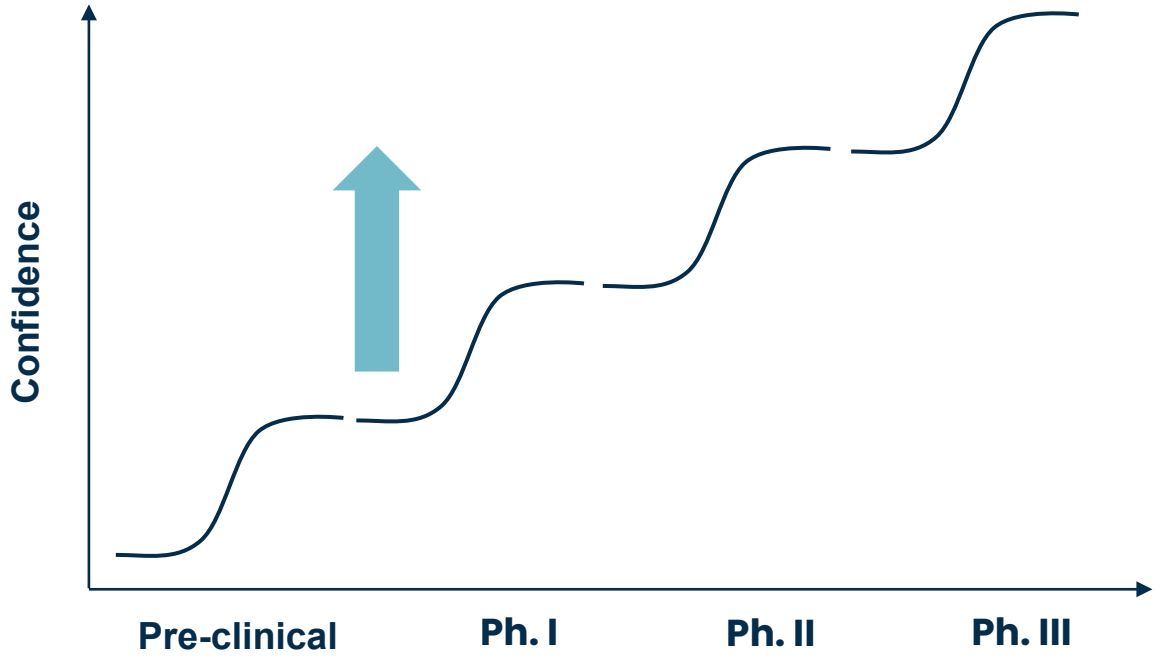
HbA1c | HdL/BMD/LPa | ELF

CTX-I | PRO-C3 | Imaging

Biomarkers reflecting disease activity



Value shift to Phase Ib (vs Phase II)



Clearer go / no-go decision

Efficacy shift (measurable in 1b)

3x higher success rate for clinical trials[1]

Directing resources to the right development

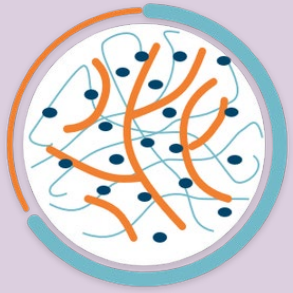
NORDIC BIOSCIENCE

Prevalence and mortality of extracellular matrix-related chronic diseases

Rosa C Christiansen, Ms, Cecilie L Bager, PhD, Andrea Heinz, PhD, Anne C Bay-Jensen, PhD, Diana J Leeming, PhD, Prof Dinesh Khanna, MD, Federica Genovese, PhD, Florian Rieder, MD, Georg Schett, MD, Joachim H Mortensen, PhD, Kim Henriksen, PhD, Nicholas Willumsen, PhD, Prof Philip G Conaghan, MBBS, Prof Raghu Kalluri, PhD, Scott L Friedman, MD, Signe Holm Nielsen, PhD, Signe Larsen, Ms, Prof Stephane Heymans, MD, Prof Toby M Maher, MD, Prof Søren Brunak, PhD, Prof Morten A Karsdal, PhD

Disease definitions

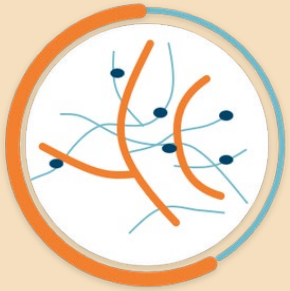
Fibrotic diseases



Excessive
ECM formation

Chronic disorders characterised by excessive ECM formation relative to degradation.

Tissue destruction diseases



Excessive
ECM degradation

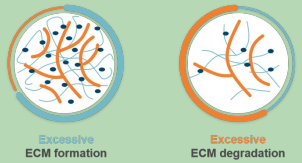
Chronic disorders characterised by excessive ECM degradation relative to formation.

Non ECM diseases

Balanced
turnover

Disorders not characterised by chronic persistent dysregulation of ECM homeostasis.

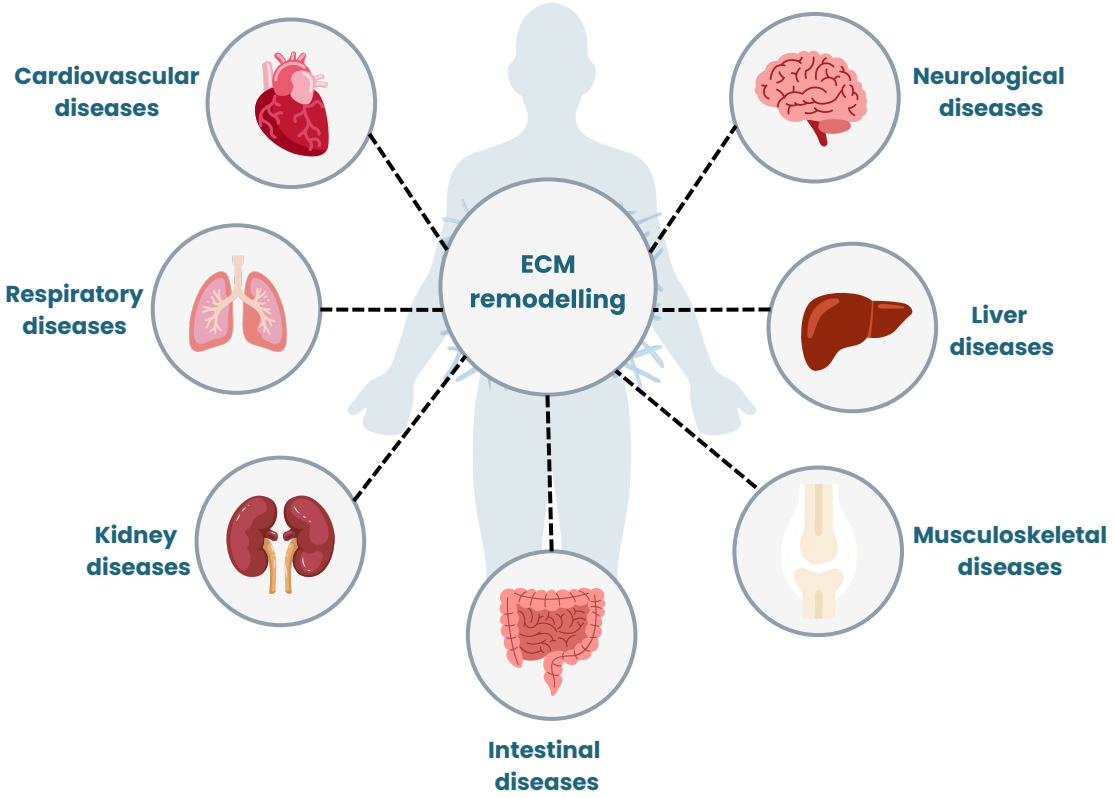
ECM-related diseases



Chronic disorders characterised by chronic ECM dysregulation and include both fibrotic diseases and tissue destruction diseases.

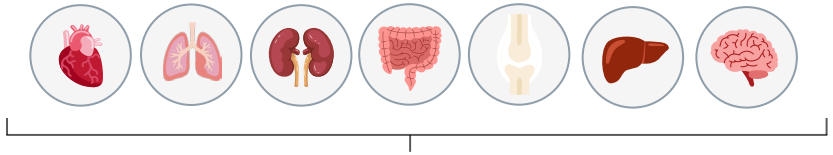
ECM as the common denominator

Extracellular matrix (ECM) remodelling is a shared biological mechanism that contributes to diseases across **multiple organ systems**



SHARED MECHANISM, TYPICALLY STUDIED IN ISOLATION

Seperate disease specific research and estimates



No unified estimate to capture the total disease burden

? **TOTAL DISEASE BURDEN REMAINS UNKNOWN**

Despite a shared biological mechanism, diseases related to chronic ECM dysregulation are typically studied in isolation, likely underestimating their true population burden

Study design

Study population and data sources

8.504.378
unique individuals

5.945.094
Danish residents alive end of 2024

UK Biobank validation cohort
2006-2019

199 4 — 202 4

Primary data sources

Danish National Registries

Central Person Registry
All residents
↓
Study population

National Patient Registry
All hospital visits
↓
Prevalence analysis

Cause of Death Registry
All deaths
↓
Mortality analysis

External validation

UK Biobank
Cohort with ~ 500.000 UK residents
↓
Valiidation of main results

ECM disease classification

ICD-10 level 2 diagnoses
n = 1701

Predefined **definitions** of chronic ECM remodelling categories;
Fibrotic disease, Tissue destruction disease, Non ECM disease, Unknown

Disease expert 1
Independent review

Double blinded disease classification

Disease expert 2
Independent review

Third-expert adjudication in case of disagreement

ECM disease classification

- **Fibrotic disease**
- **Tissue destruction disease**
- **Non ECM disease**
- **Unknown**

