



How do extracurricular factors (socioeconomic + personal) influence the risk of infection in synthetic versus. nonsynthetic grafts?

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Worldwide 2.2 million bone grafting procedures happen every year to fix bone problems like injuries and diseases that wear down the bones. Doctors are using synthetic bone substitutes more and more in these procedures because they are easy to get and do not cause problems at the site where the bone is taken from. Synthetic bone grafts can be made from different materials, such as polymethylmethacrylate, which is also called PMMA, custom-made PMMA, custom-made titanium mesh and custom-made ceramics like alumina ceramics and hydroxyapatite. There are also options like bone morphogenetic proteins, demineralized bone matrix and composite grafting materials. All of these are used in procedures. Because these synthetic grafts are put into the body they are grouped based on how they work with the body. Some help the bone grow, some encourage the bone to heal. Some can be absorbed by the body. However PMMA does not help the bone grow or heal. Research shows that PMMA is the commonly used material that does not have any biological properties. Custom-made PMMA grafts are the same. The problem with synthetic bone grafts is that they can cause infections and be rejected by the body compared to using the patients own bone. This is because the body sees the graft as foreign and can react to it. Synthetic grafts also do not have living cells, which can make it harder for them to become a part of the existing bone. This can create an environment where bacteria can grow easily making infections more likely.

Overall synthetic bone grafts are useful when the patients own bone cannot be used. However they can cause problems like infections and rejection. All of these sources show that synthetic bone graft materials are very different and work in ways.. They all have some important limitations compared to using the patients own tissue. Materials like PMMA and other custom-made synthetics can provide support. They do not have the properties that help the bone grow naturally. Even when these synthetic grafts have additives that help the bone heal they still do not work well as the patients own bone. The body sees these materials, as foreign which can cause problems and make infections more likely. This is why synthetic grafts can cause infections, rejection and delayed healing compared to using the patients own bone.

Now bone grafts are not always easy to deal with. The truth is, people who do not have a lot of money face health problems when they are getting better. One study found that people who earn wages are almost twice as likely to have a bone fracture as people who earn higher wages (Zhao et al., 2024). These bone fractures can lead to problems like getting an infection, which can make it take longer to get better.

Other research also shows that people with incomes are more likely to get an infection after having bone graft surgery. A study looked at different factors and found that people, with lower incomes,

who are older and who have other health problems are more likely to get an infection after surgery (Chang et al., 2016). Worrying about money makes it even harder to get better. People who do not have a lot of money often feel more stressed and anxious because of their bills. One study found that people who worry about money are more likely to feel stressed and anxious especially if they do not have a lot of money (Kim et al. 2022). When people are stressed their bodies are less able to fight off infections, which can make them more likely to get sick. Not having insurance can make things even worse by making people worry more about money and feel more stressed which can make them more vulnerable when they are getting better. Bone grafts are a thing and people need to be aware of the risks, especially bone grafts.

Overall, these findings heavily suggest how socioeconomic factors can significantly shape a patient's recovery process. Individuals with lower income levels face greater risks of complications - such as fractures and postoperative infections - due to both biological and environmental disadvantages. The research shows a clear pattern: lower wages are linked with higher fracture risk, and patients with limited financial resources are more likely to develop infections after bone-grafting procedures. Additionally, financial stress - often intensified by costly medical treatments - can heighten psychological distress, which may further hinder recovery. Together, these studies emphasize that financial status and related stressors are not peripheral issues but central determinants of health outcomes.

Not to mention, chronic conditions such as obesity and diabetes play a significant role in delayed healing and increased infection risk following bone graft procedures. Diabetes, in particular, is well documented as a major risk factor for infections due to its negative effects on immune function, circulation, and wound healing. According to StatPearls, "*Diabetes presents a significant risk factor for all kinds of infections*" (Klekotka & Mizgala-Izworska, 2023). Poor glycemic control impairs leukocyte function and reduces the body's ability to fight pathogens, making diabetic patients more susceptible to postoperative complications, including infections at surgical and graft sites. These risks are not limited to bone grafts but extend to surgical procedures overall. Obesity further compounds these risks and is strongly associated with the development of type 2 diabetes. Obesity contributes to chronic inflammation, impaired immune response, and reduced tissue oxygenation, all of which hinder wound healing. One review notes that "*obesity increases the risk of type 2 diabetes mellitus, hypertension, obstructive sleep apnea, osteoarthritis, cardiovascular diseases, and certain types of cancers*" (Hruby & Hu, 2015). Because obesity is a leading contributor to type 2 diabetes, individuals with obesity are more likely to experience diabetes-related complications, including an elevated risk of infection. The relationship between obesity, diabetes, and infection risk is particularly relevant in bone graft procedures, which rely heavily on adequate blood supply and immune response for successful healing. While both obesity and diabetes independently increase the risk of postoperative infection, diabetes poses a more direct and significant threat due to its profound impact on immune system function. Together, these chronic conditions substantially increase the likelihood of infection and delayed recovery following bone graft surgery.

