

# The Intersection of Heart Disease and Breast Cancer: A Clinical Cardiologist's Perspective

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October 20, 2022

# Case Example

- 57-year-old woman with a history of obesity and high blood pressure was referred to a cardio-oncology clinic during therapy for breast cancer
- She had completed 4 cycles of chemotherapy with doxorubicin as well as 3 months of trastuzumab (Herceptin) of a planned 12-month course
- She was asymptomatic, however her echo showed changes

# Baseline



# 3-month echo

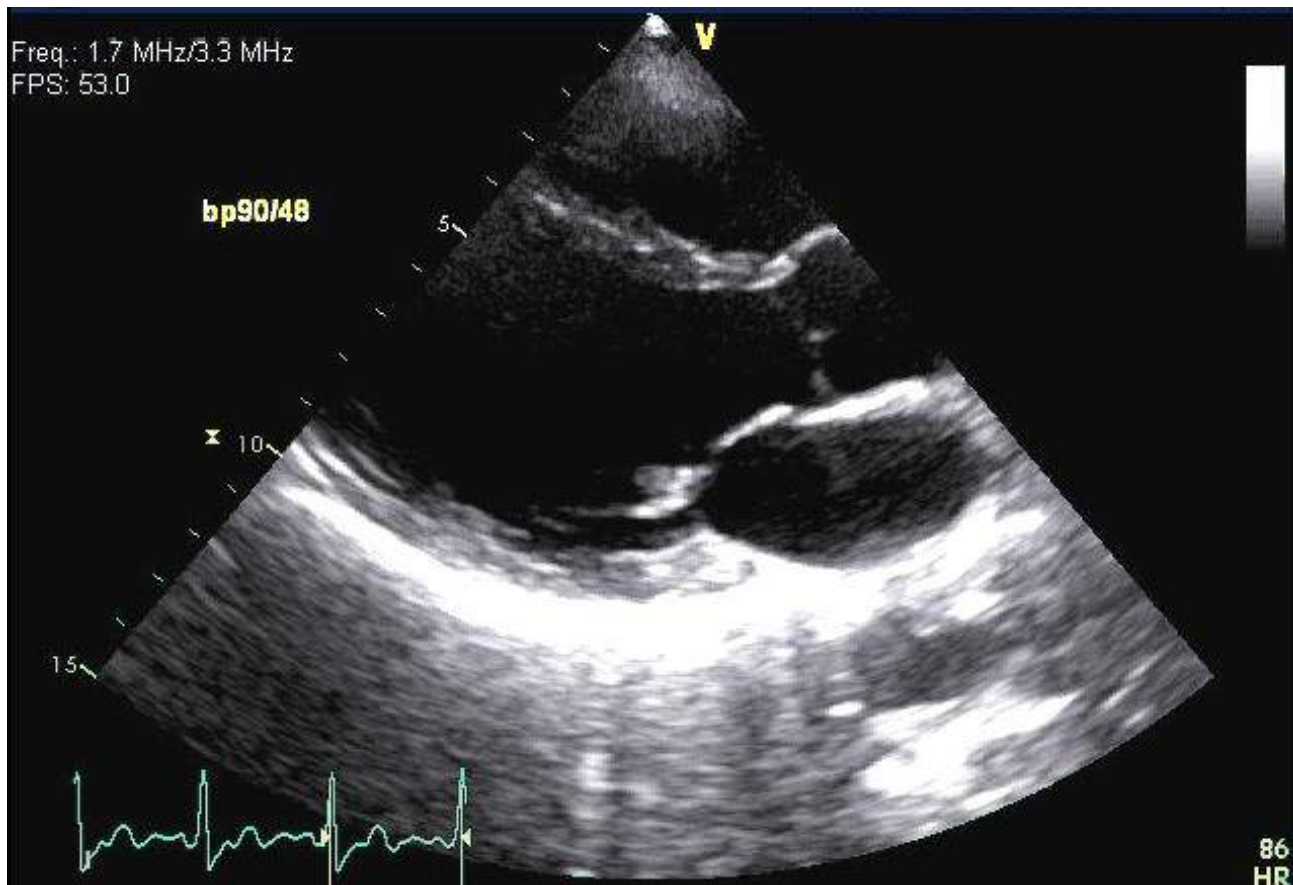


Left ventricular ejection fraction (LVEF)  
decreased from 60% to 49%

# Therapy

- Medical therapy with carvedilol and lisinopril
- Transition to a whole-food plant-based diet low in sodium (<2 grams/day)
- Moderate physical activity of at least 30 minutes, 5 days/week

# Following Treatment







# Outline

- Scope of the Problem, Risk Factors and Prevention
- Chemotherapy cardio-toxicity
  - Anthracyclines
  - Trastuzumab
- Prevention – The Whole-Food Plant-Based Diet