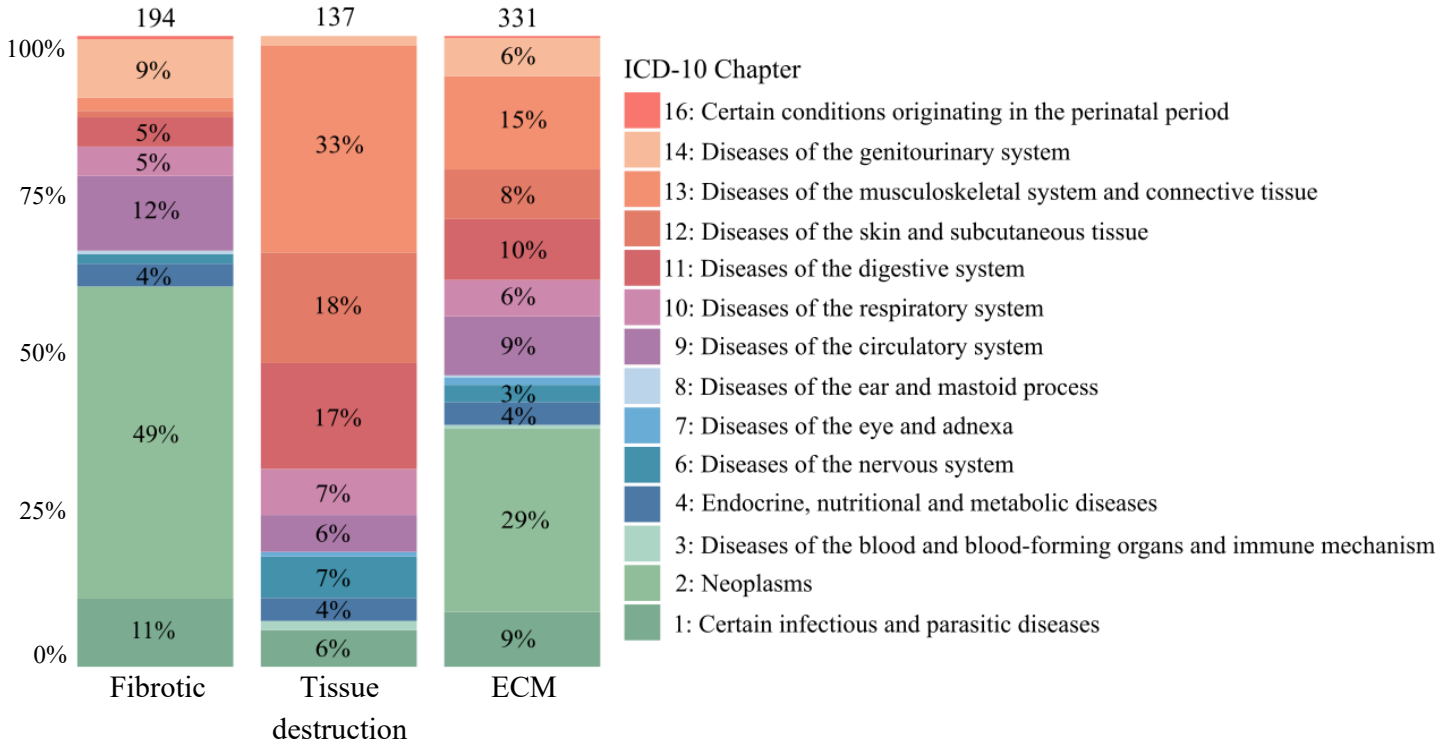
ECM-related diseases

331 ECM-related diseases span multiple organ systems

Main results

Fibrotic disease	**194**
Tissue destruction disease	**137**
Non ECM disease	1341
Unknown	29

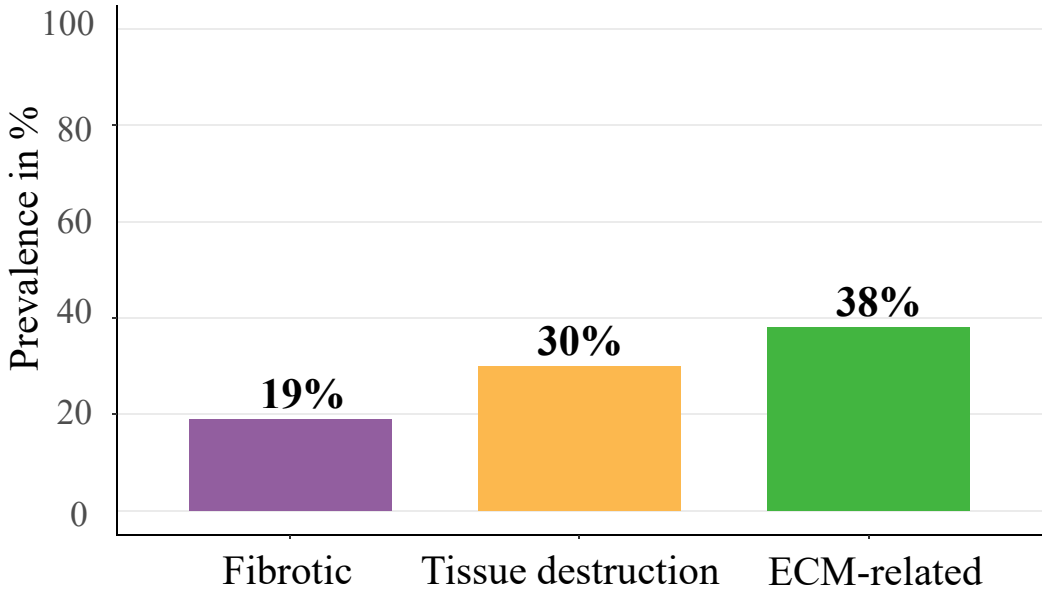
331 ECM-related diseases



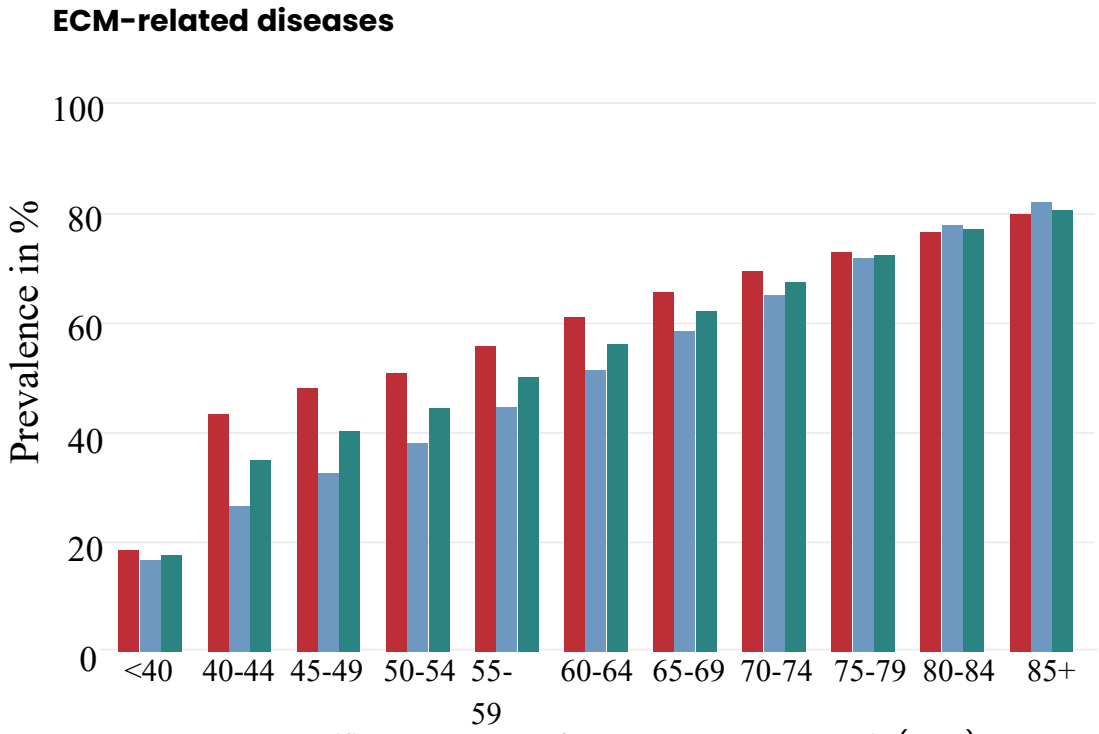
Proportion of diseases across disease categories by ICD 10 chapter- ECM diseases comprise fibrotic diseases and tissue destruction diseases within one unified group of diseases*.

ECM-related diseases affect **38%** of the population, with prevalence increasing steadily with age

Main results



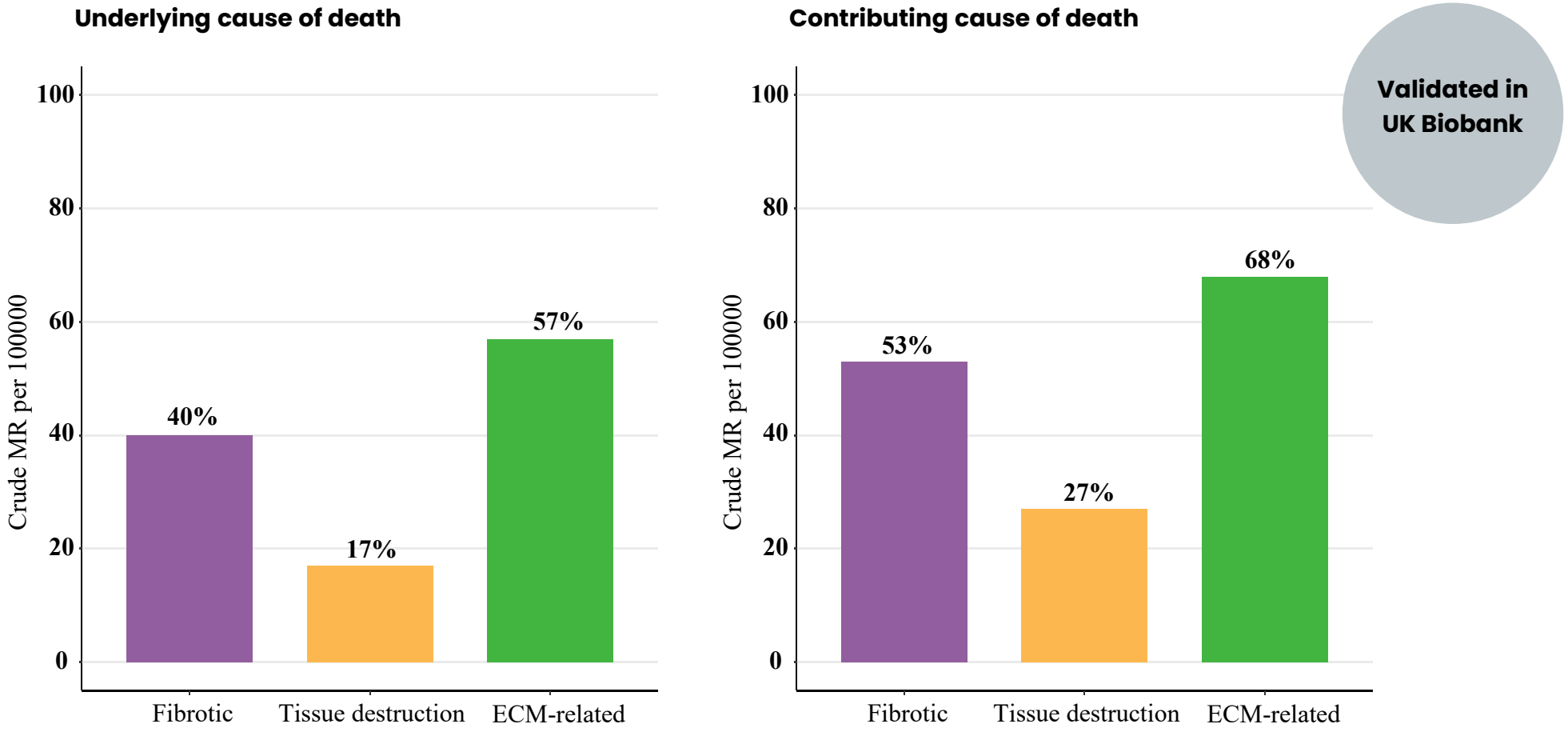
Total prevalence of extracellular matrix (ECM)-related diseases in 2023, Denmark.



