Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Beta glucans

Evidence Summary

β-glucans are a type of fiber with good safety. Soluble grain-derived glucans may benefit cardiometabolic health. Insoluble fungal-derived glucans may benefit immune health. Effects are very modest.

Neuroprotective Benefit: Beta-glucans may modulate the microbiome in a neuroprotective manner.

Aging and related health concerns: Yeast/Fungal β-glucans may modestly boost immune responses, but clinical impacts are minor. Oat/Barley β-glucans can modestly benefit cardiometabolic health as part of a high-fiber diet.

Safety: Beta-glucans from diverse sources are generally safe and well-tolerated. They may pose safety risks to those allergic to source foods and those taking immunosuppressant medications.

Availability: OTC and from food (Oats/Barley/Mushrooms/Yeast)	**Dose**: Not established. Common doses are around 100-300 mg/day yeast/fungal β-glucan as oral capsules. Oat/barley health claims require an intake of ≥3 g/day.	**Chemical formula:** Varied **MW**: Varied (high MW β-glucans are more bioactive) Common linkage structures include: Linear β-(1,3;1,4)-D-glucans (Grains) Branched β-(1,3;1,6)-D-glucans (Yeast/Fungi)
Half life: Varied depending on structure and route of administration	**BBB**: Not penetrant	
Clinical trials: Dozens of small clinical trials have been conducted testing soluble beta-glucans for cardiometabolic conditions, and insoluble yeast/fungal beta-glucans for immune potentiation for preventing infection or part of cancer treatment.	**Observational studies**: Beta-glucan is a source of fiber. High fiber diets have been associated with reduced risks for mortality from a variety of causes.	

What is it?

Beta-glucans are polysaccharides comprised of D-glucose monomers linked with (1-3), (1-4), or (1-6) β-glycosidic bonds in a linear or branched manner [1]. They are located in the cell walls of a variety of organisms, such as cereal grains, bacteria, fungi, and algae. The beta-glucans from these difference sources are structurally distinct, and the structure of the β-glucans is a key determinant of their biological properties [1].
Cereal grains, such as oats and barley, are generally structured as linear β-(1,3;1,4)-D-glucans, in which the glucose units are connected by β (1-3) and β (1-4) bonds.

Bacteria tend to produce extracellular linear (1,3)-β-glucans, such as the high molecular weight polysaccharide, Curdlan, which can form an elastic gel.

Some yeast and fungi produce branched β-(1,3;1,6)-D-Glucans.
Other commonly observed structures are fungal side-chain-branched β-(1,4;1,6)-D-glucans and bacterial cyclic β-(1,3;1,6)-glucans.

In general, β-glucans with lower branching and lower polymerization, as is characteristic of β-glucans from plants with β-(1-4) linkages, are soluble, whereas β-glucans with higher polymerization and more branching, such as fungi with β-(1-4) bonds, are insoluble [1]. The structure also impacts their immunostimulatory potential. β-(1-3) glucans are the most potent immunostimulators, particularly those containing β-(1-6) sidechains, as is observed in many yeast and other fungal-derived forms.

Other structural properties also contribute to their functional properties, such as molecular weight and chemical modification [1]. Consequently, the manner in which beta glucans are extracted/processed can greatly affect their physiological effects.
As such, beta-glucans cannot be considered interchangeable, and even different preparations from the same source may have different effects. This can make it challenging to compare studies using different preparations of beta-glucans, since the effects cannot necessarily be considered generalizable. When applicable and available, the characteristics of the preparation and/or brand are identified when discussing the results of clinical studies testing beta-glucans.

Due to this structure-function relationship, there is no single 'best' type of beta-glucan. Instead, different kinds are better suited toward some activities than others [2]. And while there is likely to be variation across preparations, general trends can be observed regarding the physiological properties associated with different classes of beta-glucans.

Soluble, **cereal grain-derived beta-glucans**, particularly those from oat and barley, have been associated with benefits for cardiometabolic health, which is recognized in the form of health claims by numerous government health organizations around the world [2].

Yeast/mushroom/fungal-derived (insoluble) beta-glucans are used for immune support [2]. They have been tested in a variety of clinical studies for protection against illness, particularly upper respiratory infections. They are also used as an adjuvant for standard cancer chemotherapy and/or immunotherapy [1]. One form in particular, known as lentinan, which is derived from shiitake mushrooms, is approved for use in Japan in combination with chemotherapy.

Neuroprotective Benefit: Beta-glucans may modulate the microbiome in a neuroprotective manner.

Types of evidence:

- 1 clinical trial testing yeast β-glucan in MCI
- Several observational studies for associations between β-glucan rich foods and cognition/dementia risk
- Several laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

An association specifically between beta-glucan consumption and cognitive trajectories has not yet been established. However, associations between beta-glucan-rich foods and cognition and/or dementia risk have been observed. Greater intake of dietary fiber, in general, has been associated with a lower risk of dementia, but since this pattern was observed for a variety of sources, it includes but is not limited to beta-glucan fiber [3]. Oats and mushrooms are excellent sources of different types of beta-glucans. There is evidence from clinical studies supporting a potential positive impact of oats on cognitive function, however, the quality of the evidence is moderate due to high heterogeneity across studies and a lack of clarity around dosing [4]. Mushroom consumption has also been associated with a lower risk of dementia and better preservation of some cognitive domains in observational studies, though the degree of potential benefit is variable [5; 6]. These observational studies suggest that consumption of high-fiber, beta-glucan-containing foods, as part of an overall healthy diet, is beneficial for brain health.

Human research to suggest benefits to patients with dementia:

There is limited clinical evidence regarding the impact of beta-glucan supplementation in patients with dementia.

A randomized placebo-controlled trial was conducted testing yeast-derived β-glucan (Angel Yeast Co.) at a dose of 250 mg twice per day for six months in 138 patients with mild cognitive impairment (MCI) (NCT06083350). The primary outcome was cognitive function based on the Montreal Cognitive Assessment (MOCA). Secondary outcomes included profiling of the gut microbiome, immune profiling, plasma Aβ40 and Aβ42, and additional cognitive tests.
According to a news source related to nutrition/supplements, the key findings of this trial were announced at a trade show indicating a beneficial effect on the gut microbiome and some measures of cognition, though details have not yet been released.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

Beta-glucans have shown evidence of neuroprotection in preclinical Alzheimer's disease (AD) models. The two primary mechanisms of neuroprotection are related to the modulation of the gut microbiome and the modulation of immune/inflammatory responses. The two mechanisms are interrelated, since the metabolites produced by the microbiome have been shown to have immunomodulatory properties.

