BHOF
Bone Health & Osteoporosis FOUNDATION™
Healthy Bones, Build Them for Life

Osteoporosis Medications: Biologics & Biosimilars

BHOF Building Strength Together® Support Groups

November 7, 2024

How Can Osteoporosis Medicines Help?

- The skeleton is an active vital organ. It keeps you healthy through a constant process of repair, renewal, and mineral release. This process is called remodeling.

- The bone remodeling cycle consists of two distinct stages: (1) bone resorption (breakdown and removal) and (2) bone formation (generation of new bone). As we age, the remodeling process can become unbalanced. More old bone gets removed than new bone gets created.

- The goal of osteoporosis therapy is to try to restore the balance of bone resorption and formation to reduce bone loss.

- It can be done by slowing resorption through use of antiresorptive medication or by promoting bone formation using anabolic medication. By doing so, these therapies lower the risk for fractures, which is the goal of treatment.

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Diagnosis of Osteoporosis → Treatment Categories

T-score –2.5 or below in the lumbar spine, femoral neck, total proximal femur, or 1/3 radius

Low-trauma spine or hip fracture (*regardless of bone mineral density*)

T-score between –1.0 and –2.5 ***and*** a fragility fracture of proximal humerus, pelvis, or distal forearm

T-score between –1.0 and –2.5 *and* high FRAX® (or if available, TBS-adjusted FRAX®) fracture probability based on country-specific thresholds

Shobach D et al. *J Clin Endocrinol Metab*. 2020 Mar 1;105:dgaa048 (Endocrine Society Guidelines)
Camacho PM et al. *Endocr Pract*. 2020;26(supp 1):1-46 (AACE/ACE Guidelines)
LeBoff M, et al. *Osteoporos Int.* 2022. doi.org/10.1007/s00198-021-05900-y (Bone Health and Osteoporosis Foundation)
Menopause. 2021;28(9):973-997 (NAMS – North American Menopause Society)
Chelmow D, et al. Obstet Gynecol. 2021;138(3):494-506. (ACOG – American College of Obstetrics and Gynecology)
Pinkerton JV, et al. Obstet Gynecol. 2022;139(4):698-717 (ACOG)

Treating the Whole Person: Non-pharmacologic Interventions

Strength/Resistance training
≥2 days/week

Balance training
Daily for ≥15-20 minutes

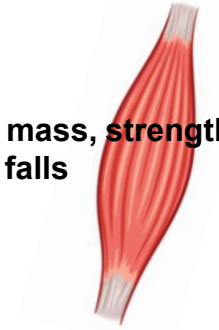
Aerobic exercise
≥5 days/week, ≥30 minutes

Vitamin D
1000 IU/day or more

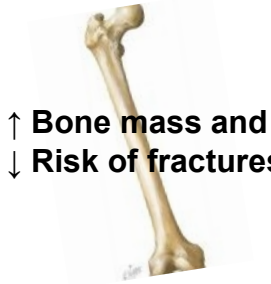
Calcium
1200 mg/day total from all sources

Protein 1-1.5 g/kg/day to preserve muscle mass and function

Balanced diet



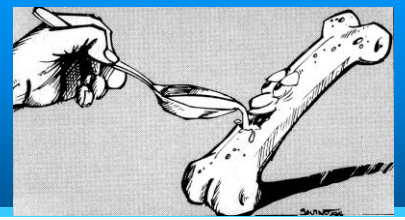
↑ Muscle mass, strength and balance
↓ Risk of falls



↑ Bone mass and strength
↓ Risk of fractures

Kirk et al. J Cachexia Sarcopenia Muscle. 2020; www.bonefit.ca

Osteoporosis Treatment Options



- Anti-remodeling (antiresorptive) agents *(inhibit resorption more than formation)*
  - Estrogen, Estrogen/Progestin, Estrogen/Bazedoxifene
  - Estrogen agonist/antagonist (raloxifene)
  - Bisphosphonates
    - alendronate, risedronate, ibandronate, zoledronate
  - RANK ligand inhibitor (denosumab)
  - Calcitonin
- Osteoanabolic agents *(activate bone formation)*
  - Remodeling stimulators (*increase formation and resorption)*
    - Parathyroid hormone receptor activators (teriparatide, abaloparatide)
  - Modeling stimulator *(increases formation, decreases resorption)*
    - Sclerostin inhibitor (romosozumab)

