The Immuno-Metabolic Program-Clinical Guide

Analyzing immuno-metabolic function allows for a deeper understanding of a patient's health while creating tangible opportunities for meaningful intervention. Key to this program are the Systemic Immune -Inflammation Index (SII) and Systemic Inflammation Response Index (SIRI), two signals hidden inside every CBC with differential.

In consultation with **Dr. Jeffrey Bland, PhD, FACN, FACB, CNS · Founder, Big Bold Health**

01 | A Pioneer's Approach, Distilled Into a Program

Dr. Jeffrey Bland has spent decades shaping how clinicians approach inflammation, metabolism, and chronic disease. An internationally recognized educator, author, and researcher, he is a pioneer in systems-based medicine and the founder of Big Bold Health.

His concept of **immunorejuvenation** (supporting healthy immune function through targeted lifestyle, nutritional, and metabolic strategies) has influenced a generation of integrative practitioners. That framework is now operationalized in a single, structured lab order and protocol.

> *"A patient can have 'normal' individual cell counts and still show an elevated SII or SIRI, a signal that something in the immune-metabolic system warrants a closer look."*

02 | The Gap Standard Labs Leave Open

A patient presents with joint stiffness, persistent fatigue, or cognitive impairment. The CBC and standard metabolic panel return within reference ranges. This is a frequently encountered clinical pattern: symptomatic inflammatory burden that does not register as an out-of-range value on any individual line of a lab report.

SII and SIRI are computed directly from a CBC with differential; no new blood draw is required. Both indices derive from cell counts available in most clinical settings and recombine them into a single composite signal.

Worked Example

CBC Value	Result	Flag
Platelets	**312 K/µL**	Normal
Neutrophils	**5.1 K/µL**	Normal
Monocytes	**0.7 K/µL**	Normal
Lymphocytes	**1.4 K/µL**	Normal

$$\textbf{SII} = (312 \times 5.1) \div 1.4 = \mathbf{1136.6}$$

Above the protocol threshold of > 348; flagged despite three individually normal cell counts.

$$\textbf{SIRI} = (5.1 \times 0.7) \div 1.4 = \mathbf{2.55}$$

Above the protocol threshold of > 0.99; a corroborating signal derived from a distinct cellular component.

03 | How the Indices Are Calculated

SII — Systemic Immune-Inflammation Index

$$\text{Platelets} \times \text{Neutrophils} \div \text{Lymphocytes}$$

Platelets contribute to thrombo-inflammatory processes, reflecting the close relationship between thrombosis, hemostasis, and immune activation. (Mezger 2019) Neutrophils reflect front-line innate inflammation; lymphocytes, in the denominator, represent adaptive immune regulation. (Leliefeld 2015) Described in the literature as a marker of platelet-neutrophil interaction. (Mezger 2019)

Protocol threshold: SII > 348

SIRI — Systemic Inflammation Response Index

$$\text{Neutrophils} \times \text{Monocytes} \div \text{Lymphocytes}$$

SIRI incorporates monocytes, adding a tissue-level signal; recruited monocytes differentiate into macrophages within inflamed tissues and contribute to the initiation, propagation, and resolution of inflammatory responses. (Dash 2024) This index is complementary to, and mechanistically distinct from, the platelet-driven signal captured by SII.

Protocol threshold: SIRI > 0.99

04 | What's Included in the Immuno-Metabolic Program

A panel, initial draft interpretation, and protocol initial draft curated by Dr. Jeffrey Bland- ready for you to review, edit, approve, and to use in practice.

The Panel

Marker	Goal	Notes
CBC with differential	—	Source data for SII, SIRI, and NLR
High-sensitivity C-reactive protein (hsCRP)	**< 1.0 mg/L†**	General inflammatory marker, read alongside the indices
Glycated hemoglobin (HbA1c)	**< 5.5%†**	Glycemic control over ~3 months
Uric acid	**< 5.0 mg/dL†**	Metabolic and inflammatory relevance (Murea 2019)
Fasting glucose	**72-85 mg/dL**	Point-in-time glycemic status
Fasting insulin	**< 5 µU/mL**	Early marker of insulin resistance (Thomas 2019)
Standard lipid panel	—	Cardiovascular risk context
Comprehensive metabolic panel (CMP)	—	Core metabolic and organ function

† Goal ranges for hsCRP, HbA1c, and uric acid reflect Dr. Bland's clinical protocol. See the protocol disclaimer below.
SII THRESHOLD > 348 SIRI THRESHOLD > 0.99

> SII and SIRI are calculated for you and included in the initial draft interpretation when using the Immuno-Metabolic Program.

05 | What Elevated SII and SIRI Are Associated With

A growing body of observational research has linked elevated SII and SIRI to adverse outcomes across multiple organ systems, while mechanistic studies of their constituent immune cell populations provide biological rationale for these associations. (Xia 2023)(Ke 2026)(Dash 2024)(Leliefeld 2015)(Mezger 2019) Associations describe correlation, not diagnosis—elevated indices are risk-stratification signals meant to prompt closer clinical attention, not stand-alone criteria for any specific condition.