# Scope of the Problem – The Intersection of Cardiology and Oncology

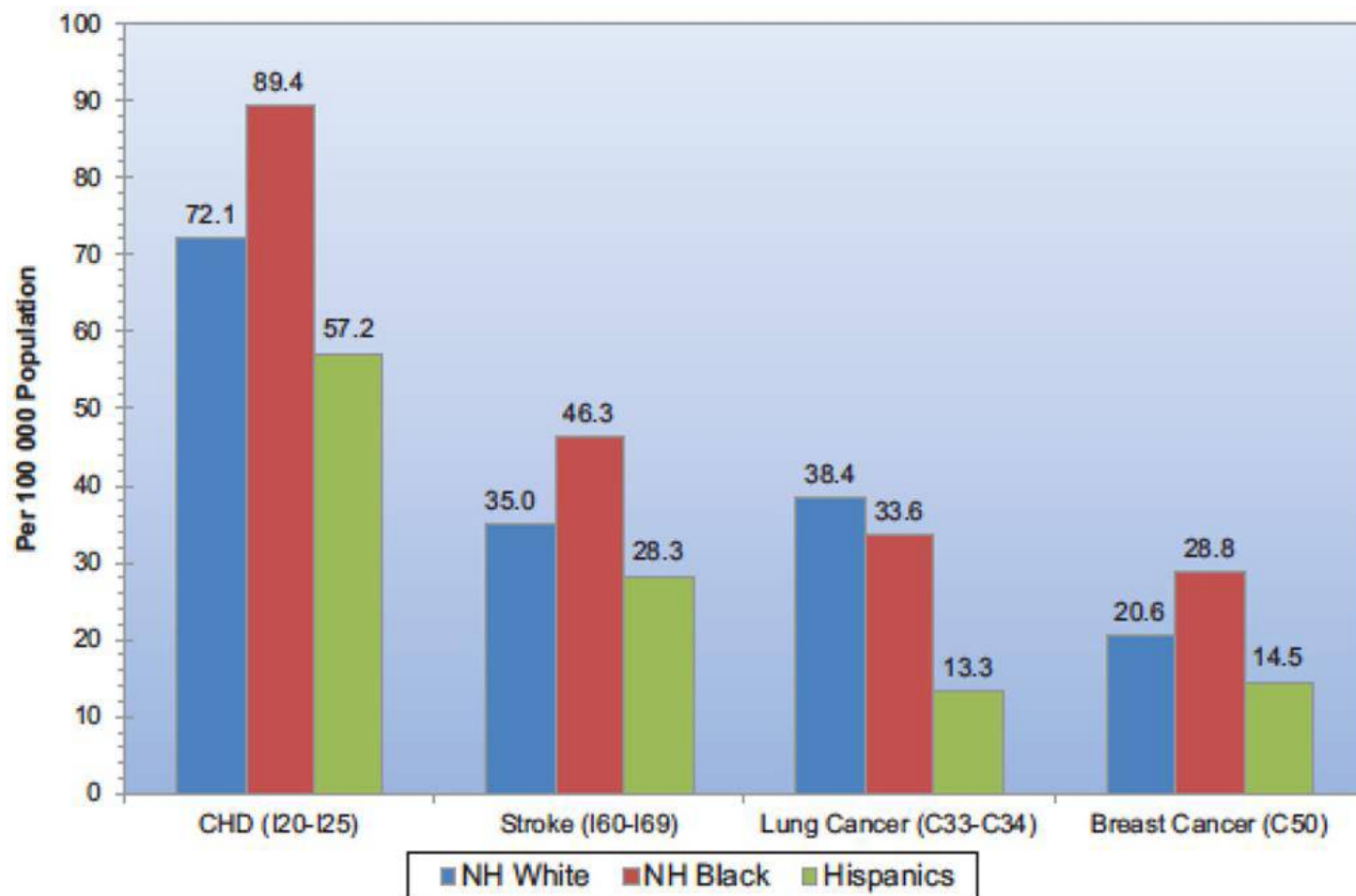
- 18 million cancer survivors projected to be 22 million by 2030
- Cancer patients are living longer
  - Higher odds of developing CV disease
- Changing therapies/targeted therapies
  - Improved cancer outcomes
  - More side effects, including cardiovascular

# Sites of New Cancer Cases and Deaths – 2022 Estimates

Estimated New Cases	Male					Female		
Prostate	268,490	27%				Breast	287,850	31%
Lung & bronchus	117,910	12%				Lung & bronchus	118,830	13%
Colon & rectum	80,690	8%				Colon & rectum	70,340	8%
Urinary bladder	61,700	6%				Uterine corpus	65,950	7%
Melanoma of the skin	57,180	6%				Melanoma of the skin	42,600	5%
Kidney & renal pelvis	50,290	5%				Non-Hodgkin lymphoma	36,350	4%
Non-Hodgkin lymphoma	44,120	4%				Thyroid	31,940	3%
Oral cavity & pharynx	38,700	4%				Pancreas	29,240	3%
Leukemia	35,810	4%				Kidney & renal pelvis	28,710	3%
Pancreas	32,970	3%				Leukemia	24,840	3%
All sites	983,160					All sites	934,870	