These findings demonstrate how chronic conditions like obesity and diabetes significantly influence the risk of complications during the bone-graft healing process. Diabetes, which weakens the immune system, is shown to be a major risk factor for a wide range of infections, making recovery more difficult and less predictable. Obesity further contributes to this

issue by increasing the likelihood of developing type 2 diabetes and other health problems that can interfere with healing. Because obesity and diabetes are closely linked, their combined effects place patients at a heightened risk for postoperative infections. Overall, these conditions play a substantial role in determining recovery outcomes, with diabetes presenting the greater threat.

While on the topic of health decreasers, stress also plays a major role, similar to diabetes and other health issues, in the body's ability to heal, and high stress levels are associated with an increased risk of infection. When the body is under stress, it struggles to rest effectively, which is a crucial component of recovery. According to a large population-based study, stress-related disorders were associated with all studied life-threatening infections, demonstrating that stress is a significant contributing factor to infection risk (Song et al., 2019). Additionally, chronic stress negatively affects immune function. The Cleveland Clinic explains that stress increases the production of cortisol, a hormone that can temporarily enhance immunity by reducing inflammation. However, prolonged exposure to elevated cortisol levels causes the body to adapt, leading to increased inflammation and weakened immune defenses, which raises susceptibility to infections (Cleveland Clinic, 2022). Together, these findings show that sustained stress can impair immune regulation and significantly increase the risk of infection.

Overall, these findings make it clear that stress is a powerful factor influencing healing and infection risk. When someone experiences high levels of stress, the body struggles to rest and repair itself properly, which slows recovery. Research shows that stress-related disorders are linked with a wide range of serious infections, emphasizing how deeply stress can affect the immune system. Long-term stress also leads to consistently elevated cortisol levels, which eventually cause increased inflammation rather than protection. This inflammation then makes the body more vulnerable to infection. Altogether, stress significantly disrupts the healing process and raises the likelihood of complications.

Donor (allograft) bone or tissue undergoes a rigorous, multistep screening and processing protocol before being approved for clinical use. First, potential donors are carefully evaluated through a comprehensive medical history review, social and behavioral risk assessment, and physical examination. Screening criteria established by the American Association of Tissue Banks (AATB) and regulations from the U.S. Food and Drug Administration (FDA) are used to exclude donors with risk factors for transmissible diseases, such as intravenous drug use or high-risk behaviors (American Academy of Orthopaedic Surgeons [AAOS], n.d.; FDA, 2020). After tissue harvest, grafts are processed under sterile, controlled clean-room conditions. During processing, bone marrow, lipids, and debris are removed, and the tissue is disinfected using chemical detergents or aqueous solvents, often in combination with antibiotic solutions. The grafts are then thoroughly rinsed to eliminate residual processing agents (Tomford, 2000). Finally, grafts may undergo terminal sterilization—most commonly low-dose gamma irradiation—to inactivate bacteria, viruses, fungi, and spores. Alternatively, tissues may be aseptically packaged and subjected to microbiological testing before release to ensure the absence of contamination (AAOS, n.d.; Tomford, 2000). Despite these stringent safeguards, donor tissue grafts carry inherent biological and ethical risks. Biologically, there remains a small but unavoidable risk of disease transmission, as no screening or sterilization method can detect or eliminate all potential pathogens (Tomford, 2000; Regen

Allograft, n.d.). Ethically, the use of cadaveric or deceased donors raises concerns regarding informed consent, donor anonymity, equitable allocation, and transparent communication of risks and benefits to recipients. Donor-related variability—including donor health, bone quality, handling, and storage conditions—can influence graft performance. For example, “fresh-frozen” allografts may avoid high-dose irradiation or harsh chemical sterilization to preserve biological and structural properties, but this approach can involve a trade-off between improved graft integrity and a slightly higher residual infection risk (Regen Allograft, n.d.; Tomford, 2000). Compatibility between donor and recipient can also influence graft success, although this factor appears less critical for bone allografts than for solid organ transplantation. Experimental animal studies have shown that deep-frozen bone allografts can remodel and integrate effectively even when donor and recipient are mismatched at the major histocompatibility complex (MHC), with no detectable alloantibody response and biomechanical properties comparable to syngeneic grafts (Friedlaender et al., 1984). Clinically, reviews of large bone-graft series suggest that properly processed allografts demonstrate relatively high integration and volume-retention rates, though they are generally slightly lower than those of autografts. One review reported approximately 85% integration and 80% volume retention for allografts, compared with roughly 95% integration and 90% volume retention for autografts (Younger & Chapman, 1989). Processing methods, particularly irradiation versus non-irradiation, can significantly affect biomechanical strength and long-term outcomes, highlighting the importance of both biological compatibility and graft processing history (Younger & Chapman, 1989).