Modulation of gut microbiome: The fermentation of dietary fiber, such as beta-glucans, within the gastrointestinal tract can alter the composition of the gut microbiome, as well as their functional output of immunomodulatory and neuromodulatory short chain fatty acids (SCFAs) [7]. A comparison study of grain (oat), bacterial (curdlan), and fungal (mushroom)-derived beta glucans found that while all had anti-inflammatory and neuroprotective effects in a mouse model, they had differential impacts on the gut microbiome [8].

A clinical trial testing the black yeast (*Aureobasidium pullulans*) AFO-202 strain-produced β-glucan, Nichi Glucan (500 mg/day for 90 days) with conventional treatment in 18 children with autism spectrum disorder found that the supplementation modulated the gut microbiome [9]. The study authors speculate that the types of changes observed in the composition of the microbiome have an immunomodulatory effect which could help protect against pathological protein aggregation, though this is merely conjecture at this point.

Trained immunity/immunomodulation: Beta-glucans, particularly those derived from fungal sources, have been identified as inducers of trained immunity [10]. Various inducers of trained immunity have been associated with reducing dementia risk and show evidence of neuroprotection in preclinical animal models [11]. This suggests that the manner in which the immune system is modulated by trained innate immunity inducers may be neuroprotective. To date, the role of trained immunity in beta-glucan-mediated neuroprotection has not yet been clearly established.

Alzheimer's disease: POTENTIAL BENEFIT IN PRECLINICAL MODELS

Lentinan: The β-glucan derived from shiitake mushrooms, known as lentinan, has been shown to inhibit the conversion of Aβ and α-syn into toxic fibril-forming beta-sheet structures *in vitro*, and attenuate the aggregation of these toxic proteins in *C. elegans* overexpression models [12]. Lentinan supplementation also mitigated cognitive deficits in mouse models overexpressing Aβ, tau, or α-syn [12; 13].

Yeast beta-glucan: Supplementation with macro-molecular yeast-derived β-glucan (100 mg/kg/day for 1 month) altered the composition of the gut microbiome in APP/PS1 AD model mice in a manner that increased the production of neuroprotective SCFAs, including propionic acid, butyric acid, and valeric acid, and secondary bile acids [14]. This was accompanied by a reduction in neuroinflammation and Aβ plaque deposition, along with better cognitive performance. Similarly, macro-molecular yeast-derived beta-glucan supplementation (100 mg/kg/day for 1 month) also modulated the composition of the gut microbiome in a model of Aβ1-42 (injected i.c.v.), which was associated with reductions in Aβ pathology and neuroinflammation, and better cognitive performance [15].

APOE4 interactions: Not established

Aging and related health concerns: Yeast/Fungal β-glucans may modestly boost immune responses, but clinical impacts are minor. Oat/Barley β-glucans can modestly benefit cardiometabolic health as part of a high-fiber diet.

Types of evidence:

- 1 meta-analysis of trials testing β-glucans for URTIs
- 1 meta-analysis of trials testing fungal β-glucans in cancer therapy
- 1 meta-analysis of trials testing β-glucans for fatigue
- 1 systemic review of trials testing β-glucans in cancer therapy
- 3 reviews of β-glucans for cancer therapy
- 1 systematic review of trials testing β-glucan for various health outcomes
- 1 scoping review of trials testing β -glucans for anti-infective properties in children
- 4 clinical trials in healthy adults on immune modulation
- 9 clinical trials in healthy active adults/athletes on URTIs/immune response
- 3 clinical trials testing b-glucans as vaccine adjuvants
- 1 clinical trial in older adults on URTIs/Immune response
- 1 FDA health claim for oat/barely β-glucans and cardiovascular health
- 4 EFSA health claims for oat/barely β-glucans and cardiovascular health
- Numerous observational studies for fiber with mortality or cardiovascular health outcomes
- Numerous laboratory studies

Lifespan: EXTENSION IN *C. ELEGANS* FOR IMMUNOMODULATORY β-GLUCANS

There is no direct evidence linking beta-glucans to lifespan, however, there is some indirect supportive evidence. Dietary fiber intake has been associated with a lower risk of mortality from a variety of causes, including cardiovascular disease, metabolic disease, and cancer [16; 17; 18; 19]. This includes dietary fiber from whole grains, which is enriched in beta-glucans.

Studies in the nematode worm, *C. elegans*, indicate that different forms of β-1,3 beta-glucans can extend lifespan in *C. elegans* through a mechanism dependent on daf-16 (FoxO) signaling, which is involved in stress resistance [20; 21]. One study found that the effect of particulate paramylon, an insoluble β-1,3-glucan produced by the mixotrophic algae *Euglena gracilis*, on lifespan, was also dependent on the upregulation of clec-196, an ortholog of the mammalian β-glucan receptor, dectin-1, which is involved in innate immune system regulation [20]. A separate study found the lifespan extension afforded by lentinan, a purified β-1,3 glucan extracted from *Lentinus edodes* (shiitake mushrooms), involved increased resistance to oxidative stress. These studies suggest that at least some types of beta-glucans can induce pathways that have previously been associated with lifespan extension in *C. elegans* [21]. Similar to reports of other therapeutic agents that engage these pathways in the worm, the capacity for them to translate to maximum lifespan extension in higher-order organisms, such as humans, is unlikely, but provide a mechanism by which they may promote healthspan. This would be consistent with the protective effects observed in epidemiological studies.

Infectious disease: POTENTIAL VERY MODEST BENEFIT FOR YEAST/FUNGAL β-GLUCAN

Beta glucans have been identified as mediators of trained immunity [10]. Due to these immunomodulatory properties, they have been widely tested for their ability to reduce infection risk or severity when used as adjuvant for vaccines or as a stand-alone treatment [2]. While the vast majority of mechanistic studies have been conducted in preclinical systems, clinical studies have also been conducted in a variety of populations, many of which support the notion that beta-glucans can modestly boost immune responses [2; 7].

Beta-glucans are widely used in agriculture and aquaculture to boost immune responses in animals, as a way to help cut down on the overuse of antibiotics [22; 23].