Estimated Deaths	Male					Female		
Lung & bronchus	68,820	21%				Lung & bronchus	61,360	21%
Prostate	34,500	11%				Breast	43,250	15%
Colon & rectum	28,400	9%				Colon & rectum	24,180	8%
Pancreas	25,970	8%				Pancreas	23,860	8%
Liver & intrahepatic bile duct	20,420	6%				Ovary	12,810	4%
Leukemia	14,020	4%				Uterine corpus	12,550	4%
Esophagus	13,250	4%				Liver & intrahepatic bile duct	10,100	4%
Urinary bladder	12,120	4%				Leukemia	9,980	3%
Non-Hodgkin lymphoma	11,700	4%				Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,710	3%				Brain & other nervous system	7,570	3%
All sites	322,090					All sites	287,270	

# CV Disease and Cancer in Women: Age-Adjusted Mortality Rates



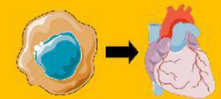
Source: Mehta LS, et al. Circulation 2018

# Cancer ↔ CV Disease

**Cardio-Oncology Syndrome (COS):** Neoplastic disorders and Cardiovascular disease whereby direct or indirect mechanisms associated with the one condition induces acute or chronic presence of the other

## **COS Type I** (Direct)

Progressive development of cancer leads to CV disease



## **COS Type II** (Indirect)

Cancer associated treatments causing CV disease



## **COS Type III** (Direct)

Progressive scarring and remodeling of heart and kidney causing a pro-oncogenic environment



## **COS Type IV** (Indirect)

CV disease associated treatments and diagnostics causing a pro-oncogenic environment



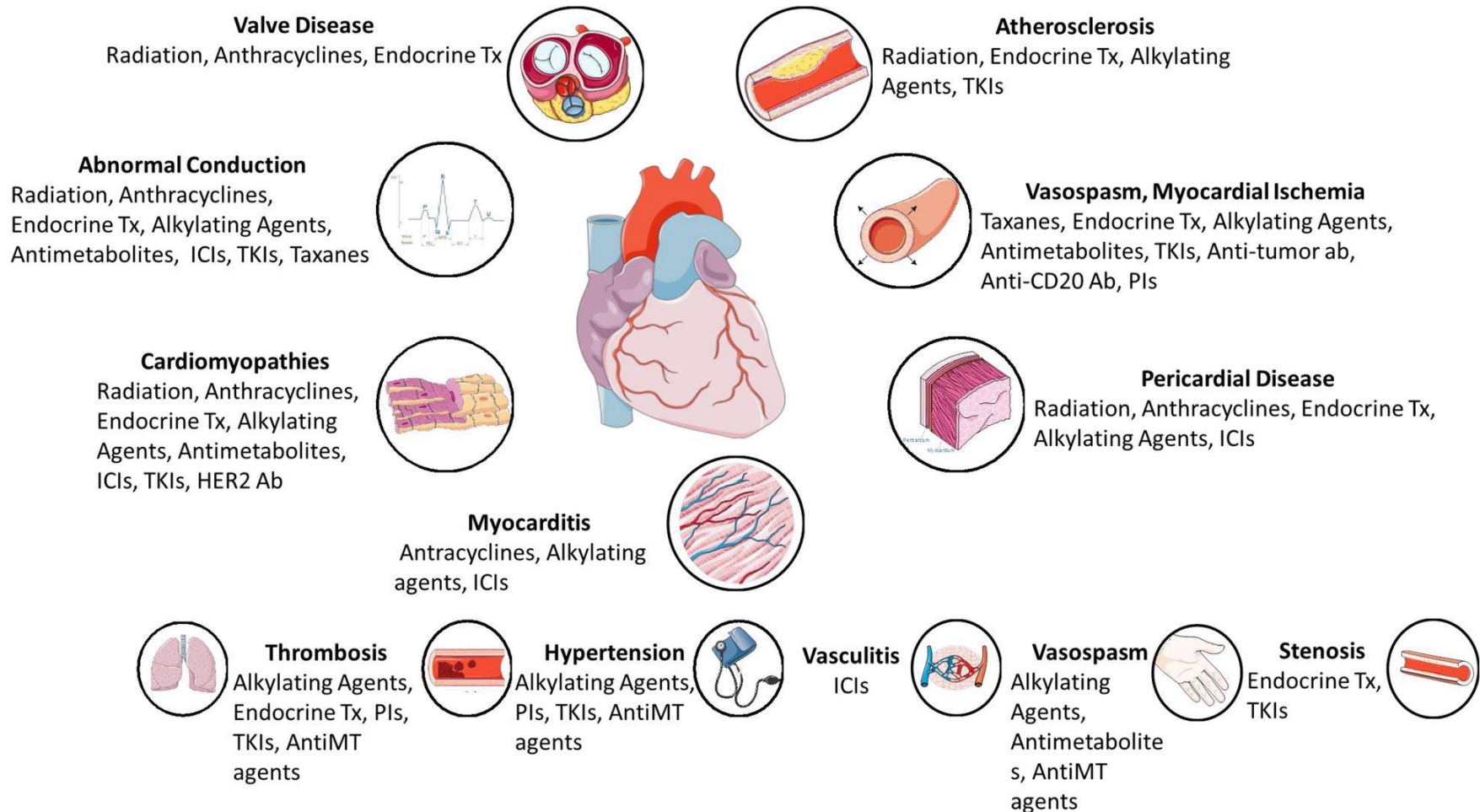
## **COS Type V** (Secondary)