Age- and sex-specific prevalence of and extracellular matrix (ECM)-related diseases in 2023, Denmark.

More than half of all underlying causes of death are ECM-related (57%)

Main results



Mortality percentage for fibrotic, tissue destruction, and extracellular matrix (ECM)-related diseases by cause of death in Denmark in 2024. Fibrotic diseases are shown in purple, tissue destruction diseases in blue, and ECM-related diseases in green.

Review

JOURNAL
OF HEPATOLOGY

A framework and shared vocabulary to identify actionable protein biomarkers and enable optimal precision medicine: Myth-busting with unicorn biomarkers

Morten A. Karsdal[1,*], Anne-Christine Bay-Jensen[1], Daniel Guldager Kring Rasmussen[2], Aleksander Krag[3,4], Stine Johansen[3,4], Quentin M. Anstee[5,6], Diana J. Leeming[1], Federica Genovese[1], Arun J. Sanyal[7], Cecilie L. Bager[1], Robert J. Benschop[19], Salvador Augustin[20], Darren Ruane[21], Neeraj Adya[21], Jörn M. Schattenberg[22], Ali Mobasheri[23,24,25,26], Veronica Miller[8], Maja Thiele[3,4], Roberto A. Calle[9,10], Patrick Bossuyt[11], Adam Platt[12], Signe H. Larsen[1], Kim Henriksen[1], Vincent Bonneau[15], Bruno Golding[15], Mohamed Hassanein[16], Sumanta Mukherjee[17], Sarah Harris[18], Zoltan Derdak[13], Suneil Hosmane[14], Paresh Thakker[13], Virginia B. Kraus[27]

Summary

Not all biomarkers are equal, and some arguably should not be classified as biomarkers at all. Despite an explosion in putative biomarker discoveries from high-throughput proteomic technologies, very few advance beyond initial excitement to become validated, clinically actionable tools. Most stall in a biomarker 'valley of death', where promising signals fail to meet robust technical, scientific, and regulatory standards for clinical use. We propose a framework to distinguish between unvalidated protein findings and validated biomarkers with specific utility. We highlight the need to separate exploratory protein measurements from biomarkers that meet predefined analytical criteria and progress through validation, including qualification as a reasonably likely surrogate endpoint (RLSE) or a validated surrogate endpoint (VSE). This review article delineates differences

Lilly, Roche, Takeda, Lilly, Janssen, Madrigal, Pfizer, Novo, Astra, GSK & BMS

A Unicorn Biomarker

Prognostic

Predicts disease progression and outcomes

Genetically validated

Linked to disease through genetic evidence

Regulatory supported

Endorsed by regulatory agencies for clinical use

Diagnostic

Accurately identifies disease presence/subtype

Scientifically understood

Reflect biological processes supported by strong scientific data

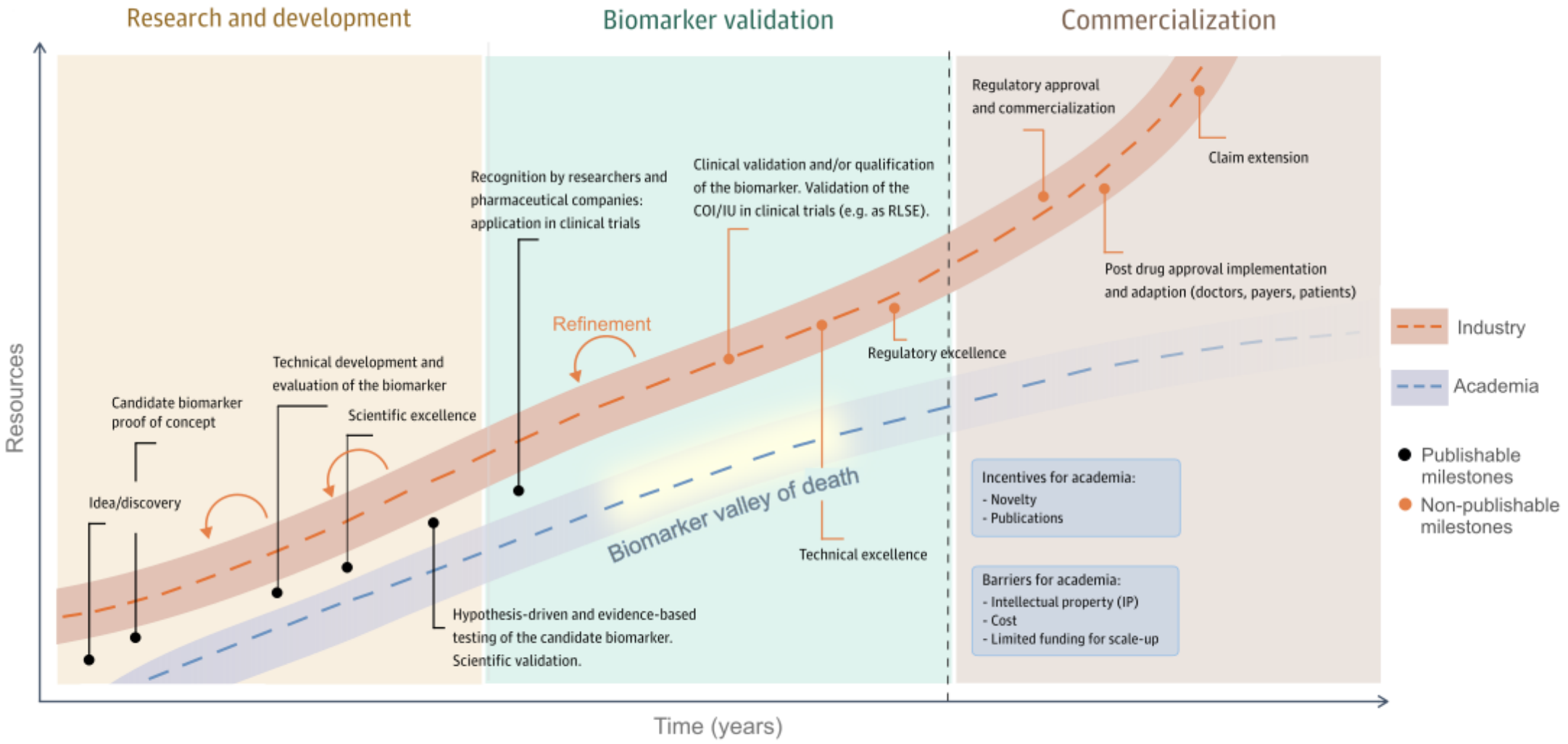
Pharmacodynamic-RLSE

Measures treatment response in real time

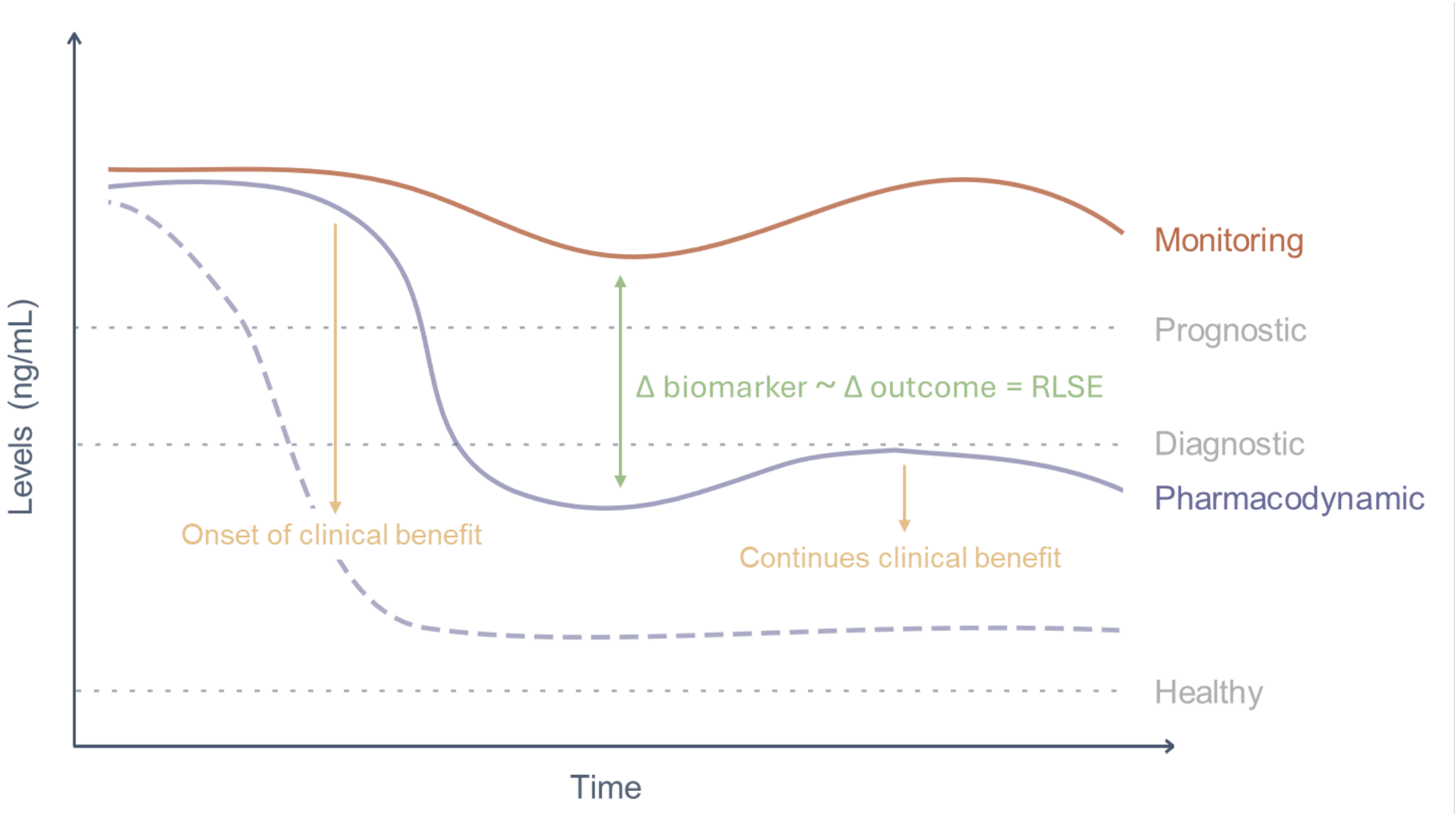
Technically validated

Precise, accurate, reproducible, and robust

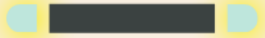
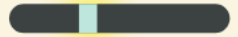
The “Biomarker Valley of Death”