The functional properties of beta-glucans are largely shaped by their structural and molecular properties, including molecular weight, linkages, branching structure, degree of modification, and

solubility [1]. These properties impact their ability to interact with various pattern response receptors (PRRs) on immune cells as well as their processing by the gut microbiome [1; 7]. Preclinical studies have characterized the structure-function relationship of various beta-glucans and identified properties associated with immunomodulation [24; 25].

Several studies have compared the immunomodulatory effects of yeast (*Saccharomyces cerevisiae*)-derived whole-glucan particle and soluble β-(1,3; 1,6)-D-glucan [24; 25]. The β-1-3 and β-1-6 glycosidic bonds in the fungal glucans allow for their recognition and engagement with the phagocytic C-type lectin receptor, dectin-1, which is encoded by the gene *Clec7a*, and is expressed on myeloid-lineage cells, such as macrophages and dendritic cells [24]. This interaction with dectin-1 is a key determinant feature of the downstream immune response associated with a particular type of beta-glucan. While both the particulate and insoluble types were found to be able to interact with the dectin-1 receptor, only the particulate β-glucans led to the activation of dectin-1, resulting in the uptake (phagocytosis) of the beta-glucan and activation of the dendritic cells and macrophages [25]. The activated myeloid cells promote the activation and expansion of cytotoxic T cell subsets via antigen presentation and cytokine secretion [25]. This immune program facilitates pathogen clearance, and is anti-tumorigenic. The soluble beta-glucans also show immunomodulatory properties via complement receptor 3 (CR3) by priming immune cells to be more permissive to other immunomodulatory agents [25]. They may also modulate the inflammatory milieu through the gut microbiome, but the soluble forms generally do not have strong immunomodulatory effects on their own.

The function of greatest interest is the capacity of beta-glucans to induce trained innate immunity. Trained immunity refers to the metabolic and epigenetic rewiring of innate immune cells in response to a stimulus, which allows the immune cells to elicit a stronger response to future stimuli [26] Trained immunity-inducing stimuli are often pathogen-derived components, referred to as pathogen-associated molecular patterns (PAMPs) [26]. Since some types of fungi are pathogenic to humans, it makes sense that as components of fungal cell walls, beta-glucans can act as PAMPs [24]. Furthermore, it explains why fungal-derived beta-glucans have the capacity to modulate immune responses, whereas, grain-derived beta-glucans largely lack this capacity. Furthermore, since different immune responses may be needed to combat different fungal pathogens, it follows that beta-glucans derived from different fungal sources would modulate immune responses in slightly different ways.
While the engagement of the dectin-1 receptor is important, it is not fully determinant for trained immunity [24]. One study comparing the responses induced by β-glucans from different sources found that the metabolic reprogramming was a critical feature [24]. Consistent with other inducers of trained

immunity, beta-glucans drive glycolytic reprogramming [24]. However, whether or not the cells maintain oxidative metabolism may determine whether training occurs. Those that induce training enhance the metabolic status of the immune cell, by upregulating glycolysis while maintaining oxidative metabolism [24]. Uptake of the beta-glucan into the cell following activation of dectin-1 drives pathways that promote this metabolic reprogramming. These activated myeloid cells can then migrate to lymphoid tissues, such as the bone marrow and lymph nodes, where they can potentially shape immune profiles in a lasting manner [24]. Preclinical studies in rodents suggest that orally administered fungal beta-glucans do not elicit dramatic changes within the bone marrow [24], which may at least partially explain the modest immunomodulatory effects observed in clinical studies.

Clinical studies:

Many small clinical studies have found that yeast/fungal-derived beta-glucans are associated with reduced incidence and symptoms of upper respiratory infections (URTIs) [2]. However, many of these outcomes involve participant reporting and could be subjective. The impact of beta-glucans on immune system responses has been less clear due to the high degree of variability across studies stemming from differences in beta-glucan preparations, study populations, and immunological outcomes. Furthermore, most studies assessing impacts to URTIs did not pair participant immune responses with infection incidence. There is evidence to suggest that supplementation with particulate/non-soluble fungal-derived beta-glucans can elicit some changes to the immune system, which may modestly enhance immune responses to pathogens. Whether this has any meaningful impact on protecting against infection may depend on an individual's baseline immune status as well as the type of pathogen. Generally healthy individuals with modestly dampened immune systems, such as athletes, older adults, and children, may be most likely to notice a small benefit. Whereas, as has been observed with other inducers of trained immunity, further immune enhancement may not readily occur in healthy immunocompetent adults. Meanwhile, the immune modulation may not be robust enough to overcome chronic disease-related immunosuppression.

Several caveats need to be considered when interpreting the clinical studies of beta-glucans. First, many of the studies were funded by manufacturers of beta-glucan supplements. Second, the composition of the placebo-control could impact the interpretation of the results [27]. Many studies use a simple sugar-based placebo. While the doses are typically very low, these could potentially also influence blood sugar, the gut microbiome, and immune responses. Different preparations could potentially impact the immune system in different ways, so the selection of the immune endpoints may determine whether an immunomodulatory effect is observed. Finally, responsiveness to beta-glucans appears to be influenced

by genetics [28], and likely also by microbiome composition, such that the characteristics of the study population may be very important to determining the outcomes.

Healthy subjects: MODEST/ VARIABLE IMMUNE EFFECTS (YEAST/FUNGAL β-GLUCANS)
A meta-analysis including 2,465 participants ranging in age from 2 to 59 years old from 13 RCTs assessed the efficacy of yeast β-glucans in reducing the incidence, severity, and duration of URTIs [29]. The analysis found that yeast β-glucans reduced the incidence of URTIs (Odds Ratio [OR]: 0.345, 95% Confidence Interval [CI] 0.192 to 0.620), the average number of URTIs (Standardized Mean Difference [SMD]: - 0.315, 95% CI - 0.500 to - 0.130), and the duration of URTIs (SMD: - 0.312, 95% CI - 0.561 to - 0.064). The use of different URTI severity metrics precluded a formal meta-analysis for this outcome, but reductions in severity were observed in the majority of the included studies. However, there was high heterogeneity across the studies, likely stemming from use of different age populations, dosing schedules, and formulations. Due to the high heterogeneity and low participant numbers for the studies, it is difficult to make clear conclusions regarding how beta-glucans can be used most effectively for immune support. This is further complicated by the high degree of variability in the type of immune responses elicited by yeast/fungal beta-glucans across participants in different clinical studies. There are likely to be numerous sources of this variability, including, the individual characteristics of the participants, microbiome differences, ethnicity, the specific formulation of the beta-glucan, the composition of the placebo/comparator, the administration schedule, the timing of the assessment, and the types of biomarkers collected. Based on cell culture studies, all of the formulations in the studies described below would be expected to have the capacity to impact the immune system.