Systemic and genetic conditions causing both cancer and CV disease

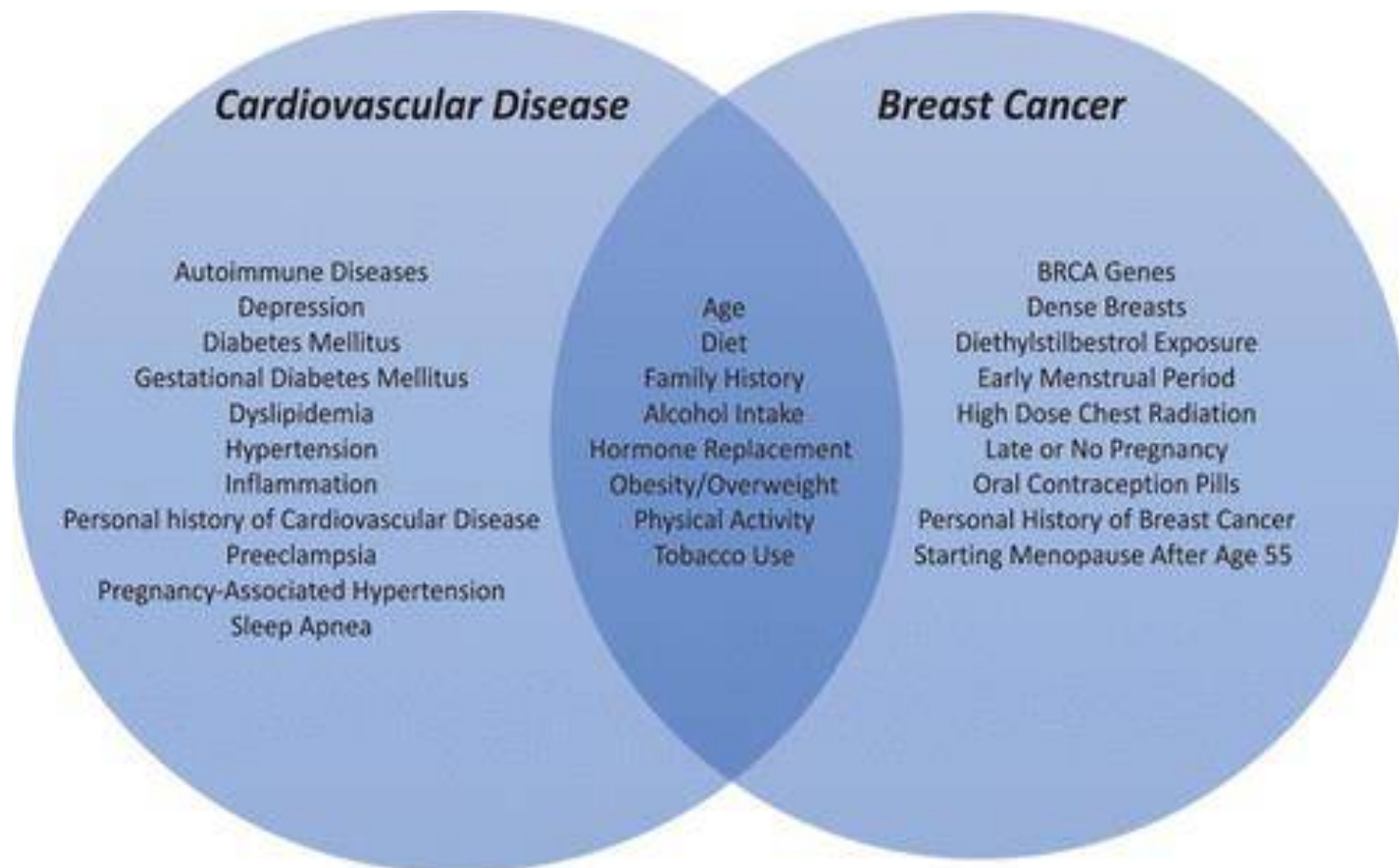




# Types of cardiovascular toxicity



# Risk Factors for CV Disease and Breast Cancer



# Anthracyclines



# Anthracyclines - Basics

- Have been used since the 1950s in adults and children
  - breast cancer, lymphoma, GU/Gyn cancers, ALL/AML, and sarcomas
- “Red Medicine”
- See heart failure and LV dysfunction
  - Incidence rises with increasing doses (7%, 18%, and 65% at cumulative doses of doxorubicin 150 mg/m<sup>2</sup>, 350 mg/m<sup>2</sup>, and 550 mg/m<sup>2</sup>, respectively)