Biomarker Nomenclature & Dynamics



One protein – 1000 possibilities

	TOTAL PROTEIN	PRO-PEPTIDES	DEGRADATION PEPTIDES	CRYPTIC SIGNALLING	POLYMERIZATION	POST-TRANSLATIONAL MODIFICATIONS
						
ESTIMATED NUMBER OF VARIANTS	1	2-10	>1000	1-2	1-5	1-50
FUNCTIONAL IMPACT	No	Yes	Yes	Yes	Yes	Yes
EXAMPLE		All fibrillar collagens such as type I collagen	Degradation of all proteins, such as CTX-I, CTX-II, CTX-III, C3M and C6M	Signaling fragments of collagen such as Vastatin and Decastatin	All collagens and CRP	Glycosylations such as Hba1c and many other PTMs

Patients, Payers, Diagnostics & Drug Developers

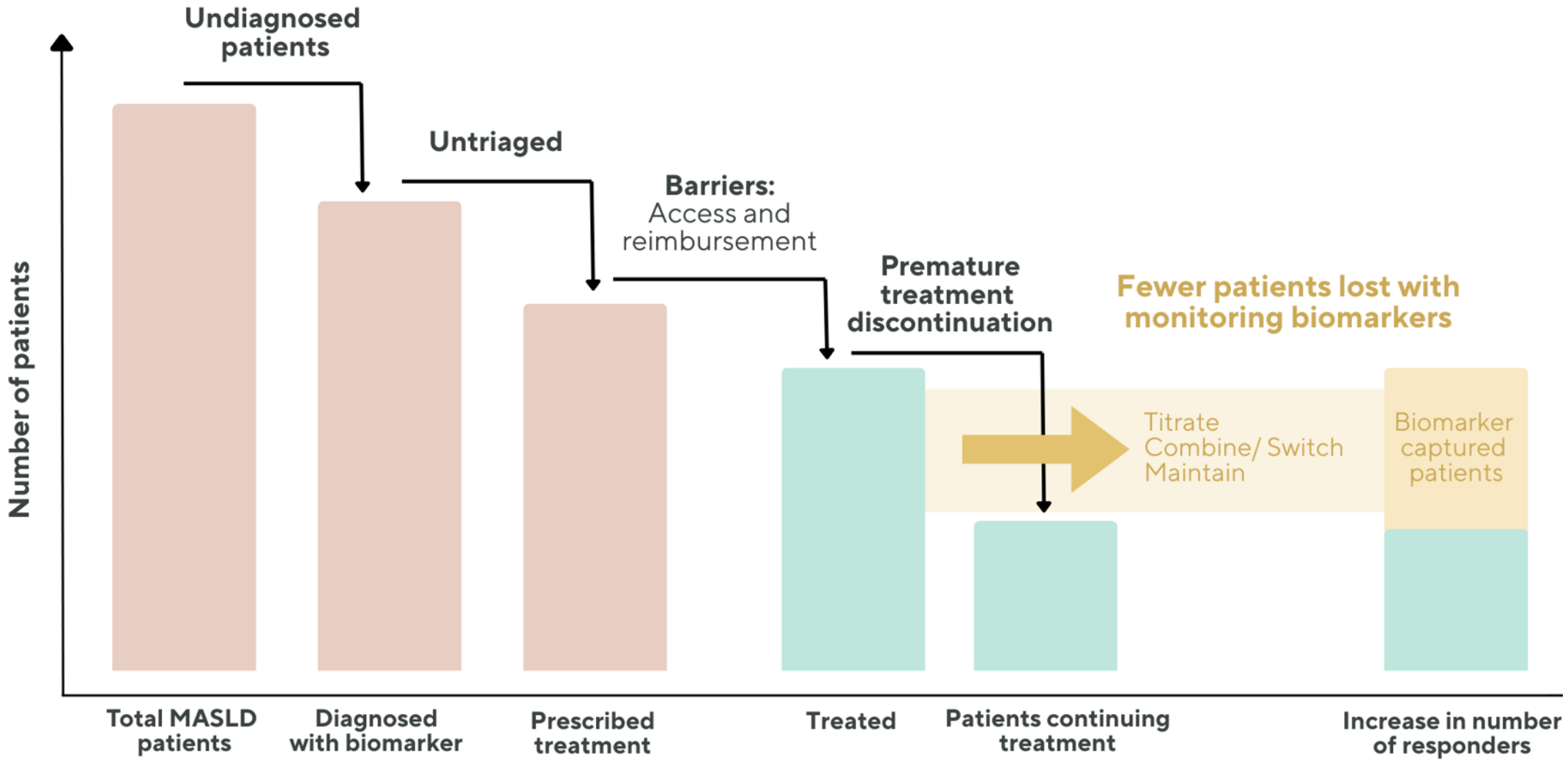


Table 2. Modifie
Endpoint(s) at a T
novel biomarker
biomarker develo

U.S. FOOD & DRUG ADMINISTRATION

Considerations for Discussion of a New Surrogate Endpoint(s) at a Type C PDUFA Meeting Request

/ Surrogate
positioning a
ints that most

Relationship of the SE with the Clinical Outcome	Unicorn Biomarkers as RLSEs
Rationale for Using the SE as a Primary Endpoint	
What is the clinical outcome the SE proposed to predict?	Due to their biological link to the disease process based on hypothesis-driven approaches and extensive validation in multiple publications, their association with clinical outcomes should be well-substantiated. The biomarker needs to be directly linked to the proven critical path of the disease in question.
What is the rationale for using an SE rather than the clinical outcome measure (e.g., feasibility, study duration, sample size, etc.)?	Due to a close connection with the underlying disease biology, changes in Unicorn Biomarker levels typically occur earlier than changes in organ function; changes observed through imaging or clinical endpoints (as illustrated in **Figure 6**). This allows for the detection of pharmacodynamic effects sooner and in fewer patients, enabling faster and more efficient trials. Introducing new and clinically relevant RLSEs can alleviate the operational, patient, and cost burdens of Phase 3 trials. For instance, in the case of MASLD, liver biopsies are currently utilized as RLSEs. However, from a clinical standpoint, liver biopsies are seldom used for diagnosis, indicating that relevant non-invasive tests utilized in the clinical setting could serve as effective replacements for these RLSEs, thus facilitating faster access to novel treatments for patients.
What evidence exists to support the relationship between the SE and the clinical outcome of interest (e.g., epidemiologic studies,	Unicorn Biomarkers, consequent to their extensive literature, rely on multiple sources of evidence, both randomized clinical trials (rCTs) and epidemiologic studies with outcomes, and preferably including cellular

	thus being treatment-agnostic.
If the SE is proposed based upon prior publications and general scientific community acceptance, discuss the current body of evidence and the use of the SE in clinical studies.	Often supported by independent studies and widely published, these biomarkers are accepted by the scientific community. Importantly, several different lines of evidence from multiple different research groups should support the biomarkers, e.g. FNIH and IMI both support the use of consortia to generate the evidence needed for biomarker development and utilization.
If the course of disease is typically acute, what is the expected long-term sequelae and could a change in the SE also reflect these clinical outcomes (e.g., reduction in viral shedding with influenza and reduced incidence of hospitalization due to complications from illness)?	While in the MASLD space, decompensation events are acute; the predecessor of liver fibrosis is fibroblast activity and other biological processes [24]. Changes in these biomarkers happen prior to acute events [25]. Changes in the biomarker in MASLD phase III studies should be associated with changes in current RLSE (Liver histology) and outcome.
Relationship of the SE with the Causal Pathway(s)	
What is known about the causal pathway(s) for the intended disease? What is the relationship of the SE to this pathway(s)?	Unicorn Biomarkers, consequent to their prognostic, diagnostic and pharmacodynamic performance criteria, reflect the underlying disease biology and often capture downstream processes that drive disease progression. For example, collagen formation and degradation biomarkers quantify fibrosis balance, a disease pathology that may be shared by more than 50 chronic diseases[26]. Because fibrosis drives organ dysfunction and poor clinical outcomes, biomarkers related to fibrogenesis and fibrolysis provide a scientifically understood and broadly applicable potential surrogate endpoint across diseases where fibrosis is causal. Consistent with this, fibrosis and accumulation of collagens are on the causal pathway in liver fibrosis, and in fibrotic diseases more broadly.
Does the intended disease or use have multiple causal pathways? If so, what is the evidence that the specific pathway the SE monitors is the primary pathway leading to the outcome being assessed?	In liver, multiple causal pathways are at play, such as alcohol, liver fat, bile acids, but they all result in a similar end point, fibroblast activation and collagen formation, which may be quantified by collagen formation biomarkers. That has been shown repeatedly to be a primary causal pathway associated with disease progression and poor outcomes in these contexts[25].

If the SE is on a single causal pathway, what is the evidence that this pathway is the predominant mechanism for pathogenesis?	Some Unicorn Biomarkers are RLSE on a single causal pathway. For example, HbA1c in diabetes. HbA1c reflects chronic blood glucose levels and lies on the single predominant causal pathway of hyperglycemia. In direct alignment, collagen accumulation is central to all fibrotic diseases.
If the SE is not on the causal pathway, what is the rationale, the evidence, and the strength of evidence that leads to the conclusion that a change in the SE will be predictive of a change in the clinical outcome of interest?	Unicorn Biomarkers, consequent to the prognostic and diagnostic performance criteria, are most often on the causal pathway. They are hypothesis-driven biomarkers with a clear link to disease pathology. All Unicorn Biomarkers should be on the causal pathway.
Threshold for Change Required to Demonstrate Clinical Relevance	
How much do changes in the SE reflect changes in the clinical outcome or the probability of the clinical outcome occurring?	This is a chicken-and-egg dilemma: evidence is required to show changes and timing of changes in the Reasonably Likely Surrogate Endpoint in predicting clinical outcomes. The magnitude of change in SE must be correlated to established approvable clinical outcome. Therefore, this requires independent validation (post-hoc analysis) of results of trials with different MoA showing the same relationship of SE to clinical outcome.
What is the extent and timing of change in the SE that would predict the outcome of interest?	The magnitude and timing of change are context-specific and depend on the biological pathway, mechanism of action of the therapy, and disease progression rate. Typically, Unicorn Biomarkers are sensitive to therapeutic response before clinical outcomes manifest, as they reflect the underlying disease biology, making them valuable tools for early decision-making. The extent and timing of biomarker changes are typically evaluated through longitudinal and interventional studies (phase II and III) conducted during the development of a Unicorn Biomarker and its utilization in industry-sponsored clinical trials.
Is the change in the SE stable or does it only occur for a short time? Would timing of sample collection be feasible?	This pertains to the variation of the underlying disease reflected by the surrogate biomarker, as to whether it remains stable or is transient. Fibrogenesis and fibrolysis present a balance that fluctuates in liver disease patients over time (hot vs. cold; extended duration of quiescent disease; etc.)