β-glucan source	Dose	Duration	Population	Placebo	Outcomes
Baker's yeast β-glucan (Glucan 300®)	1,000 mg/day	7 days	15 men (Netherlands)	None	No immune effects
Baker's yeast β-glucan (Wellmune®)	180 mg/day	12 weeks	39 adults (Japan)	Matched capsules	Increase in some dendritic cell activation markers (CD80)
Baker's yeast β-glucan (Wellmune®)	50 mg/day →125 mg/day →250 mg/day	Each dose for 2 weeks, total 6 weeks	20 adults (USA)	Maltodextrin	Variable changes in immune-related mRNAs
Reishi β-glucan/Immulink MBG®	200 mg/day	84 days	135 adults (Taiwan)	dextrose monohydrate	Increases in T cells (CD4 and CD8) and NK cells

A randomized, controlled, open-label trial (NCT01727895) in 15 healthy male volunteers in the Netherlands found that an oral preparation of yeast β-glucan (1,000 mg) taken once per day for seven days was barely detectable within the serum and had no meaningful impacts on *ex vivo* leukocyte activity or cytokine production [30]. The study utilized a water-insoluble β-glucan derived from baker's yeast (*Saccharomyces cerevisiae*) reported to have a purity of ≥83% by the manufacturer (Glucan 300®, Beta-1,3D Glucan; Transfer Point).

A randomized, double-blind, placebo-controlled trial (UMIN000049706) assessed the impact of dietary β-1,3;1,6-Glucan from baker's yeast for 12 weeks on dendritic cell activation in 39 adults (average age ~44) in Japan [31]. This study used Wellmune® (Kerry Inc.) as the source of the baker's yeast beta-glucan. Active and placebo capsules were specially formulated to be identical with the exception of the beta-glucan. Participants in the active arm received a total dose of 180 mg β-1,3;1,6-glucan (divided amongst two capsules), administered once daily. CD14+ monocytes were isolated from participant PBMCs and differentiated *ex vivo* into conventional dendritic cells (CD11c+, HLA-DR+). Co-stimulatory marker profiles were assessed as indicators of dendritic cell activation. Conventional type 1 dendritic cells (cDC1), which are involved in antigen cross-presentation to cytotoxic T cells and important for pathogen control, had higher levels of the co-stimulatory marker CD80 in beta-glucan-treated participants, though levels of the co-stimulatory markers CD86 and CD40 were not significantly altered. Modest impacts on mucosal immune markers were also observed including nasopharyngeal and oropharyngeal secretory immunoglobulin A (s-IgA). No between-group differences were observed for measures of serum IgA, NK cell activity, neutrophil phagocytosis, or the systemic inflammation marker, C-reactive protein (CRP). Several reported URTI symptoms were reduced in the group taking beta-glucan, however, the study did not assess the relationship between cellular immune responses and patient responses regarding URTIs. This study highlights how the selection of the immune-related marker can influence whether a detectable effect is observed.

An exploratory study assessed the impact of yeast beta-glucan supplementation on immune maturation mRNA in blood from 20 healthy adult participants (age 31±4 years) in the US without inflammatory or metabolic conditions [32]. This study used a preparation of 100% baker's yeast beta-glucan (Wellmune®, Kerry Inc.) administered orally at a dose of 50 mg/day for the first two weeks, 125 mg/day for the next two weeks, and 250 mg/day for the last two weeks of the study. The placebo comparator was composed of maltodextrin. They identified changes in mRNAs associated with immune responses, including those related to antigen presentation, T cell signaling, myeloid responses, and immune cell activation. Many were changed during specific two-week dosing windows, which could be a reflection of how both

duration and dose affect the effects of beta-glucan on the immune system. The high degree of variability both across subjects and over time highlights the challenge of identifying biomarkers that can provide clear and consistent evidence of whether beta-glucan supplementation is meaningfully impacting immune function.

A randomized controlled trial (ISRCTN48306294) assessed the impact of β-1,3; 1,6 D-glucan derived from *Ganoderma lucidum* (Reishi mushroom) for 84 days on immune parameters in blood-derived immune cells in 135 healthy adult participants (average age 37-39) in Taiwan [33]. The study used the commercial preparation of Reishi β-glucan/Immulink MBG® (Super Beta Glucan Inc.) with an oral dose of 200 mg/day, in comparison to a placebo capsule comprised of 200 mg of dextrose monohydrate. The dose was selected based on human equivalent dosing for a rodent study that detected cytokine changes in response to Reishi β-glucan. Differences in multiple immune cell subsets were identified within 12 weeks between Reishi β-glucan and placebo groups. These include increases in total lymphocyte count (14.1 ± 20.9% vs. 2.8 ± 12.8%), absolute CD3+ T-cell counts (15.0 ± 9.9% vs. 1.0 ± 2.5%), absolute CD4+ T-cell counts (13.4 ± 22.2% vs. -8.0 ± 17.2%), absolute CD8+ T-cell counts (14.6 ± 22.8% vs. 2.4 ± -22%), CD4: CD8 ratio (12.9 ± 11.2% vs. -2.2 ± 1.7%), NK cell counts (19.5 ± 6.4% vs. -2.0 ± 8.9%) and NK cell cytotoxicity (83.1 ± 30.0% vs. -4.5 ± -8.7%), and serum IgA concentration (10.0 ± 38.3% vs. 2.1 ± 11.8%). The durability of these effects as well as their clinical relevance remain to be established.

Children: POTENTIAL MODEST BENEFIT (YEAST/FUNGAL β-GLUCANs)
A scoping review assessed the anti-infective properties of beta-glucans in children ≤12 years old [34]. The most commonly used sources of beta-glucans were pleuran and baker's yeast beta-glucan. The majority of the 12 included studies saw an association with a lower incidence of URTIs and/or symptoms, though caution is warranted in the interpretation as many were open-label studies. Higher molecular weight beta-glucans showed greater immunomodulatory activity.

Older adults: UNCLEAR/MODEST BENEFIT (YEAST β-GLUCANS)
A randomized, double-blind placebo-controlled trial (EudraCT number 2011-004910-41) did not find significant effects of baker's yeast beta-glucan (Wellmune®; Biothera) at a dose of 250 mg/day for 90 days during winter on URTIs or serum cytokines in community-dwelling older adults (aged 50 to 70) in the UK [35]. There was an increase in (LPS-)stimulated IFN-γ in blood, from beta-glucan-treated participants at day 45, which in some studies is used as a marker of trained immunity, but this augmented IFN-γ response was not maintained at the 90-day timepoint in this study.