# Toxicity Types

- Acute
  - During therapy (can be during infusion and within 2-3 days of administration)
  - E.g, palpitations due arrhythmias, EKG changes, and chest pain due to myopericarditis
- Subacute
  - Within 1 year
- Chronic
  - Late effects
  - Can be as late as 10-20 years due to a “second hit”

# Monitoring

- Transthoracic Echocardiogram (TTE) is the main way to monitor patients
- Assess baseline LV function prior to therapy, after 4 cycles, and 6-12 months after completion of therapy
- Long-term monitoring is not well defined

# Perspective

- Cardiac dysfunction affects cardiovascular outcomes as well as oncological therapeutic options
- LVEF at the end of chemo and the cumulative dose are independently associated with cardiotoxicity
- With therapy, over 80% of patients recover LVEF either fully or partially
- Cardiac surveillance based only on symptoms (e.g., shortness of breath or leg swelling) might miss the opportunity to treat early

Trastuzumab

# Monoclonal Ab Tyrosine Kinase Inhibitor – Trastuzumab (Herceptin)

## The New England Journal of Medicine

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VOLUME 344

MARCH 15, 2001

NUMBER 11

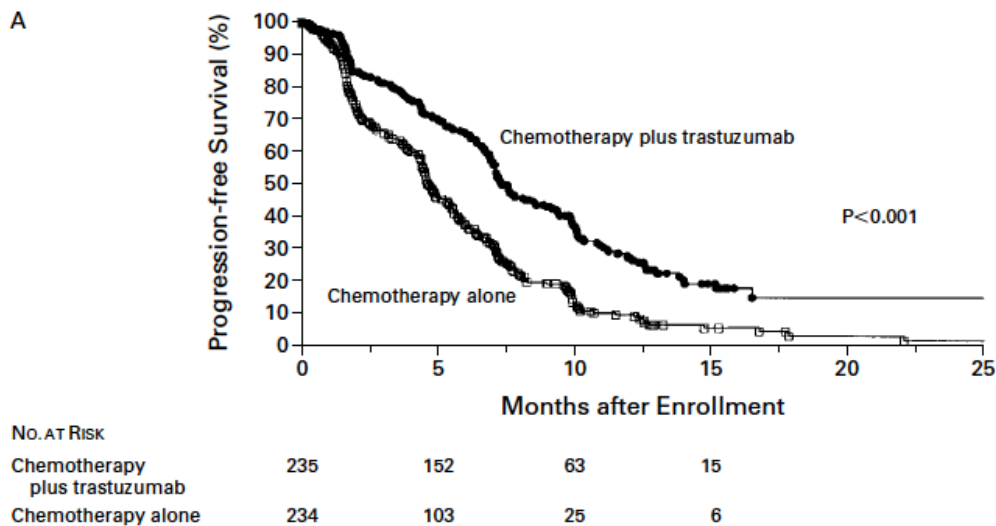


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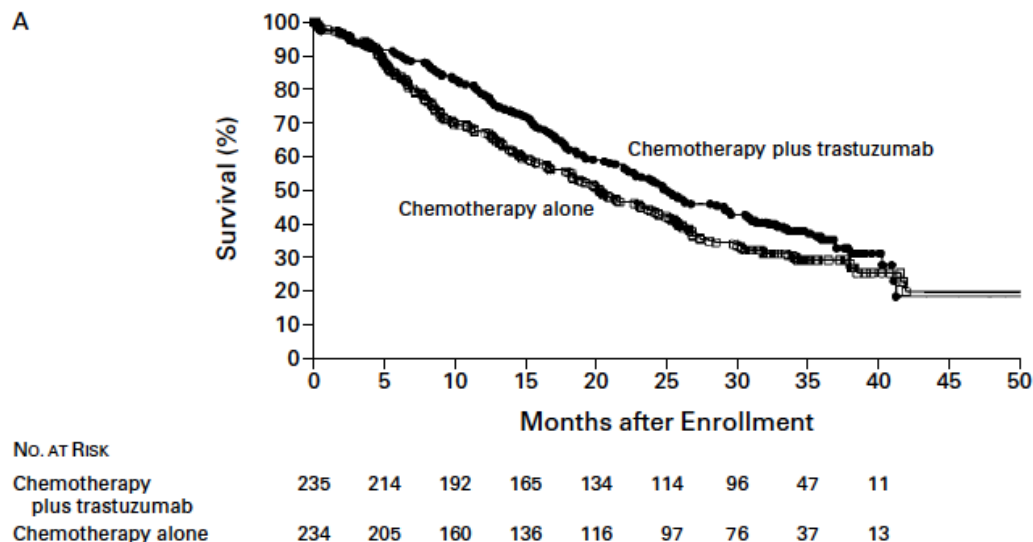
### USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2