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If a minimum threshold for change has been selected (both size and duration), how was this value determined (include studies conducted and data generated)? If available, is there available information about the sensitivity and specificity of any measurement tools used?	This is another chicken-and-egg dilemma: Often, Unicorn Biomarkers are CLSI-validated, which includes assay sensitivity, limits of detection/quantification, and precision, which is crucial for a reliable threshold for change. Its performance needs to be benchmarked (in correlating with or predicting) against the clinical outcome of interest in a clinical trial(s). These minimal clinically significant changes need to be validated with the biomarker in multiple studies from phase II and III.
Consistence of SE Response under Various Conditions	
How does the SE predict the clinical outcome across different subgroups of the targeted population (e.g., demographic, disease severity, co-existing conditions, concomitant medications typical of the population)?	Extensive validation across multiple cohorts - including varying disease severities, and common co-morbidities, supports their robustness as Reasonably Likely Surrogate Endpoints, reflecting the considerable path of development and validation.
Is there data showing that the SE predicts the clinical response similarly across relevant subgroups?	Unicorn Biomarkers should be linked to core disease mechanisms and have been tested in diverse populations during their development. From this, it is established if they capture biological changes that occur consistently across subgroups within the same group of diseases, regardless of demographic or clinical differences. For example, liver fibrosis is a common denominator, irrespective of whether the underlying insult arises from alcohol or metabolic disease, albeit this needs to be carefully validated.
Reliably Quantifying Changes in the Clinical Outcome Before and After Treatment	
Are there scoring systems or measurement tools commonly used in clinical practice, supported by high-grade clinical evidence, and recognized by clinical expert groups, to assess baseline disease status and/or the effect of treatment on the clinical outcome?	This depends on the Unicorn Biomarker and disease area. In the liver fibrosis field, for example, multiple commonly used biomarkers, including VCTE and ELF, are currently under consideration by the FDA and FNIH as potential RLSE, even as liver biopsy maintains its current RLSE status. Meanwhile, commonly used tests such as FIB-4 are being complemented by newer biomarkers such as the ADAPT-score (which includes PRO-C3) and Li
Predictive Value of Therapeutic-Induced Changes i the SE	
What is the evidence that a therapeutic-induced change in the SE will be predictive of a change in the clinical outcome (e.g., the SE is a correlation vs. the SE has actual predictive value)	This is on cur trials v therap Agenc clinica MOAs are needed to provide a biomarker agnostic of MOA.

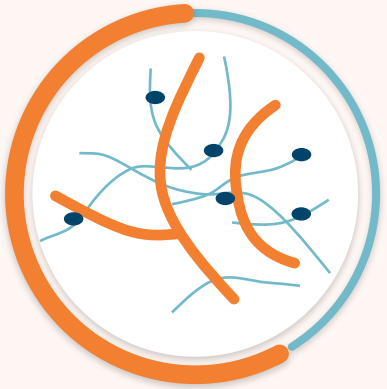
NaF and BMD . More fractures
Torcetrapib – 80% higher mortality
Bardoxolone affected GFR but not outcome
Novartis & Lpa last week

Off-Target Effects of the Therapeutic Product	
Are there any pharmacological effects that could influence the SE but that are unrelated to modifying the disease process (e.g., renal blood flow and creatinine)?	Part of becoming a Unicorn Biomarker is CLSI investigations documenting the technical performance, as well as many interference experiments, allowing a deep understanding of tissue origin, disease process responsible for the epitope, to finally help establish whether changes in biomarkers reflect true disease biology or are off-target pharmacodynamic effects or even obstructive interference.
Operations Manual	
Does the operations manual include a detailed process from specimen collection to results reporting (e.g., information on sample collection and handling, sample processing, testing, results gathering, and interpretation)	The pre-analytical steps are essential and are part of the measurements in a CAP-CLIA certified laboratory, and such are GLP guidelines under a clinical. Due to the high level of validation for Unicorn Biomarkers, the entire process from specimen collection to results-reporting has been thoroughly investigated and standardized. This includes detailed protocols on sample stability and handling to ensure robustness and reproducibility across different settings.
Performance Characteristics of the Measurement Tool(s)	
To what extent have the performance characteristics of the measurement tool (e.g., sensitivity, specificity, within laboratory precision and between laboratory reproducibility, and sample stability under expected handling conditions) been studied?	Unicorn Biomarkers are often evaluated according to CLSI guidelines, which ensure rigorous analytical validation. This validation confirms that the assay produces reliable, consistent, and accurate results across various laboratories and study settings. It also meets the quality requirements expected by regulatory authorities and clinical laboratories.
Is there a description of the sample type(s) that were used to generate the data for these studies included in the briefing package (e.g., prospective or retrospectively collected patient samples, left-over banked samples, samples spiked with defined levels of analyte)?	Cohort characteristics, real-world representativeness, audit trace and logs are needed to reflect patient populations and document sample stability. Preanalytical characteristics are often overlooked and important for assay performance. As a Unicorn Biomarker needs to comply with CLSI validation protocols, this aspect should be carefully dealt with.

The Liver Regenerates

ECM alterations during disease progression – and we regenerate

Inflammation



Excessive
ECM degradation

Release of degradation fragments into the blood

Healthy tissue

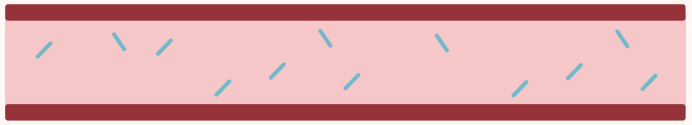
Balanced
turnover

Low release of fragments

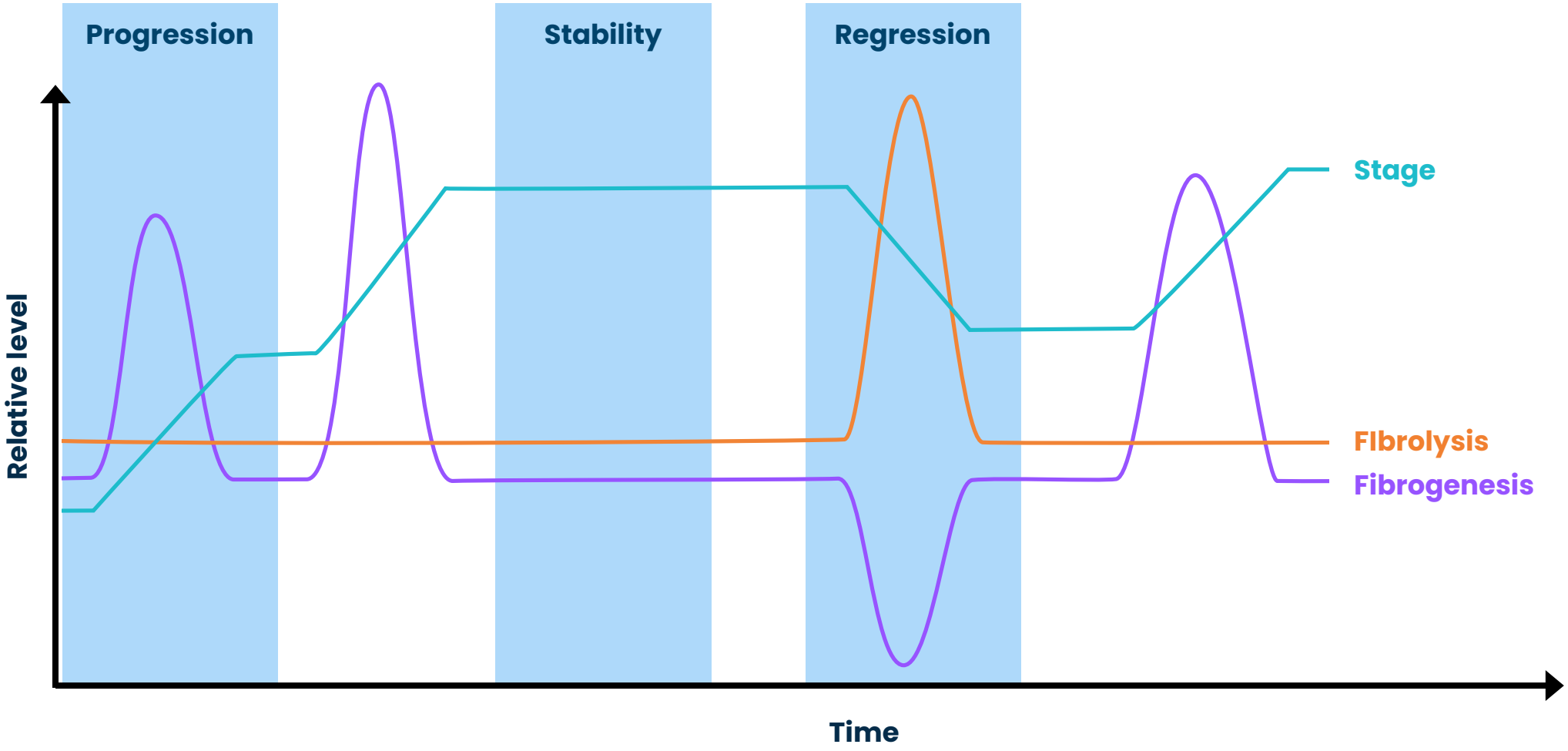
Fibrosis

Excessive
ECM formation

Release of formation fragments into the blood



Fibrosis stage and activity are independent!