> A 20-year NHANES cohort of 42,875 US adults found that those in the highest SIRI category had a 39% higher risk of all-cause mortality and a 39% higher risk of cardiovascular mortality than those in the lowest. Similar associations have subsequently been reported in chronic kidney disease and coronary artery disease cohorts. (Xia 2023)(Gu 2024)(D.-S. Liu 2025)

NLR — Neutrophil-to-Lymphocyte Ratio

Category	Represents	Associated Findings
Cardiovascular & mortality	Vascular disease & survival	All-cause mortality, cardiovascular disease, coronary disease, heart failure, stroke (Xia 2023)(He 2022)(Ke 2026)
Metabolic	Glucose metabolism & metabolic health	Insulin resistance, metabolic dysfunction (Thomas 2019)
Musculoskeletal	Bone & muscle health	Sarcopenia (Xie 2024)
Respiratory, renal & cancer	Lung, kidney & oncologic outcomes	COPD, chronic kidney disease, cancer (Song 2024)(Gu 2024)(Hu 2014)(Qi 2016)
Brain & lifestyle	Mood, cognition & exposures	Depression, cognitive decline, dementia, sleep problems/OSA, sensorineural hearing loss (Bai 2025)(Xiao 2023)(Algul 2025)(He 2026)(Zhou 2024)

Associations With Elevated SIRI

	Represents	Associated Findings
Cardiovascular & mortality	Vascular disease & survival	All-cause mortality, cardiovascular death (Xia 2023)(Ke 2026)(Gu 2024)(D.-S. Liu 2025)
Metabolic & organ health	Liver, kidney & blood	Metabolic dysfunction-associated steatotic liver disease (MASLD; formerly NAFLD/NASH), chronic kidney disease, anemia (Yin 2024)(Gu 2024)(Li 2026)
Respiratory, infection & cancer	Lung, sepsis & oncologic outcomes	COPD, sepsis, cancer (Jia 2025)(Zhu 2025)(Jiang 2021)
Brain & lifestyle	Mood, cognition & physical activity	Depression, cognitive decline; physical activity (Li 2025)(Wang 2025)(X.-Y. Liu 2025)

Associations are largely observational and often bidirectional — an elevated index may reflect, rather than cause, the conditions shown. (Xia 2023)(Ke 2026) Some contributing factors, like sleep, activity, and air pollution exposure, are modifiable. (He 2022)(X.-Y. Liu 2025)(Xu 2025)

06 | The Immuno-Metabolic Program by Dr. Jeffrey Bland on Fullscript

01 Intake & draw: The platform handles intake and the blood draw directly with the patient — at a Quest location or via mobile phlebotomy.

02 Computed results: SII and SIRI are surfaced alongside the rest of the panel — no manual calculation required.

03 Initial Draft interpretation: Built on Dr. Bland's methodology, an initial draft interpretation flags meaningful patterns for clinical review.

04 Initial Draft plan: An initial draft plan spanning nutrition, lifestyle, and supplementation follows the same protocol logic curated with Dr. Bland. Interventions should be directed at established clinical risk factors rather than at reducing SII or SIRI values alone. Providers can review, approve, and edit, before anything reaches the patient.

05 Longitudinal retest: Patients are prompted to retest at a provider-set interval, so SII and SIRI can be tracked over time — both may change over time and have been associated with lifestyle-related factors such as sleep quality, physical activity, and other inflammatory exposures.

07 | Who Tends to Be a Good Fit

Given the foundational role of immune and metabolic health, this panel is appropriate for most adult patients. It may provide additional risk-stratification information in patients with conditions associated with chronic inflammation, such as the following:

- Early metabolic drift—blood sugar or cholesterol trending the wrong way before it meets criteria for diabetes or cardiovascular disease. (Thomas 2019)(Buonacera 2022)
- Low-grade, ongoing inflammation the patient may not otherwise report or recognize. (Buonacera 2022)(Mezger 2019)
- Patterns relevant to metabolic dysfunction-associated steatotic liver disease (MASLD), obstructive sleep apnea, and sensorineural hearing loss. (Yin 2024)(He 2022)(Zhou 2024)

As with any risk-stratification tool, an elevated SII or SIRI is not intended to diagnose a specific condition; it serves as a prompt for further clinical evaluation.

Learn More

The Immuno-Metabolic Program by Dr. Bland's is available now on Fullscript. Providers can also join Dr. Bland live for a webinar on the evidence behind the program and how to recognize meaningful immune-metabolic patterns in practice.

Wednesday, August 12 · 9:00 AM PST / 12:00 PM EST

SII and SIRI thresholds and goal ranges (including hsCRP < 1.0 mg/L, HbA1c < 5.5%, and uric acid < 5.0 mg/dL) reflect Dr. Bland's own clinical protocol, developed from his practice experience. They are risk-stratification signals intended to support clinical judgment, not standalone diagnostic tests, and should not be assumed equivalent to thresholds or reference ranges used in any individual published study.

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