Exercise stress: MODEST IMMUNOMODULATORY EFFECTS/REDUCTION OF URTI SYMPTOMS (INSOLUBLE YEAST/FUNGAL β-GLUCANS)

Physical activity can modulate the immune system. High intensity exercise can stress the body in a manner that weakens the immune system, at least temporarily [36]. As a result, many studies test the efficacy of immune potentiating agents, including beta-glucans, in the context of exercise stress-induced immune dampening. Beta-glucans have been tested for performance and immune-modulating effects in the context of acute bouts of exercise as well as in athletes in the context of long-term training [2]. The ability to detect an effect is likely to be influenced by the degree to which the participants' immune systems are affected by the exercise regimen [36]. Athletes undergoing a prolonged period of intense training are more likely to be in overall immunosuppressed state, whereas the effects of an acute bout of exercise are more variable, including both pro-inflammatory and immunosuppressive features. The studies conducted to date suggest that beta-glucan supplementation may help attenuate declines in certain features of immune function in athletes undergoing periods of training, but the translation to enhanced protection from illness appears quite modest. It also does not show consistent effects on boosting performance.

β-glucan source	Dose	Duration	Population	Exercise intervention	Outcomes
Pleuran (Imunoglukan®)	100 mg/day	2 months	20 Elite athletes	Training	Preservation of NK cells/activity
Pleuran (Imunoglukan®)	100 mg/day	3 months	50 Elite athletes	Training	Preservation of NK cells; reduction in URTI symptoms
Baker's yeast β-glucan (Yestimun®)	250 mg/day	13 days	29 Recreationally active adults	Acute (treadmill)	No significant effects on muscle damage markers, modest immune effects.
Baker's yeast β- glucan (Wellmune®)	250 mg/day	10 days	60 Recreationally active adults	Acute (cycling)	Induction of monocytes ($CD14^+/CD16^+$) and cytokines: IL-4, IL-5 and IFN-γ 2hr after exercise
Baker's yeast β-glucan (Wellmune®)	250 or 500 mg/day	4 weeks	75 Marathon runners	Post marathon period	Reduction in URTI symptoms
Baker's yeast β- glucan (Wellmune®)	250 mg/day	28 days	182 Marathon runners	Post marathon period	Reduction in URTI symptoms

Baker's yeast β- glucan (Wellmune®)	250 mg/day	91 days	357 Marathon runners	45 days prior to 45 days after marathon	Reduction in URTI symptom days
Baker's yeast β- glucan (Wellmune®)	250 mg/day	91 days	(69 active/133 placebo) Marathon runners	45 days prior to 45 days after marathon	Reduction in URTI symptoms
Soluble Baker's yeast β- glucan	250 mg/day	91 days	(76 active/133 placebo) Marathon runners	45 days prior to 45 days after marathon	No effect on URTIs
Soluble oat β-glucan (OatVantage®)	5.6 g/day	18 days (training through event)	36 Male cyclists	3-day cycling 3hr/day	No effect on URTIs or immune measures

A double-blind cross-over study assessed the impact of baker's yeast beta-glucan on exercise-induced muscle damage and inflammation in 16 male and 15 female healthy volunteers (average age 30). The participants were supplemented with 250 mg/day of yeast beta-glucan (Yestimun®) or maltodextrin (placebo) for 13 days, and conducted a bout of heated treadmill exercise on the 11th day of supplementation [37]. There were no group-time interaction effects on measures of muscle damage, though there was a tendency toward a faster recovery of myoglobin levels. There were also no significant differences between groups on measures of muscle function.

Immune potentiation

A double-blind, placebo-controlled study in 20 elite athletes found that supplementation with 100 mg/day β-glucan from *Pleurotus ostreatus*, known as pleuran (Imunoglukan®) for two months was associated with greater perseveration of NK cell levels and activity during the recovery period, relative to placebo [38]. A separate double blind, placebo-controlled study in 50 athletes using pleuran (Imunoglukan®) for three months, also showed a preservation of NK cell counts and their phagocytic activity with pleuran supplementation [39].

In a cross-over design study, supplementation with baker's yeast beta glucan (Wellmune WGP®) 250 mg/d for 10 days was associated with greater induction of pro-inflammatory monocytes ($CD14^+/CD16^+$) and plasma IL-4, IL-5 and IFN-γ cytokine levels two hours after a bout of 50 minutes of cycling in hot,

humid conditions, relative to placebo (rice flour) supplementation in 60 recreationally active adults [40]. Levels of salivary IgA, a marker of mucosal immunity, were also increased with beta-glucan, at this timepoint [41].
In contrast to the immune modulating effects observed for insoluble, fungal-derived beta-glucans, no clear immune modulating effects were observed in a study testing two weeks of supplementation with a soluble oat-derived beta glucan concentrate (OatVantage®) in trained male cyclists [42].

URT1s
Several studies testing insoluble yeast or fungal-derived beta-glucan have found that supplementation is associated with a reduction in URTI symptoms and symptom severity in athletes based on participant surveys [39; 41; 43; 44; 45]. However, a similar impact on the incidence and duration of URTIs overall has generally not been observed. Notably, one study comparing insoluble vs soluble baker's yeast beta-glucan found that only the insoluble form had a measurable effect on URTI symptoms [45]. This suggests that the effect on URTIs stems from the immune modulating properties of the beta-glucan.
Overall, these studies suggest that insoluble yeast/fungal beta-glucan supplementation has the capacity to modulate the immune system in a moderately potentiating manner. While this small boost to the immune system may help with anti-pathogen responses, it may not be enough to offer a clinically meaningful level of protection for most people.

β-glucan as a vaccine adjuvant: MODEST/UNCLEAR CLINICAL BENEFIT
Due to its purported ability to act as an inducer of trained immunity and potentiate immune responses, some studies have tested the potential of beta-glucans to act as a vaccine adjuvant [10]. While beta-glucans have shown promise in preclinical models, their capacity to meaningfully boost vaccine responses in a clinical setting has been quite limited to date.