Using donor (non-synthetic) grafts entails balancing the benefits of biologically relevant, “natural” bone tissue with the risks inherent to transplantation. The rigorous screening and sterilization protocols developed by tissue banks significantly reduce - though cannot entirely eliminate - the risk of disease transmission, and careful processing aims to preserve structural integrity while maximizing safety. While immunologic mismatch (e.g., MHC disparity) seems to have limited impact on bone graft healing in many contexts, the processing history (freezing, irradiation, sterilization) and donor-derived variables remain nontrivial factors in graft success. Overall, non-synthetic grafts offer a compromise: better biological compatibility and potential for integration than purely synthetic materials, but with some residual risk and variability that must be managed through stringent protocols and careful donor/graft selection.

Exercise, nutrition, and body weight each play a measurable role in bone healing after grafting. Controlled mechanical loading through low-impact exercise can stimulate osteoblast activity and enhance bone remodeling, whereas excessive or premature loading may impair graft stability; animal and clinical studies show that appropriately dosed mechanical stress accelerates callus formation and mineralization (e.g., Goodship & Kenwright, 1985; Turner, 1998). Nutritionally, adequate intake of calcium, vitamin D, protein, and micronutrients such as magnesium and vitamin K is essential, as deficiencies slow mineral deposition and collagen synthesis—two processes required for graft incorporation (Heaney, 2000; Bonjour, 2011). Body weight also influences outcomes: obesity has been associated with delayed bone healing and impaired angiogenesis due to chronic low-grade inflammation and altered cytokine signaling, while underweight patients may lack the nutritional reserves necessary for normal tissue repair (Brown et al., 2014). Together, these factors directly shape the biological environment in which the graft must integrate. Stress and insufficient sleep can significantly hinder bone healing through hormonal and metabolic pathways. Elevated stress hormones, particularly cortisol,



suppress osteoblast differentiation, reduce bone formation, and impair immune function, all of which can slow graft incorporation (Manolagas, 2000; Clow et al., 2014). Similarly, sleep deprivation alters the secretion of growth hormone, melatonin, and inflammatory cytokines, disrupting the anabolic processes needed for bone repair. Experimental studies demonstrate that chronic sleep restriction reduces bone density, weakens trabecular architecture, and delays fracture healing in animal models (Ikegami et al., 2018; Endo et al., 2015). In humans, poor sleep quality correlates with higher postoperative pain, slower recovery, and heightened stress responses, suggesting that sleep hygiene is an important modifiable factor in bone graft success. Specific habits and structured rehabilitation programs can improve graft outcomes by optimizing mechanical stability and biological healing. Gradual physical-therapy protocols that incorporate progressive loading, balance training, and range-of-motion exercises have been shown to enhance circulation, stimulate osteogenesis, and reduce postoperative stiffness without compromising graft integrity (Garrison & Choi, 2019). Additionally, lifestyle practices such as smoking cessation, adequate protein intake, and vitamin D supplementation are consistently linked to improved bone regeneration and reduced complication rates (Kanis et al., 2013). Together, these interventions help create a supportive physical and metabolic environment that facilitates graft integration.

Overall, lifestyle factors play a substantial but often underappreciated role in bone graft success. While surgical technique and graft material determine the immediate structural outcome, long-term healing depends heavily on the patient's biological environment- shaped by nutrition, exercise, hormonal balance, sleep quality, and daily habits. Optimizing these factors can significantly improve graft incorporation, reduce complications, and support faster, more resilient recovery.

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BONE GRAFT MATERIALS

AUTOGRAFT	ALLOGRAFT	XENOGRAFT	SYNTHETIC
			
PROS	PROS	PROS	PROS
<ul style="list-style-type: none">+ No immune rejection	<ul style="list-style-type: none">+ No donor site+ Readily available	<ul style="list-style-type: none">+ Abundant supply- Slower healing	<ul style="list-style-type: none">+ No risk of disease- Unlimited supply
CONS	CONS	CONS	CONS
<ul style="list-style-type: none">- Donor site morbidity- Limited quantity	<ul style="list-style-type: none">- Risk of disease transmission- Variable healing	<ul style="list-style-type: none">- Possible immune reaction- Slower healing	<ul style="list-style-type: none">- Lacks natural properties- Variable healing

Figure 1: Bone graft materials overview

Diagram adapter from (<https://dentalimplantsdallastx.com/dental-implant-and-bone-graft/>) demonstrating the patient pros and cons of specific bone grafting materials including Autograft, allograft, xenograft and synthetic materials