PERSPECTIVE

JBMR®

Treated Osteoporosis Is Still Osteoporosis

E Michael Lewiecki,[1] Neil Binkley,[2] and John P Bilezikian[3]

- **Osteoporosis is a lifelong disease that warrants lifelong attention**
- **Osteoporosis can be treated effectively, fracture risk can be reduced, but there is no "cure"**
- **Retaining the diagnosis is consistent with other chronic diseases (diabetes, hypertension, etc)**
- **Adverse consequences of changing diagnosis to "osteopenia" include**
  - False sense of security
  - Stopping medication that is still needed
  - Potential loss of insurance coverage for medication
  - Change in allowable frequency of BMD testing

Lewiecki EM et al. J Bone Miner Res. 2019;34(4):605-606.

Summary of What I Tell Patients (Andrea Singer, MD)

- All approved osteoporosis drugs increase bone density and reduce fracture risk
- Only anabolic drugs build new bone and improve structure
- Any treatment is better than none, but when fracture risk is very high, it is ideal to begin with an anabolic drug
- Anabolic therapy must be followed by an antiresorptive drug to consolidate and enhance the benefits achieved
- Osteoporosis is a lifelong disease that warrants lifelong attention
- All drugs stop working when stopped

Biologics and Biosimilars

- What is a Biologic?
- What is a Biosimilar?
- How are Biosimilars Approved by the FDA?

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Types of Drugs: Chemical vs Biologic

Chemical Drugs

- Well defined composition
- Simple structure
- Small size
- Minimal or no variation
- Often more than one target in your body
- Usually taken by mouth

Brand | Generic

Biologic Drugs

- Composition defined to a certain extent
- Complex structure
- Big size
- Significant (micro) variation
- Often highly specific
- Often must be injected or infused

Reference | Biosimilar

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Pharmacol Res. 2018 Jul;133:251-264.

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Types of Drugs: Chemical vs Biologic

Chemical Drugs

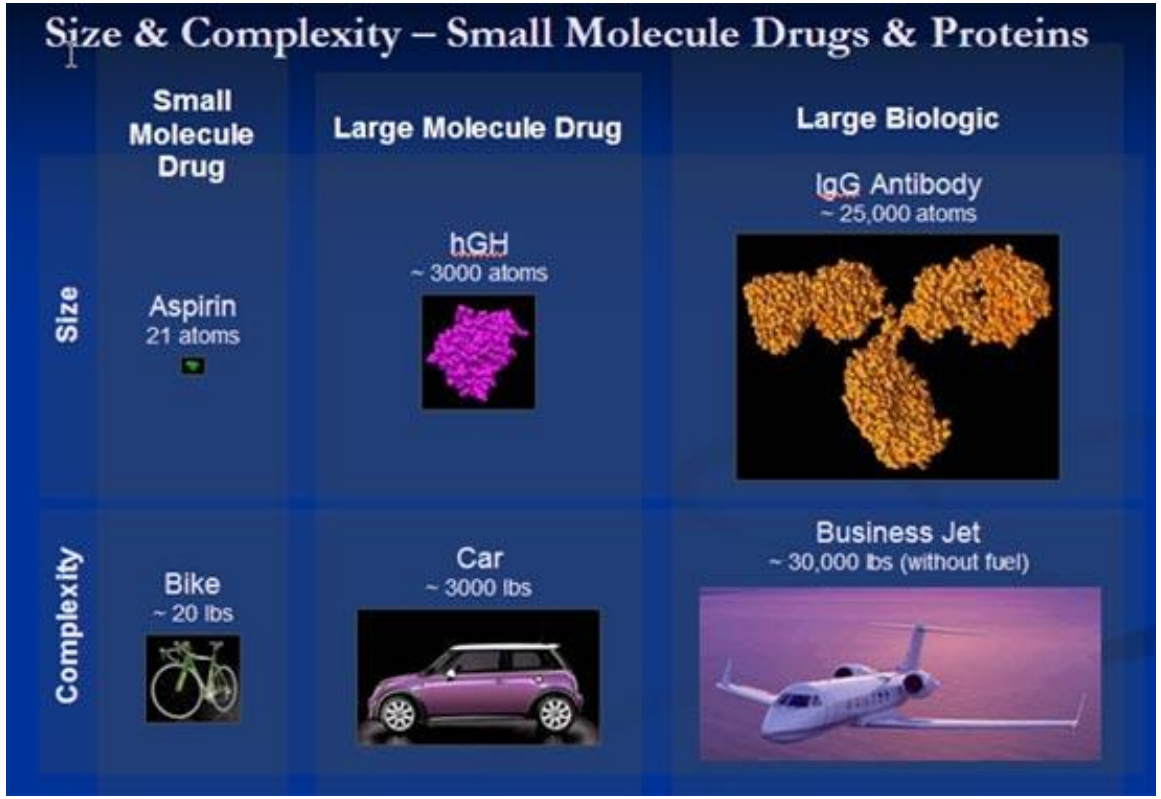
- Examples:
  - **aspirin**
  - **ibuprofen** (Motrin® - pain reliever)
  - **atorvastatin** (Lipitor® - cholesterol medicine)
  - **metoprolol** (Toprol® - blood pressure medicine)
  - **azithromycin** (Zithromax® - antibiotic)