RSV: The VN-0200 vaccine is a respiratory syncytial virus vaccine (Daichi Sankyo) containing the RSV F glycoprotein (VAGA-9001a) antigen and a β-glucan-CpG adjuvant, which is a complex of synthetic oligonucleotide and shiitake mushroom-derived beta-glucan (lentinan) [46]. The vaccine was tested using multiple doses of antigen and adjuvant in a Phase 2 trial in 342 healthy adults in Japan (NCT05547087). There were no clear immunogenetic effects of the adjuvant, with no dose-related effects on neutralizing antibodies or antigen-specific IFN-γ responses.
The other studies tested the impact of oral beta-glucan supplementation surrounding the vaccination period, for potential vaccine boosting capacity.

Covid: The impact of supplementation with 500 mg/day insoluble yeast β-glucans (≥70% purity) seven days prior and seven days following vaccination with the first dose of the ChAdOx1 nCoV-19 (AstraZeneca/Oxford) targeting SARS-CoV-2 was tested in 34 men in a randomized, blind, placebo-controlled pilot trial [47]. The production of antigen-specific IgG anti-spike (S1) and receptor-binding domain (RBD) antibodies was higher in the placebo group following the first dose. However, median levels of anti-S1 IgG (placebo: 2611.18 vs glucan: 4040.98) and anti-RBD IgG (control: 877.95 vs glucan: 1452.75) antibodies were higher in the beta-glucan group following the booster dose. The increased response to the second dose is consistent with the traditional priming effect of adjuvants. However, whether this heightened antibody response translated to more robust protection against infection or symptoms was not established.

Influenza: A supplementation regimen of 500 mg/day of yeast-derived beta-glucan (≥80% purity) (Biotec Betaglucans) starting two weeks prior and four weeks after vaccination with a seasonal quadrivalent influenza vaccine (Fall 2022) was tested as a means of boosting vaccine immune responses in 90 older adults (average age 70.7 ± 10.1) [48]. Post vaccination antibody (hemagglutination) titers to influenza A H3N2 A/Wisconsin/67/2005 were higher in the beta-glucan supplemented group, though there were no differences in post-vaccination induction of IFN-γ, suggesting that it boosted humoral, but not cellular responses. There were no differences in reported cold and flu symptoms, though levels were low in both groups, such that it is unclear whether the beta glucan supplementation had any true clinical impact.

Cancer: Beta-glucan supplementation has also been tested as a method to boost immune responses to ganglioside cancer vaccines, whose utility has been limited due to insufficient antibody production [49]. An oral gel formulation of yeast β-glucan was administered in a cyclic dosing manner (40 mg/kg/d for 14 days on, then 14 days off) in conjunction with the GD2/GD3 ganglioside vaccine (administered s.c. weeks 1, 2, 3, 8, 20, 32, and 52) in 107 patients with high-risk neuroblastoma [49]. All participants received beta-glucan supplementation from week six onwards, but one group of patients started supplementation during the first week. Higher IgG antibody (≥230 ng/mL) responses were associated with better progression free survival. The addition of beta-glucan was found to elicit higher antibody titers in a prior study. Starting beta-glucan during the priming phase also resulted in a higher anti-GD2 IgG1 antibody response. There was no effect on IgM antibodies, suggesting beta glucan may impact the class-switch transition from IgM to IgG. Despite the higher titers, there was no impact on rates of seroconversion. Genetic variation appears to be an important reason why beta-glucan supplementation did not have a robust effect on patient outcomes. Preclinical studies indicate that the immune-modulating effects of insoluble beta-glucan are mediated by the receptor dectin-1, which facilitates its

uptake. The *Clec7a* gene (encodes dectin-1) variant rs3901533 has reduced function, and homozygous carriers of this variant (C/C) show increased susceptibility to infection. This variant also hinders the ability of beta-glucan to potentiate immune function, and thus homozygous carriers of this variant failed to benefit from beta-glucan supplementation and had lower rates of seroconversion. This study highlights an important limitation of beta-glucan's potential utility as an adjuvant.

Cardiometabolic disease: MODEST BENEFIT FOR SOLUBLE GRAIN β-GLUCANS

Numerous studies have found that diets high in dietary fiber are associated with lower risk of cardiovascular disease and cardiovascular-related mortality [50]. However, most Americans consume less than the recommended 25 to 38 grams of fiber per day. The proposed beneficial mechanisms include the lowering of blood lipid levels, blood pressure, and inflammation. The best studied of these, the lowering of total cholesterol and LDL-cholesterol, are related to the ability of soluble fiber to bind to cholesterol in the small intestine and reduce its absorption [50]. Bile acids are steroid hormones derived from cholesterol which facilitate the digestion of fats. They also get trapped by the fiber gel in the intestine and excreted. Cholesterol in the blood then gets diverted to the liver to replenish the bile acids, with the result being a reduction in blood cholesterol levels [50]. Additionally, the utilization of the fiber by the resident bacteria in the colon (i.e. gut microbiome) can influence the production of bioactive short-chain fatty acids and other immunomodulatory molecules. The capacity of a given fiber to engage in these various processes depends largely on its structure. Therefore, as with other indications, different types of fiber will differentially impact different processes related to cardiovascular health.

There is evidence to support beta-glucans as at least one of the key fiber sources contributing to these cardioprotective effects. A cohort study of 4,125 older adults (aged ≥ 65) in the U.S. assessing the relationship between fiber intake and cardiovascular disease (CVD) found that relative to other fiber sources, consumption of cereal fiber, which tend to be high in beta-glucans, had the strongest association with lowering the incidence of CVD and lowering markers of inflammation, such that, depending on the marker, up to 16% of the association with CVD being mediated by the effect on inflammation [51]. Furthermore, clinical studies specifically testing beta-glucans, typically derived from oats and barley, also show effects related to cardioprotection, such as cholesterol lowering [50].

Based on this evidence, several government health agencies, including the European Food Safety Authority (EFSA) and the FDA have authorized health claims regarding beta-glucans [52]

The FDA issued a health claim regarding '***soluble fiber from certain foods and risk of coronary heart disease***.' Sources of dietary fiber eligible for this health claim include beta-glucan soluble fiber from whole oat and barley sources, including oat bran, rolled oats, whole oat flour, Oatrim, whole grain barley and dry milled barley, and barley betafiber (Code of Federal Regulations). The health claim also applies to a different source of fiber, psyllium husk (see Psyllium report). The health claim indicates that a daily intake of ≥3 g β-glucan soluble fiber from whole oats or barley, or a combination is needed to support the claim for a risk reduction in coronary heart disease.

