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The Changing Landscape of Medical Oncology

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November 7, 2019

Disclosure

This presenter has no financial interest or other relationships with manufacturers of commercial products, suppliers of commercial services, or commercial supporters.

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Objectives

- Examine the scope of systemic therapies available to oncology patients
- Discuss how changes in cancer management have impacted the patient experience
- Understand quality initiatives and their impact on contemporary oncology care
- Identify differences among the current generations and their expectations of care

Evolution of Cancer Therapy

Immunotherapy
1998 IL-2/melanoma
2011 ipilimumab/melanoma
2014 nivoulmab & pembrolizumab/melanoma
2015 nivolumab & pembrolizumab/lung cancer

Targeted therapy
1997 rituximab/lymphoma
1998 trastuzumab/Her2+ breast cancer
2001 imatinib/CML

Supportive therapy
1997 odansetron approved
1998 filgrastim approved

Chemotherapy
1956: MTX used to cure stage IV choriocarcinoma
1957: Bone marrow transplants (6 patients) published in NEJM
1958: combination chemotherapy successfully used in acute leukemia

8/27/42 JD receives 'substance X' for lymphoma

1914-1918 WWI "chemists' war"
1917 mustard gas kills 10,000 people in Ypres, Belgium

Radiation
1898 Pierre and Marie Curie identify radium as a source of radiation

Surgery
1882: Halsted mastectomy, common until 1960s

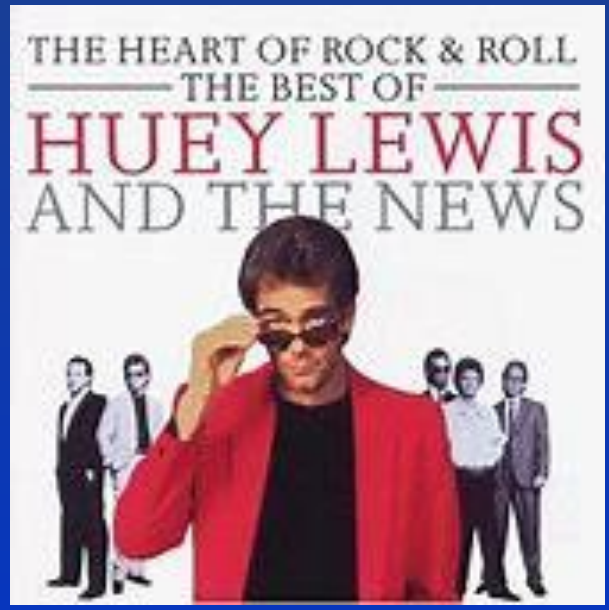
Chemotherapy

- Systemic therapy impacting replication of rapidly diving cells
- Relatively non-specific
- Side effects reflect ‘collateral damage’ to non-cancer cells
- Classic examples:
  - adriamycin
  - 5-flurouracil
  - paclitaxel

Gold Standard for New Agents

I want a new drug, One that won't make me sick
One that won't make me crash my car, Or make me feel three feet thick
I want a new drug, One that won't hurt my head
One that won't make my mouth too dry, Or make my eyes too red
I want a new drug, One that won't spill
One that don't cost too much, Or come in a pill
I want a new drug, One that won't go away
One that won't keep me up all night, One that won't make me sleep all day
I want a new drug, One that does what it should
One that won't make me feel too bad; One that won't make me feel too good
I want a new drug; One with no doubt
One that won't make me talk too much; Or make my face break out

One that won't make me nervous, Wondering what to do?
One that makes me feel like I feel when I'm with you