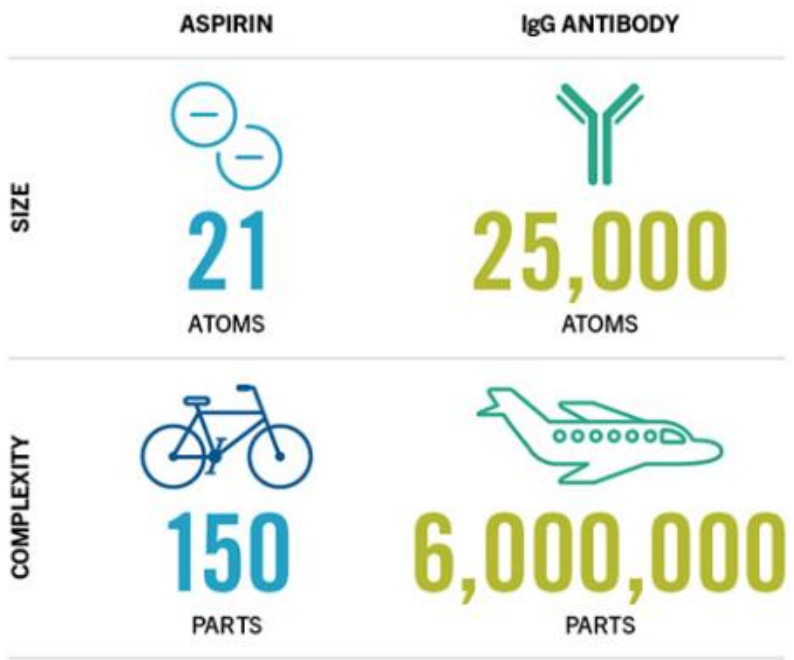
Biologic Drugs

- Examples:
  - **adalimumab** (Humira® - anti-inflammatory)
  - **denosumab** (Prolia®, Xgeva® - bone anti-resorptive)
  - **trastuzumab** (Herceptin® - breast cancer)
  - **pegfilgrastim** (Neulasta® - treats low white blood cell counts)

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Types of Drugs: Chemical vs Biologic





https://www.azbio.org/small-molecules-large-biologics-and-the-biosimilar-debate
https://www.gene.com/stories/similar-not-the-same-the-road-ahead-for-biosimilars?topic=oncology

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Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biologics

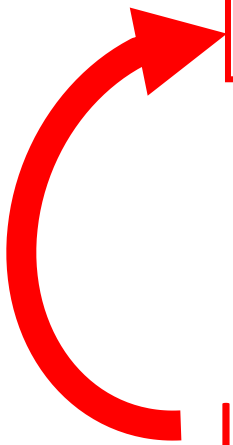
- Biologic products may be:
  - proteins that control the action of other proteins and cells in your body
  - genes that control production of proteins
  - modified human hormones
  - cells that produce substances that suppress or activate components of your immune system

https://www.medicinenet.com/biologics_biologic_drug_class/article.htm

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biologics – How they are Made

- A biologic drug is made:
  - by a living organism (e.g., antibodies)
  - or contains parts of a living organism (e.g., vaccines, blood components)