Multi-organ fibrosis & the quality of weight loss – balancing weight and additional benefits just right

1. Large reduction of fat mass
2. Minimum/positive effect on lean mass
3. Positive effect on insulin sensitivity
4. Preservation of energy expenditure
5. Prevention of bone loss
6. Reset satiety point

1. Sustained over time/durability
2. Improved QoL
3. Improved mobility
4. Reduced joint/bone/muscle pain
5. Prevention/remission of co morbidities
6. Minimizes use of other drugs
7. **Kidney, CVD and Liver**

DIABETES, OBESITY AND METABOLISM
A JOURNAL OF PHARMACOLOGY AND THERAPEUTICS

REVIEW ARTICLE

The Goldilocks for chronic weight management—Balancing quantity with quality of weight loss

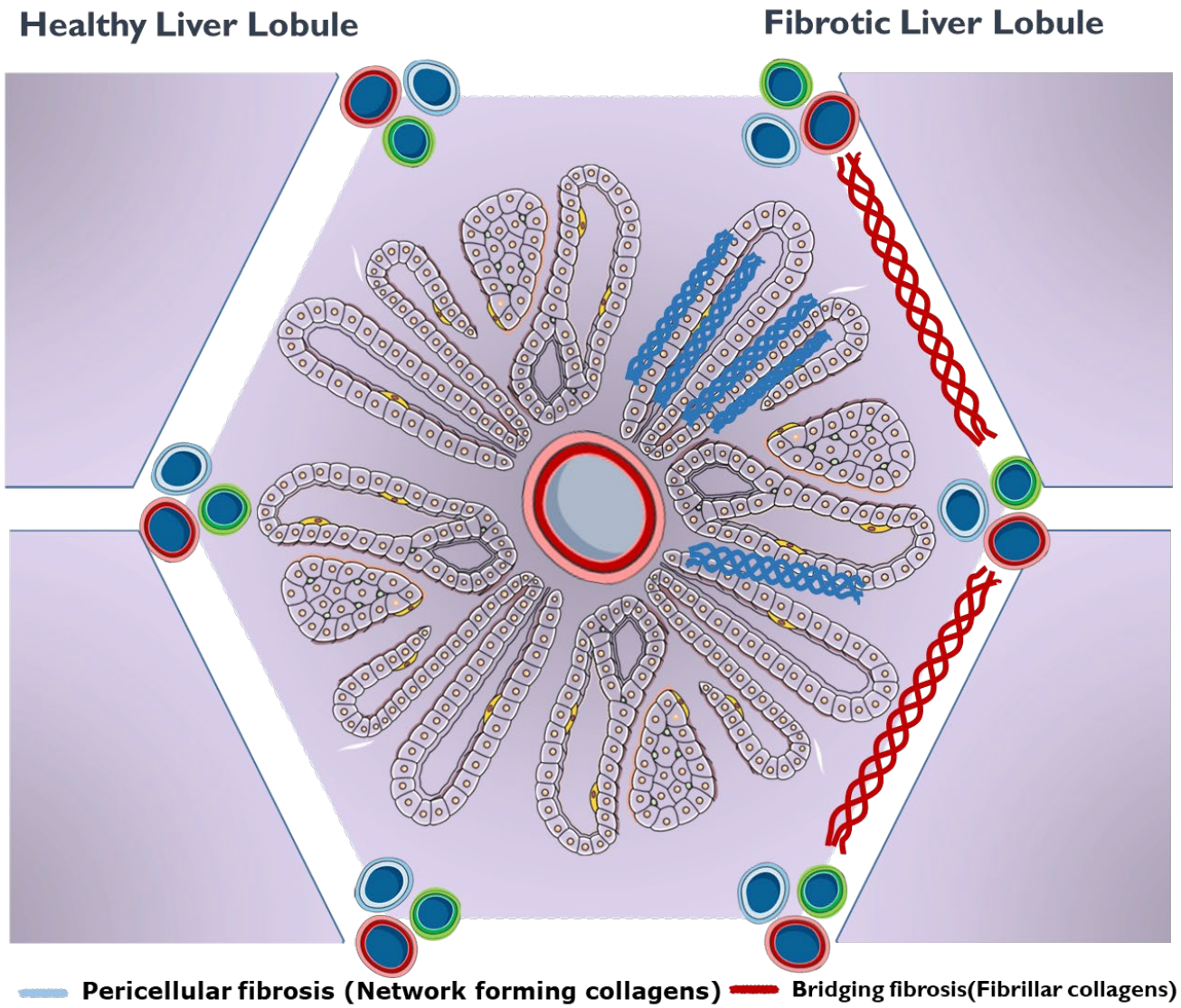
Kim Henriksen PhD ✉, M. V. Chakravarthy PhD, C. L. Bager PhD, A. T. Larsen PhD, K. E. Mohamed PhD, M. A. Karsdal PhD

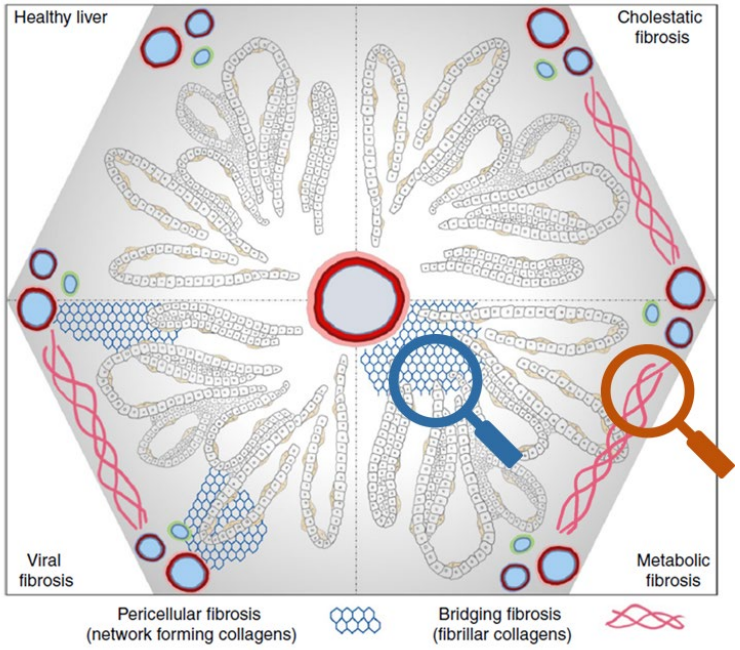
The quality of the weight loss – Key organ biomarkers in obesity trials

Monitoring comorbidities and tissue

Biomarker monitoring	Bone (CTX-I, N-MID)	Cartilage (CTX-II, C2M, PRO-C2)	Synovium (C3M, PRO-C4)	Heart (PRO-C6)	Liver (PRO-C3)	Kidney (PRO-C6 uC3M)	Muscle
	▪ CTX-I and N-MID reflects bone resorption rates and formation rates ▪ Enable assessment of osteopenia risk from weight loss intervention	▪ CTX-II and C2M indicate cartilage breakdown. ▪ PRO-C2 is reflective of cartilage formation ▪ Supports evaluation of OA progression or improvement	▪ C3M and PRO-C4 is associated with synovial and systemic inflammation ▪ Supports evaluation of OA related inflammation and improvement	▪ PRO-C6 assess endotrophin ▪ PRO-C6 is associated with cardiovascular risk ▪ Supports monitoring of cardiovascular risk improvement	▪ PRO-C3 assess pro-fragment of type III collagen ▪ PRO-C3 is associated with risk of liver fibrosis ▪ Supports monitoring risk of liver complications and fibrosis	▪ PRO-C6 assess endotrophin ▪ PRO-C6 is prognostic for kidney outcome ▪ Supports monitoring risk of kidney outcomes	▪ Creatinine ▪ Myosin
GLP-1	–	?	?	+	+	+	+
Tripple	+	+	?	+	+	+	+
DIET	–	+	+	?	+	?	?
Amylin	?	?	?	?	?	?	?

Fibrosis is not just fibrosis!- but a commen denominator!