DENNIS J. SLAMON, M.D., PH.D., BRIAN LEYLAND-JONES, M.D., STEVEN SHAK, M.D., HANK FUCHS, M.D.,  
VIRGINIA PATON, PHARM.D., ALEX BAJAMONDE, PH.D., THOMAS FLEMING, PH.D., WOLFGANG EIERMANN, M.D.,  
JANET WOLTER, M.D., MARK PEGRAM, M.D., JOSE BASELGA, M.D., AND LARRY NORTON, M.D.\*

# Marked increase in progression-free survival and overall survival with trastuzumab



Lower rate of death at 1 year:  
22% vs 33% ( $p = .008$ )



# Cardio-toxicity with Trastuzumab

- **63/235** patients with symptomatic or asymptomatic cardiac dysfunction
- Trastuzumab discontinued in 18/235 (8% overall) patients overall due to cardiac dysfunction, most of whom received an anthracycline as well.
- **Continued use of trastuzumab did not cause deterioration of cardiac function in most patients.**
- Cardiac function improved in 75% of patients who received trastuzumab who received standard medical therapy for LV dysfunction.



# Risk Factors for Cardio-toxicity

- Combination with anthracyclines
  - Either concomitant or past
  - Increases at higher doses ( $>250 \text{ mg/m}^2$  doxorubicin)
- Pre-existing Cardiac Conditions
  - HF, LV systolic dysfunction, CAD, Afib, Htn, HLD
- DM
- Obesity ( $\text{BMI} \geq 30 \text{ kg/m}^2$ )
- Renal Failure
- Age ( $\geq 60$ )
- Black Race

# Drug Monitoring (per FDA)

- Baseline LVEF measurement immediately prior to initiation of Trastuzumab
- LVEF measurements every 3 months during and upon completion of Trastuzumab
- LVEF measurements every 6 months for at least 2 years following completion of Trastuzumab as a component of adjuvant therapy
  - This would come out to 9 echos/person for a typical 1-year course

# Drug Discontinuation

- Withhold Trastuzumab for  $\geq 16\%$  absolute decrease in LVEF from pre-treatment values or an LVEF value below institutional limits of normal and  $\geq 10\%$  absolute decrease in LVEF from pretreatment values
- Measure LVEF every 4 weeks if agent is held for cardiomyopathy
- Trastuzumab may be resumed if, within 4–8 weeks, the LVEF returns to normal limits and the absolute decrease from baseline is  $\leq 15\%$
- Permanently discontinue Trastuzumab for a persistent ( $> 8$  weeks) LVEF decline or for suspension of Trastuzumab dosing on more than 3 occasions for cardiomyopathy

# An Ounce of Prevention: The Whole-Food Plant- Based Diet

# A whole-foods plant-based diet means eating foods:

- That are whole with little to no processing
- That come from plants, including vegetables, whole grains, nuts, seeds, legumes and fruits
- With no animal products (no dairy, eggs, etc.) and small amounts of healthy fats



# Why a whole-food plant-based diet?

- The more fruits and vegetables we eat the less room we will have for high fat, high sodium, high cholesterol and processed foods
- Processing robs foods of vital nutrients and their main purpose which is to nourish
- Plants are naturally low in fat, sugar, and salt, are cholesterol free (only animals make cholesterol - beef, chicken, fish, and pork), plus high in fiber, phytochemicals, and antioxidants

# What is the difference between Vegan and WFPB diet?

Food	Vegan Diet	Whole Food, Plant-Based Diet
Fresh Vegetables	Yes	Yes
Dairy	No	No
Raw Honey	No	Yes
Refined Sugar	Yes	No
Most Breads	Yes	No
Olive Oil	Yes	No



VEGAN



WHOLE FOOD,  
PLANT-BASED



# THE PLANT-BASED HEALTHY PLATE

Use this plate to help you portion your food in a healthy way and make meal planning easier. Portions are based on a small dinner plate.

Fill one-quarter of your plate with a plant-based protein source, such as cooked beans, lentils, or tofu.



Fill half of your plate with non-starchy vegetables, such as carrots, broccoli, spinach, cabbage, green beans, peppers, zucchini, onions, greens, tomatoes, or romaine lettuce.



Fill one-quarter of your plate with healthy grains or starches, such as brown rice, whole-wheat pasta, quinoa, bulgur, corn, peas, barley, farro, amaranth, 1 slice of whole-grain bread, 2 corn tortillas, or 1 whole-wheat tortilla.