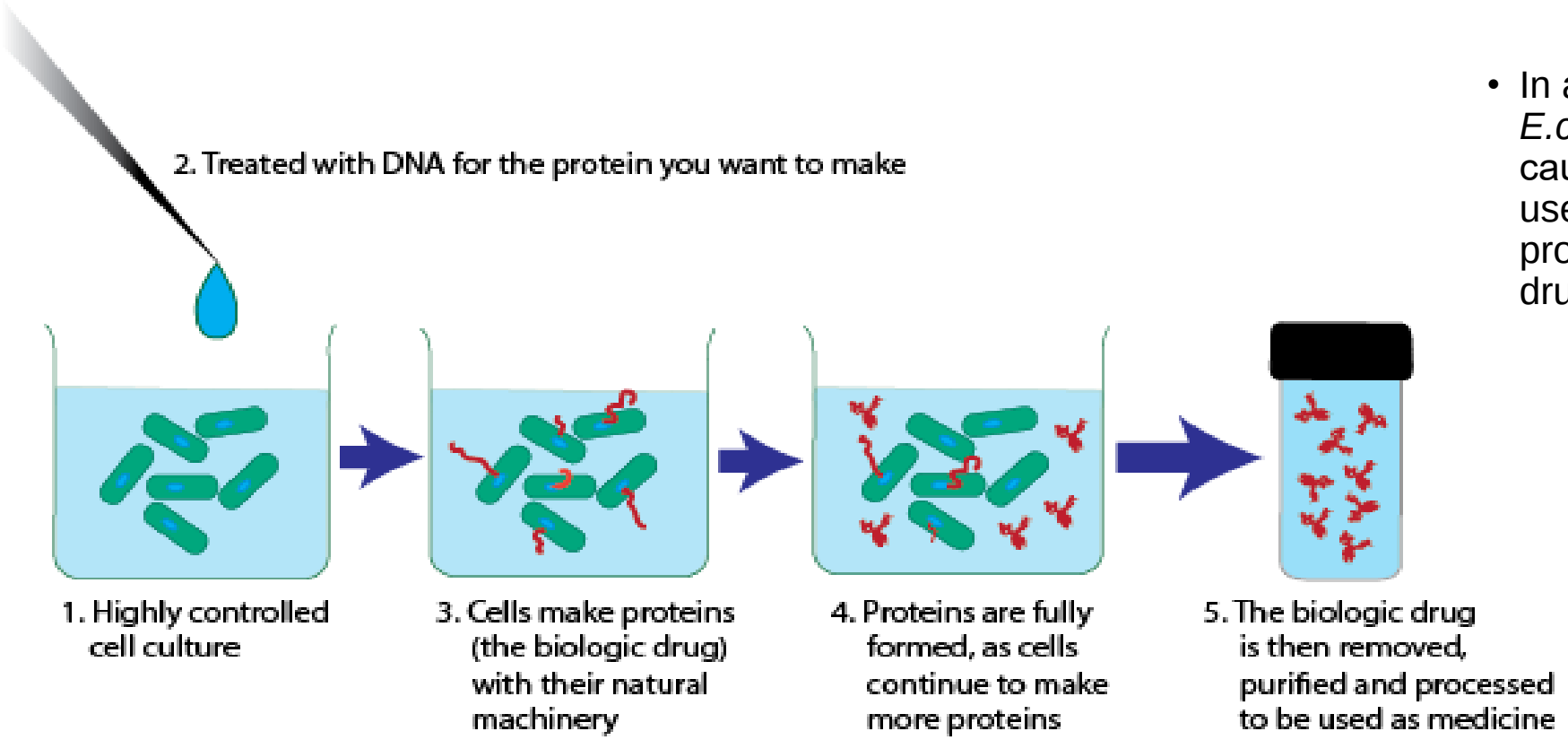


Let's look at this kind of drug

https://www.medicinenet.com/biologics_biologic_drug_class/article.htm

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biologics – How they are Made



- In a laboratory, cells (often *E.coli* cells – not the kind that cause food poisoning…) are used to produce specific proteins that become biologic drugs

https://weekly.biotechprimer.com/biomanufacturing-how-biologics-are-made/

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biologics – The Details

Question: How do you get from the strand made by the cells, to a final biologic drug?