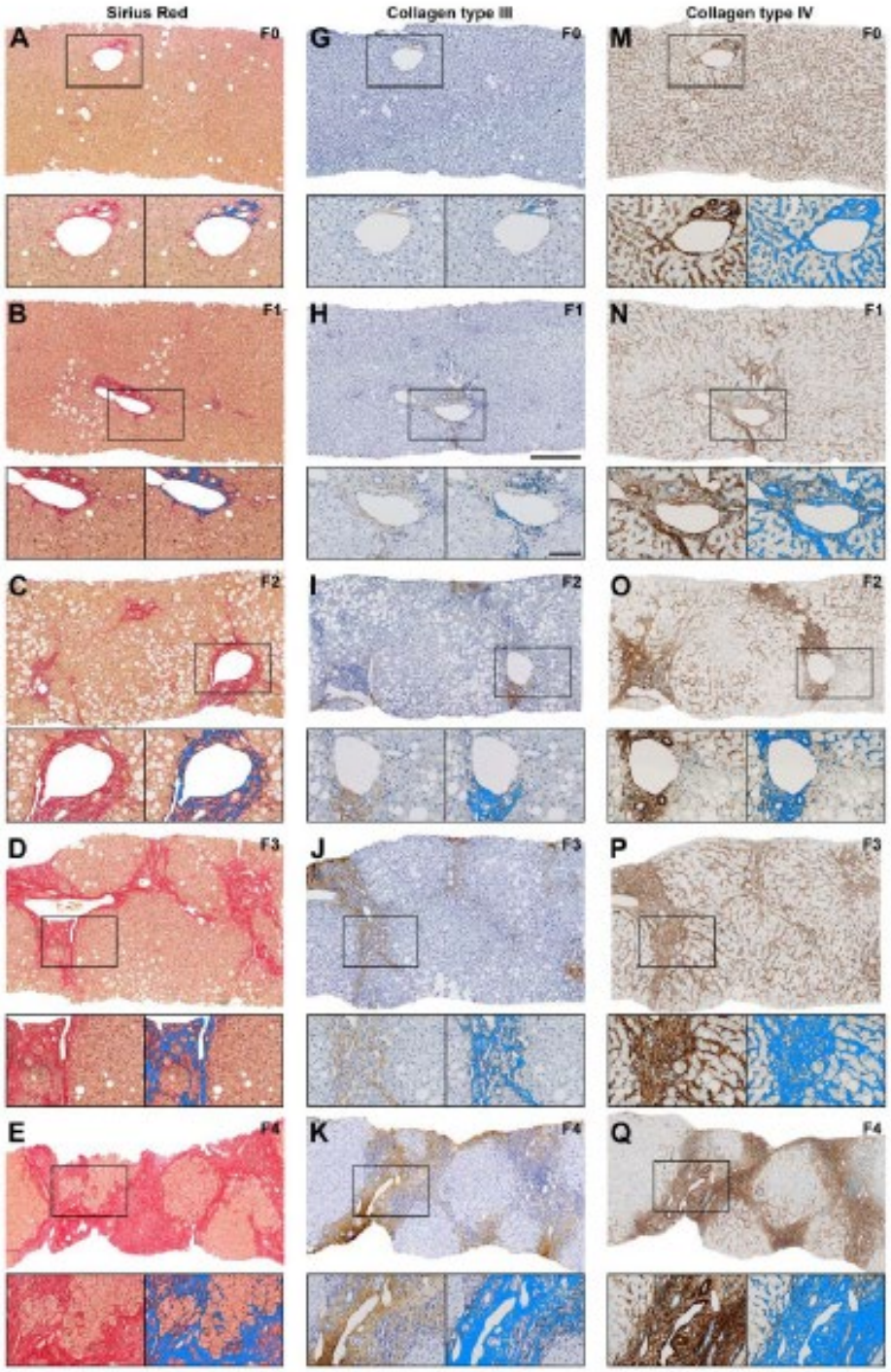




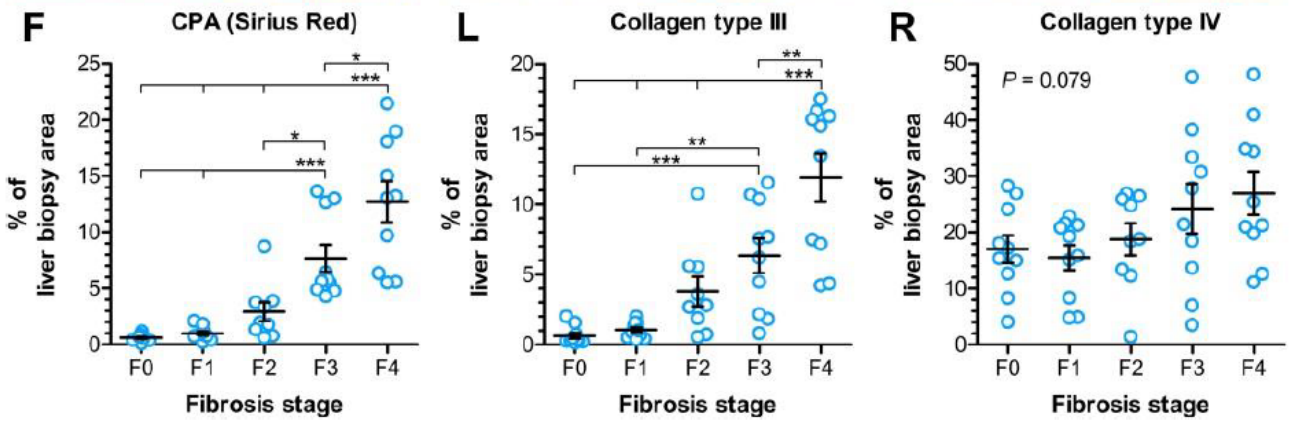
Basement membrane formation → Reparative response

Interstitial matrix → Dense matrix indicative of late stage disease

Karsdal et al. , Hepatology 2020



Type IV changes location, not amount



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Stage-dependent expression of fibrogenic markers in alcohol-related liver disease

Mia Dahl Sørensen [a,b], Maja Thiele [b,c], Aleksander Krag [b,c], Samuel Joseph Daniels [d], Diana Julie Leeming [d], Morten Karsdal [d,e], Sönke Detlefsen [a,b,*]

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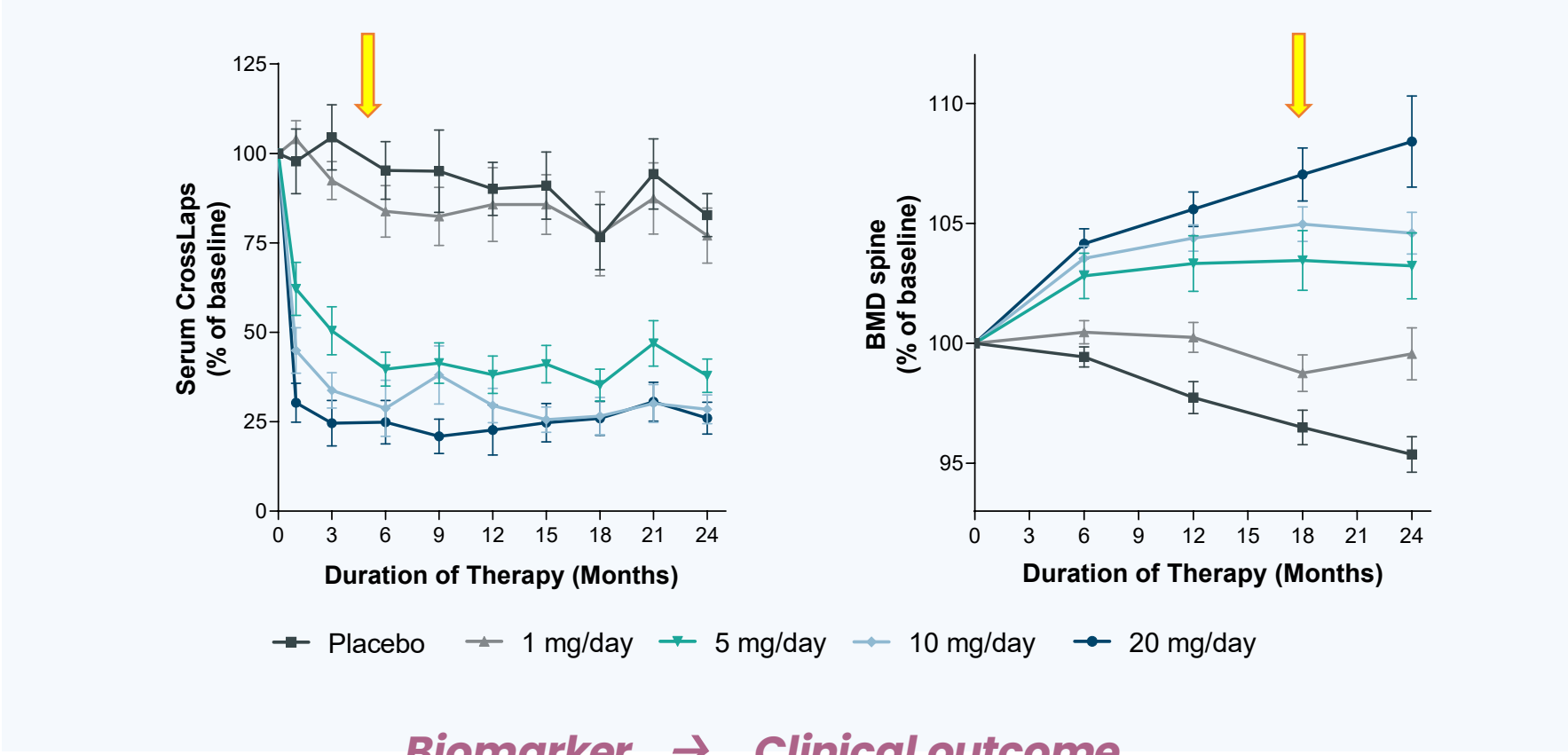
Precision Medicine – ”The Beginning”

The bone biomarker CTX-1 (serum CrossLaps) predicts bone mass change in osteoporosis patients treated with alendronate after 1 month.



Biomarker → Clinical outcome

Ravn et al., Bone, 24, 237-244; 1999

VLCD effects on fibrogenesis biomarkers in NAFLD

A high fibrogenesis endotype?

Cohort description and characteristics

Study info

Patients: NAFLD patients (n=30)

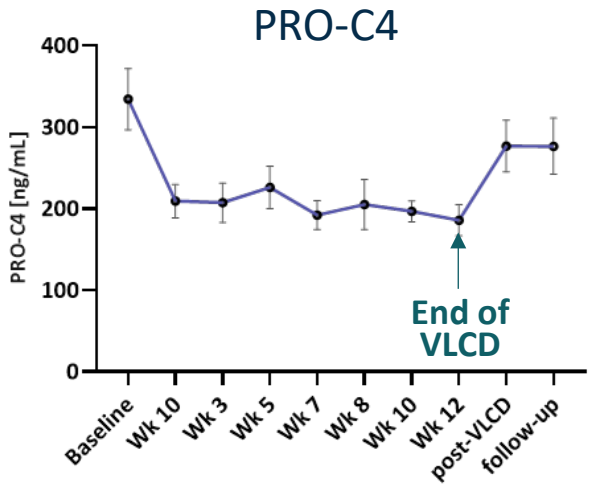
Treatment: Very low calory diet (VLCD): 800 kcal/day for 8-12 weeks

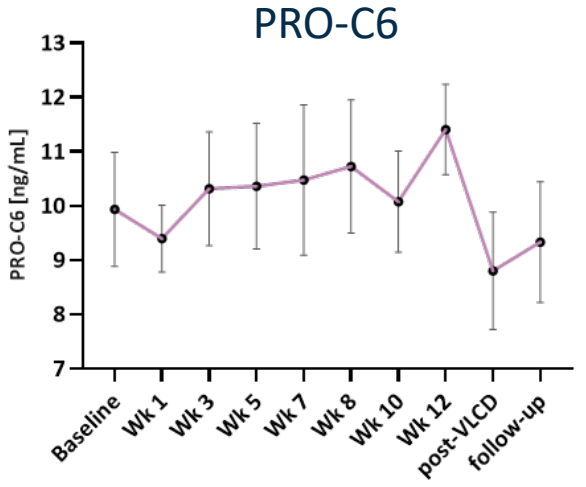
68% reached weight loss target of 10%.
Mean weight loss 13 kg

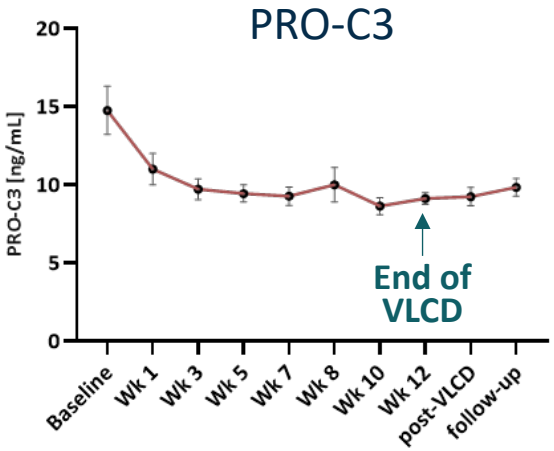
Karsdal et al , Hep. Com 2023

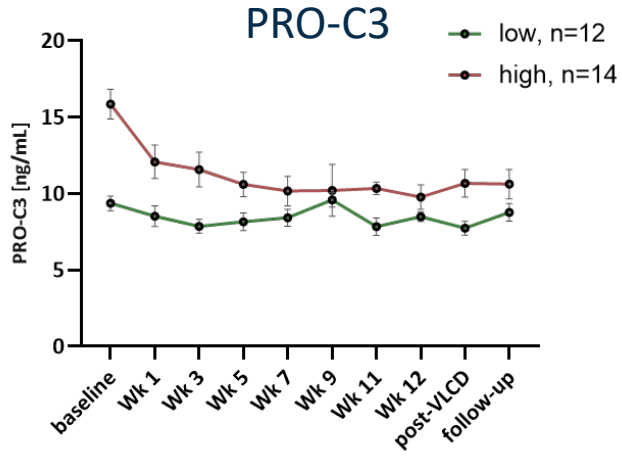
Subject Characteristics	Baseline (n=30)	Post-VLCD (n=27)	P-Value
Age (yrs)	56 ± 12		
Sex (M/F (n)	18/12		
Weight (kg)	**119 ± 25**	**104 ± 21**	**<0.0001**
BMI (kg/m²)	**42 ± 8**	**37 ± 8**	**<0.0001**
Body fat (%)	**45 ± 6.9**	**40 ± 9.1**	**0.001**