## For good nutrition also choose each day:

- 3 servings of fruit. A serving is a small orange, banana, or apple, or 1 cup of berries or melon.
- 2 to 3 cups of a milk substitute, such as almond, soy, or hemp.
- A small amount of healthy fats



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## Ideas for meals and snacks

These sample meals and snacks include foods from the shopping list below, and follow the tips on the other side. Use these ideas to build healthy, tasty meals. Or create your favorite combinations!

### Breakfast

- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>4 oz. sprouted-grain or wheat bagel with almond butter or cashew cheese</li> <li>1 cup diced melon</li> </ul>                                    | <ul style="list-style-type: none"> <li>½ cup scrambled soft tofu with 3 oz. salsa and 1 cup spinach</li> <li>1 sprouted-grain English muffin or 2 corn tortillas</li> <li>½ avocado</li> <li>½ cup mango or pineapple</li> </ul> |
| <ul style="list-style-type: none"> <li>2 oz. whole-grain muesli cereal</li> <li>½ banana, ½ cup berries</li> <li>10 walnuts</li> <li>1 cup nondairy milk</li> </ul>                     | <ul style="list-style-type: none"> <li>2 slices sprouted-grain or wheat toast</li> <li>2 Tbsp. "natural" peanut butter</li> <li>1 cup nondairy milk</li> <li>1 small apple</li> </ul>  |
| <ul style="list-style-type: none"> <li>1 cup plain almond or soy yogurt, mixed with 1 Tbsp. chia seeds and 2 Tbsp. raisins or ½ cup diced fruit</li> <li>1 small bran muffin</li> </ul> | <ul style="list-style-type: none"> <li>¾ cup brown rice</li> <li>½ cup beans</li> <li>1 cup cooked vegetables</li> <li>½ cup salsa</li> <li>½ cup avocado</li> </ul>   |
| <ul style="list-style-type: none"> <li>2 slices sprouted-grain or wheat toast</li> <li>1 cup berries</li> <li>1 cup nondairy milk</li> </ul>  | <ul style="list-style-type: none"> <li>1 cup oatmeal with 1 Tbsp. pumpkin seeds and 2 Tbsp. raisins or dried fruit</li> <li>1 cup nondairy milk</li> </ul>   |

### Snacks

- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>½ cup baked sweet potato</li> <li>2 tbsp. dried fruit or nuts</li> </ul> | <ul style="list-style-type: none"> <li>Raw vegetables with hummus or vegetable paté</li> </ul>            |
| <ul style="list-style-type: none"> <li>Fresh fruit</li> </ul>   | <ul style="list-style-type: none"> <li>Medium apple with 1-2 Tbsp. "natural" peanut butter</li> </ul>     |
| <ul style="list-style-type: none"> <li>3 cups air-popped or light microwave popcorn</li> </ul>                  | <ul style="list-style-type: none"> <li>3 large rye wafer cracker</li> <li>1½ oz. cashew cheese</li> </ul> |
| <ul style="list-style-type: none"> <li>½ cup roasted garbanzo beans</li> </ul>                                  | <ul style="list-style-type: none"> <li>Fresh nonstarchy vegetables</li> </ul>                             |

### Healthy meals start at the store. Use this shopping list to help you prepare.

- |  |  |   |
|--|--|---|
| <ul style="list-style-type: none"> <li>✓ Fruits—fresh, frozen, canned in their own juice, or dried</li> <li>✓ Vegetables—fresh, frozen, or low-sodium canned</li> <li>✓ Plain nondairy milk (fortified soy, rice, oat, or almond)</li> <li>✓ Plain nondairy yogurt (soy or almond)</li> <li>✓ "Natural" peanut or other nut butter</li> <li>✓ Cultured cashew cheese</li> <li>✓ Olive or organic canola oil</li> </ul> | <ul style="list-style-type: none"> <li>✓ Light soy sauce, tamari, or Bragg's liquid aminos</li> <li>✓ Sauerkraut or kimchee</li> <li>✓ Whole beans (canned or dried), or lentils</li> <li>✓ Hummus, bean spreads, or tahini</li> <li>✓ Tofu (silken, firm), tempeh</li> <li>✓ Avocado, olives, or sun-dried tomatoes</li> <li>✓ Unsalted nuts and seeds</li> <li>✓ Nutritional yeast</li> <li>✓ Vegetable broth</li> </ul> | <ul style="list-style-type: none"> <li>✓ 100% whole-wheat or sprouted-grain bread, rolls, or bagels</li> <li>✓ Rye wafer or whole-wheat crackers</li> <li>✓ Brown rice or whole-wheat pasta</li> <li>✓ Whole-grain cereal (oats, or muesli)</li> <li>✓ Whole grains (bulgur, whole cornmeal, hulled barley, farro, millet, whole-wheat couscous, brown rice, or quinoa)</li> <li>✓ Tortillas (corn, or whole- or sprouted-wheat)</li> </ul> |
|--|--|---|

This information is not intended to diagnose health problems or to take the place of medical advice or care you receive from your physician or other medical professional. If you have persistent health problems, or if you have additional questions, please consult with your doctor.