The EFSA has issued several health claims regarding beta-glucans, listed below.
"***Consumption of beta-glucans from oats or barley as part of a meal contributes to the reduction of the blood glucose rise after that meal.***" This claim may be used only for food which contains at least 4 g of beta-glucans from oats or barley for each 30 g of available carbohydrates in a quantified portion as part of the meal [53; 54].
"***Barley beta-glucans have been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease***." At least 3 g of barley beta-glucans should be consumed per day in order to obtain the claimed effect [55].
"***Oat beta-glucan has been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease.***" At least 3 g of oat beta-glucans should be consumed per day in order to obtain the claimed effect [56].
"***Beta-glucans contribute to the maintenance of normal blood cholesterol levels***." The claim may be used only for food which contains at least 1 g of beta-glucans from oats, oat bran, barley, barley bran, or from mixtures of these sources per quantified portion. A daily intake of 3 g of beta-glucans from these sources is needed to obtain this beneficial effect [57].

Cancer: POTENTIAL BENEFIT FOR LENTINAN/FUNGAL β-GLUCANS AS ADJUVANT TO CHEMOTHERAPY/IMMUNOTHERAPY
Beta-glucans have been used in the context of cancer, primarily as an adjuvant to immunotherapy [1]. Through their ability to engage receptors on immune cells, such as macrophages, NK cells, and neutrophils, beta-glucans have the capacity to promote a variety of immunomodulatory and anti-tumor activities [58]. Some of the key identified receptors mediating these effects include dectin-1, complement receptor 3 (CR3), lactosylceramide, toll-like receptors (TLR), and scavenger receptors [1; 58]. The engagement of these receptors drive signaling pathways involved in cell survival, cytokine production, and reactive oxygen species (ROS) production [1]. Based on these properties, they are often

paired with immunomodulatory agents, with the goal of overcoming resistance and boosting their efficacy.
These receptors and pathways will be differentially engaged depending on the structural/molecular properties of the beta-glucan, thus, not all beta-glucans are well suited for use in cancer immunotherapy. To date, high molecular weight fungal-derived beta-glucans have shown the greatest potential due to their strong engagement of immune receptors and induction of anti-cancer pathways. Additionally, cyclic β-(1,3;1,6)-glucans are being considered as candidate encapsulating agents for delivery of antitumor drugs [1].

The most extensively used beta-glucan in cancer therapy is lentinan, a β-1,3-D-glucan polymer with β-1,6 or β-1,4 branches purified from shiitake mushrooms (*Lentinus edodes*) [1]. Lentinan is used in combination with chemotherapy in China and Japan, and has been approved as a biological response modifier, for use as an adjuvant for standard (chemo)therapy in gastric cancer in Japan since 1985 [59]. While not yet approved, other preparations of fungal-derived beta-glucans have also been clinically tested as immunotherapy adjuvants, including the yeast-derived beta-glucan, BTH-1677 (odetiglucan or Imprime PGG), which has been tested in combination with anti-PD-1 therapy [58].
In contrast to its use as an immunomodulator in other contexts, where it is typically administered as an oral supplement, beta-glucans used as part of cancer immunotherapy are usually administered intravenously.
The protein bound polysaccharide mixture of beta glucans, polysaccharide-K (PSK) derived from *Trametes versicolor* (Turkey tail mushrooms) is also used as an adjuvant to chemotherapy for cancer care in Japan, where it is typically administered orally (see Turkey Tail Mushrooms Report).

A meta-analysis of 17 RCTs in advanced gastric or lung cancer with study arm sizes ranging from 15 to 149 cases, including a total of 1,423 patients assessed the impact of lentinan in combination with chemotherapy on survival and response rate [60]. Lentinan treatment was associated with a higher overall response rate (Risk Ratio [RR]: 1.28, 95% CI 1.08 to 1.55), including both complete (RR: 1.78, 95% CI 1.09 to 2.89) and partial responses (RR: 1.27, 95% CI 1.04 to 1.56). Lentinan treatment was associated with a higher 1-year survival rate (RR: 1.46, 95% CI 1.16 to 1.84), but this did not extend to the 2-year survival rate (RR: 1.16, 95% CI 0.85 to 1.56). Differences in dosing and the manufacturer of lentinan contributed to heterogeneity across studies.
A systematic review of 16 trials including 1,650 cancer patients, with study arm sizes ranging from 9 to 200 patients assessed the impact of fungal beta-glucans as adjuvants in cancer treatment [61]. While

some studies found faster recovery of white blood cell counts, the high degree of variability across studies precluded statistical analyses or generalization of the findings.
A key challenge with the use of beta-glucans in cancer therapy is that their efficacy can vary based on the formulation of the beta-glucan, and the type of cancer [28]. For example, beta-glucans treatment was associated with improved survival in the context of melanoma, but not in pancreatic cancer [28]. Some of these differences may be related to the low bioavailability, and differential penetration into the tumor microenvironments of different cancers [28].

While high fiber diets have been associated with reduced risk for several types of cancer [62], it has not yet been established whether beta-glucans, specifically, are an important driver of that risk reduction.

Fatigue: MODEST/UNCLEAR POTENTIAL BENEFIT
A meta-analysis and systematic review of 16 RCTs including a total of 1,449 participants assessed the impact of beta-glucan supplementation on measures related to fatigue and mood, including the Patient-Reported Outcomes Measurement Information System (PROMIS), Symptoms Questionnaire, Short-Form Health Survey (SF-12/SF-36), Visual Analogue Scale (VAS), Profile of Mood States (POMS), and Wisconsin Upper Respiratory Symptom Survey (WURSS-24) [63]. The included studies used beta-glucans from a variety of sources, including oats, yeast, euglena, and shiitake mushrooms, with doses ranging from 1 mg to 3,000 mg per day. Relative to placebo, β-glucan supplementation was associated with significantly reduced feelings of fatigue (SMD: -0.35, 95% CI -0.58 to -0.12), increased vigor (SMD: 0.43, 95% CI 0.22 to 0.63), and improved mood state (SMD: 0.35, 95% CI 0.09 to 0.60). Analysis of the studies suggests that it may take at least four weeks for impacts on fatigue to become noticeable.
A randomized, double-blind, placebo-controlled trial testing 250 mg/day yeast beta-glucan supplementation (ImmunoVita®) for nine months in 65 patients with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) found that the level of improvement on measures related to cognitive fatigue with supplementation were not significantly different from placebo [64].