Impact of a Very Low-Calorie Diet on ECM Biomarkers

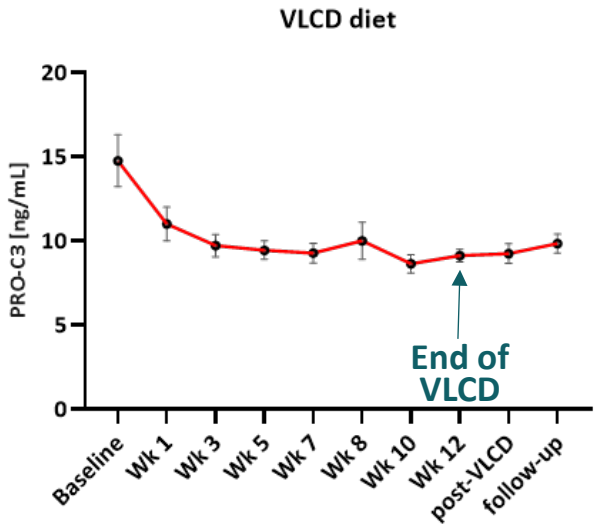


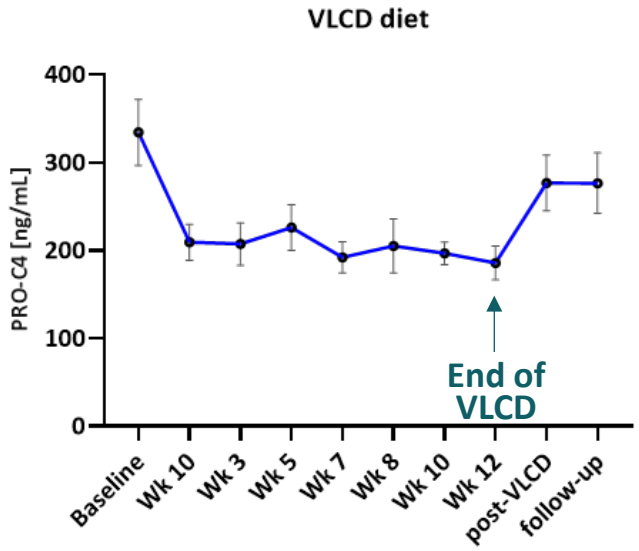


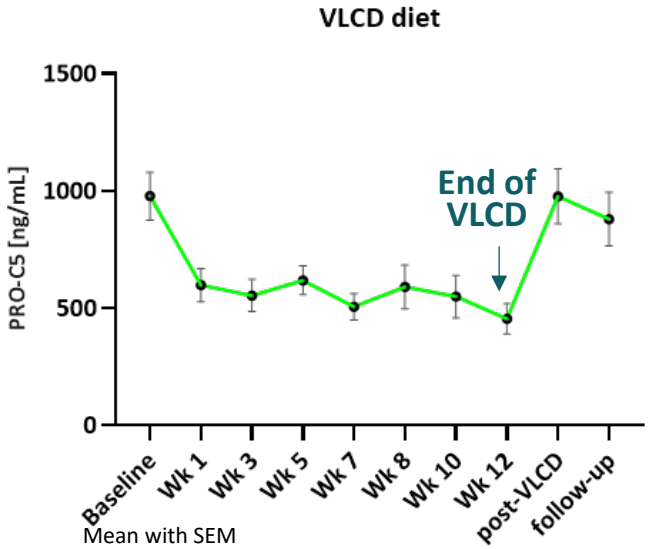




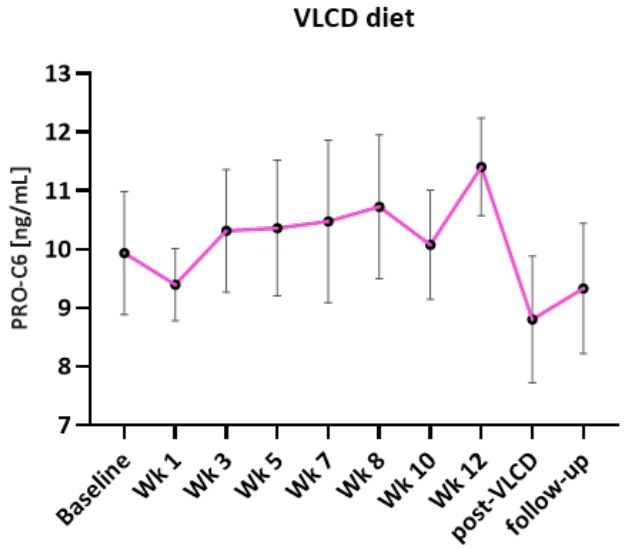
Weight dependent and independent effects







Mean with SEM



Karsdal et al , Hep. Com 2023

Weight loss and bone – a direct linear relationship

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Effect of a 16 weeks weight loss program on osteoarthritis biomarkers in obese patients with knee osteoarthritis: a prospective cohort study

E.M. Bartels † *, R. Christensen † ‡, P. Christensen † §, M. Henriksen †, A. Bennett ‖, H. Gudbergsen † ¶ #, M. Boesen † ††, H. Bliddal † ‡‡ §§

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‡ *Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense M, Denmark*
§ *Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark*
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# *Department of Rheumatology, Copenhagen University Hospitals, Glostrup, Frederiksberg and Bispebjerg, Denmark*
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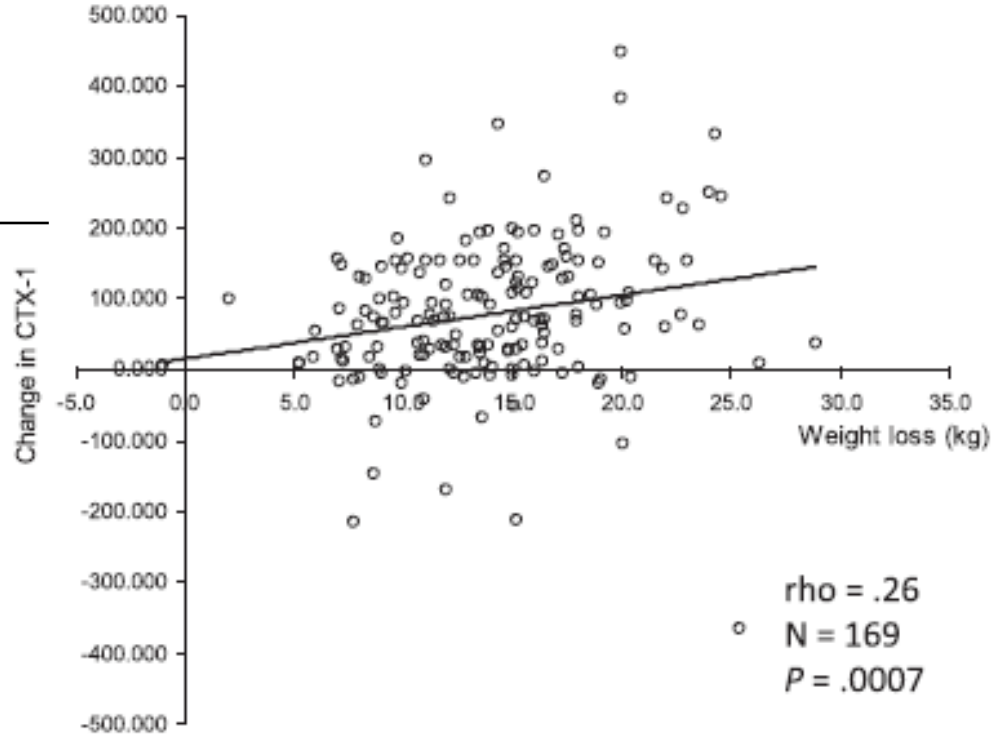
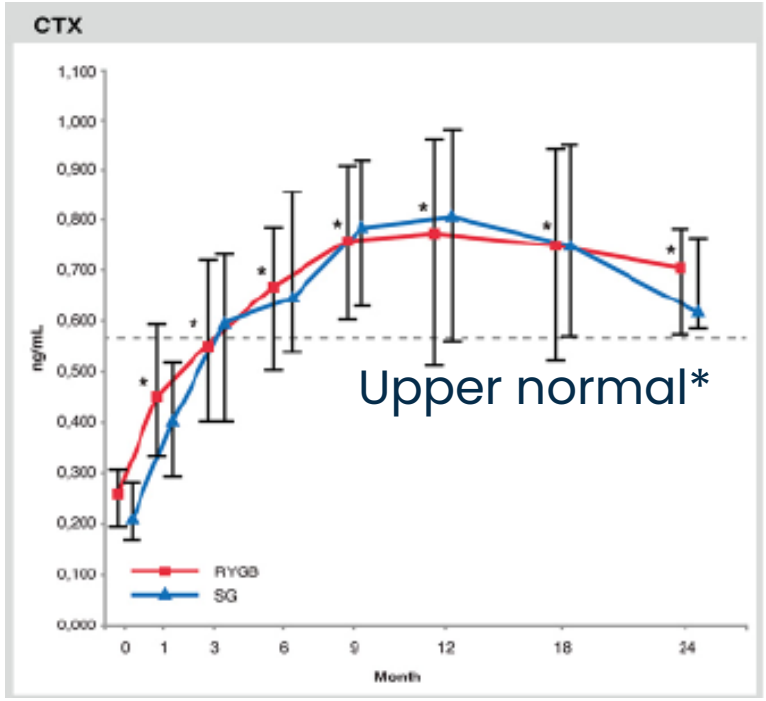


CTX-I in bariatric surgery – Massive increase exceeding the normal range (Muschitz et al, JCEM; 2015)



App. 400% increase in CTX-1!

*Reference ranges are platform and assay dependent

Bone 127 (2019) 436–445

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/bone

Full Length Article

Bone metabolism, bone mineral density and low-energy fractures 10 years after Roux-en-Y gastric bypass

Ingvild Kristine Blom-Høgestøl[a,b,*], Stephen Hewitt[a,b], Monica Chahal-Kummen[a,b], Cathrine Brunborg[c], Hanne Løvdal Gulseth[a,d], Jon A. Kristinsson[a,e], Erik Fink Eriksen[a,b], Tom Mala[a,e]

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[d] Department of Chronic Diseases and Ageing, Norwegian Institute of Public Health, Norway
[e] Department of Gastrointestinal and Pediatric Surgery, Oslo University, Norway

38% of osteoporotic subjects have a fracture

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