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### Lunch and Dinner

Add 1 cup nondairy milk to each meal (optional)

- |   |  |
|---|--|
| <ul style="list-style-type: none"> <li>4 oz. baked tofu sandwich on sprouted-grain or wheat bread with 1-2 Tbsp. avocado, lettuce or spinach, tomato, and onion</li> <li>Carrots or broccoli</li> <li>1 orange</li> </ul>                     | <ul style="list-style-type: none"> <li>2 cups stir-fried vegetables (sautéed with 1 tsp. olive oil and garlic)</li> <li>1 cup quinoa, yam, or whole-grain pasta</li> </ul>   |
| <ul style="list-style-type: none"> <li>3-4 oz. veggie (bean, lentil, soy) burger on sprouted-grain or wheat bun</li> <li>Garden salad with avocado and 1-2 Tbsp. oil and vinegar dressing</li> <li>Diced peaches or pear</li> </ul>           | <ul style="list-style-type: none"> <li>2 cups vegetarian chili</li> <li>2 Tbsp. pumpkin seeds or avocado</li> <li>1 cup cabbage slaw with lime juice</li> <li>½ cantaloupe</li> </ul>  |
| <ul style="list-style-type: none"> <li>1 cup canned black bean soup (lower sodium)</li> <li>1 cup kale (dropped into soup)</li> <li>6 whole-grain crackers</li> <li>1 apple</li> </ul>  | <p><b>Chinese cuisine</b></p> <ul style="list-style-type: none"> <li>½ cup brown rice, wild rice, or quinoa</li> <li>1 cup broccoli tofu (sautéed in broth)</li> <li>1 cup vegetarian hot-and-sour soup</li> </ul>                 |
| <ul style="list-style-type: none"> <li>1 low-fat, low-sodium frozen entrée or vegetarian entrée</li> <li>Green salad with fresh vegetables, nutritional yeast, 1-2 Tbsp. olive oil and vinegar dressing or avocado</li> <li>1 plum</li> </ul> | <p><b>Indian cuisine</b></p> <ul style="list-style-type: none"> <li>½ cup beans or 1 cup lentil soup (dal)</li> <li>1 whole-grain flatbread</li> <li>1 cup diced cauliflower, onions, and tomatoes</li> </ul>                      |
| <ul style="list-style-type: none"> <li>½-1 cup black-eyed peas</li> <li>1 cup steamed greens with a dash of hot sauce</li> <li>1 cup brown rice</li> <li>1 fresh fruit</li> </ul>   | <p><b>Mexican cuisine</b></p> <ul style="list-style-type: none"> <li>2 bean tacos made with 2 corn tortillas, 1 cup whole beans, 2 Tbsp. avocado, salsa, shredded lettuce or cabbage, and tomatoes</li> <li>Diced mango</li> </ul> |



## Chinese cuisine

- ½ cup brown rice, wild rice, or quinoa
- 1 cup broccoli tofu (sautéed in broth)
- 1 cup vegetarian hot-and-sour soup

## Indian cuisine

- ½ cup beans or 1 cup lentil soup (dal)
- 1 whole-grain flatbread
- 1 cup diced cauliflower, onions, and tomatoes

## Mexican cuisine

- 2 bean tacos made with 2 corn tortillas, 1 cup whole beans, 2 Tbsp. avocado, salsa, shredded lettuce or cabbage, and tomatoes
- Diced mango

# EVIDENCE-BASED Eating Guide:

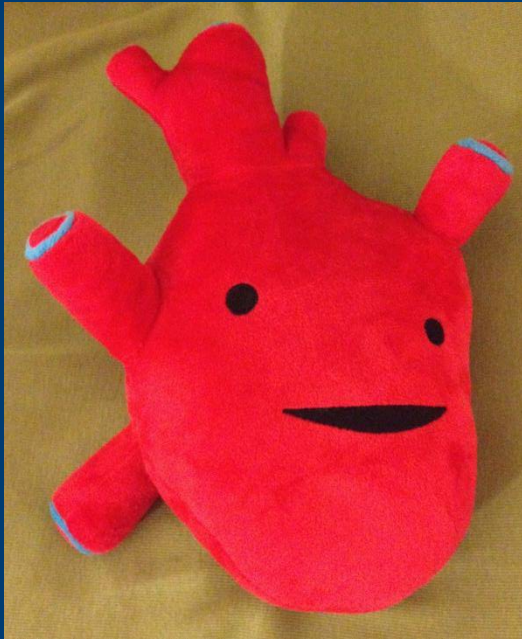
A Healthy Living Resource from  
Dr. Greger & NutritionFacts.org



# The Daily Dozen



# Thank You!



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