Answer: Protein folding

https://www.news-medical.net/life-sciences/Protein-Folding.aspx

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biologics – The Details

- Protein folding:

  VERY complex process, sensitive to the environment and conditions

  DOES NOT fold EXACTLY the same each time even with the exact same order of amino acids…but some variability has no effect on how it works in your body

https://www.news-medical.net/life-sciences/Protein-Folding.aspx

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biosimilars

A biosimilar is a biologic drug!

Biosimilars – FDA Definition

- *Biosimilar* or *Biosimilarity* – "the biological product is **highly similar** to the reference product notwithstanding minor differences in clinically inactive components" and "there are **no clinically meaningful differences** between the biological product and the reference product in terms of the safety, purity, and potency of the product"

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[PHS Act Section 351(i)(2)]

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biosimilars

- Biosimilars are tested and approved by the FDA for safety and quality (since 2015).
- They are designed to be as effective as the original reference drug.
- They work the same way in the body.
- They are made in the same dose and strength. They have the same potential side effects.
- Biosimilars drugs are made by a different manufacturer and will have different names than the original reference drug.

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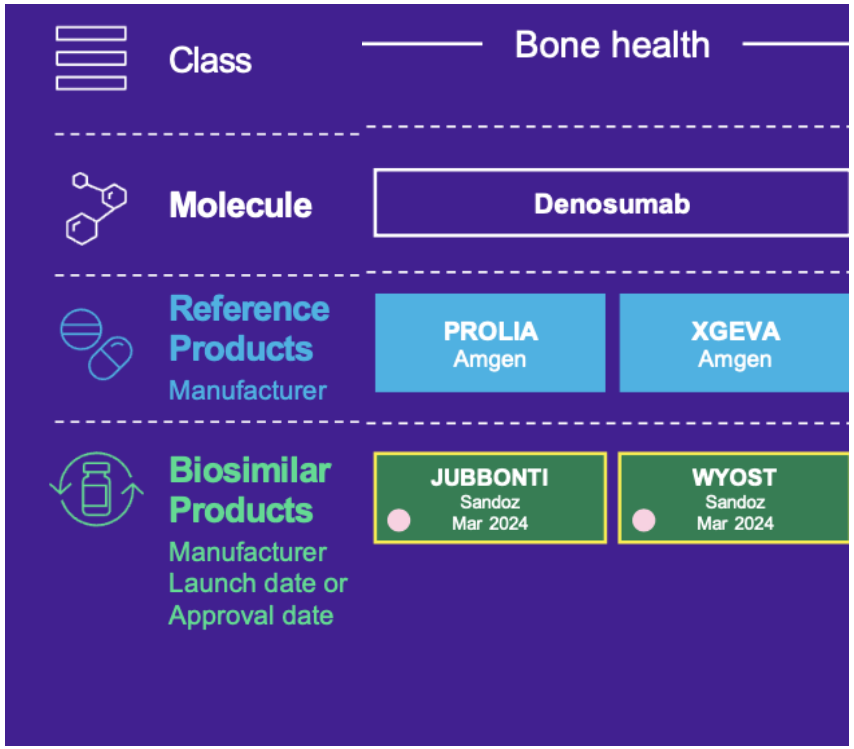
www.fda.gov/biosimilars

Available Biosimilars

- Biosimilars have been approved and launched in the U.S. since 2015

- Classes of biosimilars include Supportive Care, Oncology, Insulin, Ophthalmology, Immunomodulators, and now Bone Health

FDA Approved Biosimilars-Pending Availability



Denosumab- Treatment for:

- Osteoporosis
- Fracture risk due to chemotherapy

https://www.amerisourcebergen.com/insights/manufacturers/biosimilar-pipeline-report

Source: Biologics and Biosimilars Collective Intelligence Consortium (BBCIC)

Biosimilars for Bone Health in the Future

- The first denosumab biosimilar was approved in 2024
- Other biosimilars of bone health reference drugs are expected to be approved in the future
- Biosimilars were established by the FDA to improve patient access and affordability
- If a biosimilar is an osteoporosis treatment option for you it's important to talk to your insurance company about coverage

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Stay Connected!

- Visit www.bonehealthandosteoporosis.org and www.pathtogoodbonehealth.org for more resources
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- Stay connected on Facebook and Instagram
- If you have any questions, please contact info@bonehealthandosteoporosis.org

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Thank You!