Safety: Beta-glucans from diverse sources are generally safe and well-tolerated. They may pose safety risks to those allergic to source foods and those taking immunosuppressant medications.

Types of evidence:

- 8 meta-analyses, systematic reviews, or reviews of clinical studies
- Numerous laboratory studies

Beta-glucans from foods and supplements have generally been well-tolerated and show good safety in clinical studies in a wide variety of populations including healthy adults, children, older adults, adults with cardiometabolic conditions, and cancer patients [2; 60]. Adverse events are typically mild, such as mild gastrointestinal events. The primary safety concern is for individuals with allergies to the beta-glucan source (oats, mushrooms, yeast, etc.). Another proposed concern is the risk of immune overstimulation, however, that event has not been an issue in clinical experience to date [28].

Several forms of beta-glucans have generally recognized as safe (GRAS) status from the FDA. Listed below are some of the most commonly used beta-glucans. Beta-glucans from a variety of other specific strains submitted by various manufacturers have also been granted GRAS status.
Oat beta-glucans with intended use in food product used "as a source of fiber at levels resulting in 0.75 to 3.0 grams of beta-glucans per serving" (FDA).
Fungal beta-glucan derived from *Ganoderma lucidum* mycelium (Reishi) for use in food products "at a level of 150 milligrams β-glucans derived from *G. lucidum* mycelium per serving" (FDA).
Fungal beta-glucan derived from *Hericium erinaceus* strain BCRC 35669 (Lion's Mane) for use in food products "at levels up to 150 mg/serving" (FDA).
Bakers yeast beta-glucan derived from *Saccharomyces cerevisiae* for use in food products "at a level of up to 200 milligrams per serving" (FDA).
Similarly, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) issued a Scientific Opinion that both soluble and insoluble "Yeast beta-glucans", defined as "complex, high molecular mass polysaccharides derived from the cell wall of baker's yeast *Saccharomyces cerevisiae*" can be considered safe "at dose levels of up to 375 mg per day and in foods for particular nutritional uses (PARNUTS) at dose levels of up to 600 mg per day" (EFSA).

Drug interactions: Drug interactions with beta-glucan supplements have not been established, but different forms could affect the absorption and activity of various drugs in different ways. Soluble beta-glucans, as a source of dietary fiber, may slow digestion, which could impact drug absorption. Insoluble/fungal beta-glucans can act as immune stimulators, and thus may interact with other immune-modulating agents, particularly immunosuppressants. Beta-glucans could also potentially impact oral drug metabolism through modulation of the gut microbiome.
Moderate interactions have been identified for lentinan, including metoprolol, omeprazole, phenacetin, midazolam, and CYP1A2 substrates (WebMD).

Sources and dosing:

Oats/barley: According to the FDA, whole oat and barley sources that meet the requirements of the health claim regarding risk reduction for coronary heart disease include oat bran, rolled oats, whole oat flour, Oatrim, whole grain barley and dry milled barley, and barley betafiber, at doses of intake of β-glucan soluble fiber from these sources ≥3 grams per day. The EFSA, similarly, indicates that a daily intake of ≥3 grams per day is needed to meet the health claims regarding cardiovascular health [55]. For the health claim related to "the reduction of the blood glucose rise after a meal", the indicated dose is at least 4 grams of soluble oat/barley β-glucans per 30 grams of carbohydrate [56].

Clinically tested sources are listed below, but with the exception of lentinan, none of yeast/fungal-derived β-glucans have approved indications, and the dosing reflects manufacturer recommendations, which are not necessarily optimized.

Baker's yeast-derived β-glucans: Baker's yeast-derived β-glucan supplements have undergone the most clinical testing and shown some immunomodulatory effects in some studies. The manufacturer recommended (and clinically tested dose) for the most clinically tested baker's yeast-derived β-glucan supplement, Wellmune® from Kerry Group's ProActive Health portfolio, is 250 mg/day in the form of oral capsules, which contain a purity of ≥75% high molecular-weight whole glucan particles.

In addition to these, yeast beta-glucans can be obtained through consumption of yeast-based food products, including nutritional yeast and concentrated yeast-extract spreads.

The dose of yeast or mushroom/fungal-derived β-glucans needed to obtain a consistent immunomodulatory effect is not yet clear, as it likely varies based on the preparation.

Mushroom-derived β-glucans:

Lentinan (shitake mushroom-derived β-glucans): The pharmaceutical companies Ajinomoto and Eisai partnered to launch EA Pharma Co., Ltd. (Press release), which is involved in the distribution of pharmaceutical grade lentinan for use in cancer therapy in Japan. It is typically administered via intravenous injection at a dose of 1 to 1.5 mg/day in a hospital setting (NCATS).

Reishi mushroom-derived β-glucans: Immulink MBG® from Super Beta Glucan Inc. (200 mg/day) has been clinically tested and shown modulatory properties (contains ≥75% β-glucans). Reishi β-glucans can also be obtained through Reishi mushroom-based decoctions and supplements.

Pleuran: (*Pleurotus ostreatus*; oyster mushroom-derived β-glucans) Imunoglukan® (100 mg/day) is the source that has been tested in clinical trials and shown immunomodulatory properties.

Mushroom-derived β-glucans can also be obtained through the consumption of mushrooms as part of the diet. However, the levels of β-glucans obtained from a serving of mushrooms will vary depending on the type of mushroom. Standardized, concentrated extracts may be needed to get the level of immunomodulation observed in clinical studies.

Research underway:

According to Clinicaltrials.gov,
Beta glucan (particulate/fungal-derived) is being clinically tested for its immunomodulatory potential in cancer, including as a stand-alone supplement, and as an adjuvant for cancer immunotherapy and anti-cancer vaccines. It is also being tested for its effects on the innate and adaptive immune systems in a medical clinic setting.

Soluble forms of beta glucan (grain-derived) are being tested for their effects on glycemic control, metabolism, weight loss, and cardiovascular risk.

Search terms:
Pubmed, Google: Beta-glucans

- Alzheimer's disease, dementia, cognition, lifespan, cardiovascular, immune, cancer, fatigue, clinical trial, meta-analysis, safety

Websites visited for Beta-glucans:

- Clinicaltrials.gov
- Examine.com
- Drugs.com (Beta-Glucan; Barley; Oats; Brewer's Yeast)
- WebMD.com
- PubChem

- DrugBank.ca
- ConsumerLab.com

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