-“I Want a New Drug”, Huey Lewis and Christopher John Hayes, 1983

Targeted Therapy

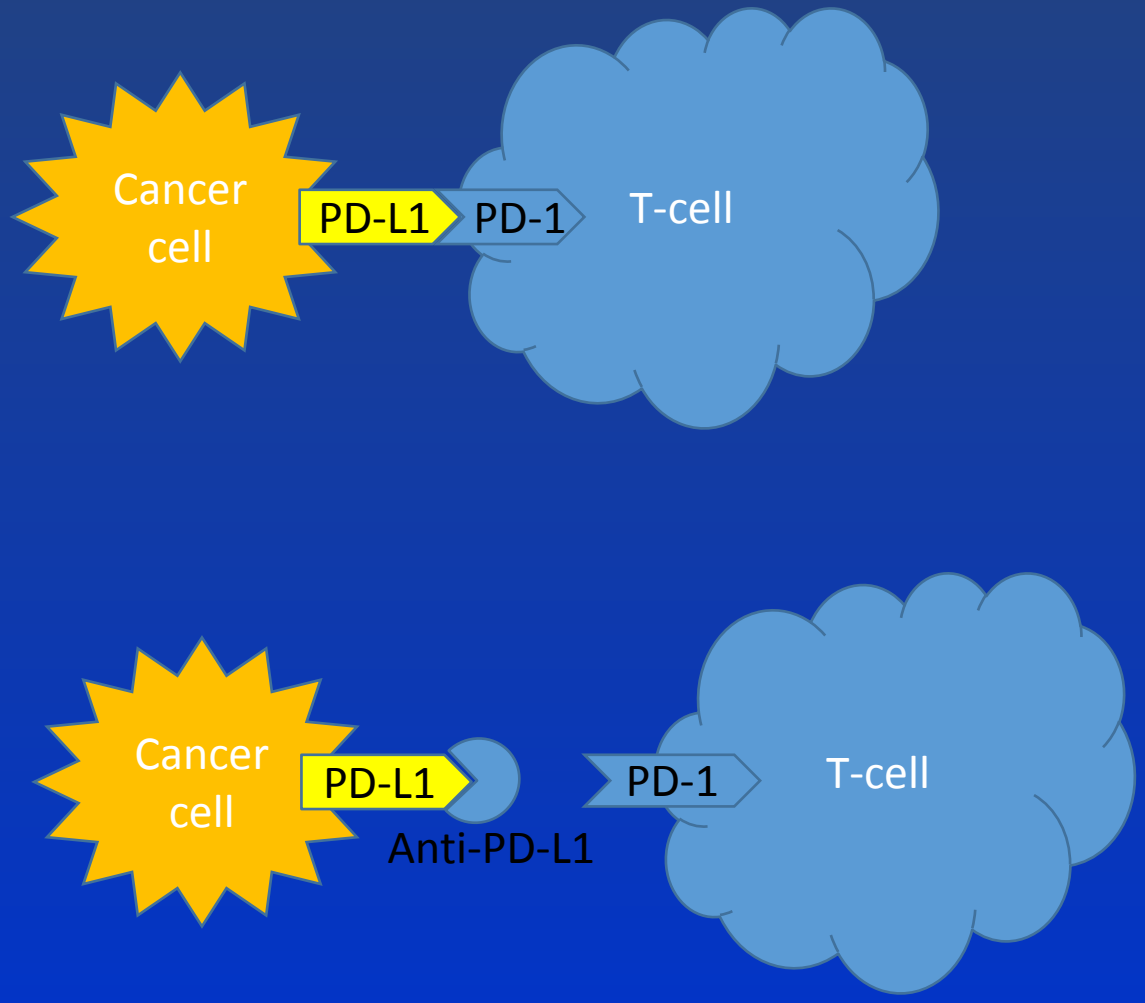
- Typically specific to proteins with limited expression on or inside cancer cell
- Less collateral damage but still potentially significant side effects
- Examples:
  - **tamoxifen:** oral agent, prevents dimerization of estrogen receptor in breast cancer patients
  - **bevacizumab:** IV anti angiogenesis agent
  - **olaparib, rucaparib:** oral PARP inhibitors used in ovarian, breast, prostate patients with BRCA mutations
  - **brentuximab vedotin:** IV antibody-drug conjugate targeting CD30 in lymphoma
  - **venetoclax:** oral BCL-2 inhibitor for CLL & AML

Immunotherapy

- Manipulates the immune system to identify and attack the cancer cell
- Side effects reflect over-active immune system or auto-immunity
- Has evolved over time
  - Promoting/increasing the natural immune response, relatively non-specific
    - Interferon, IL-2
  - Tumor specific immune response with checkpoint inhibitors
    - Ipilimumab, nivolumab, pembrolizumab, others

Blocking PD-L1/PD-1 interaction

releases the immune system to recognize and kill the cancer cell



Checkpoint Inhibitors are Approved for:

Bladder
Breast
Cervical
Colorectal
Cutaneous squamous cell
Gastric
Head/neck cancer
Hepatocellular
Lung cancer (small and non-small cell)
Lymphoma
Melanoma
Merkel call
Renal cell
MSI-H or dMMR tumors

Translational Research

- Bench to Bedside... and Back
- Basic science
- Therapeutic clinical trials
  - Physician
  - Patient
  - Research team
  - Clinic team
  - Large group/cooperative trials
  - Pharmaceutical trials
  - Investigator initiated trials

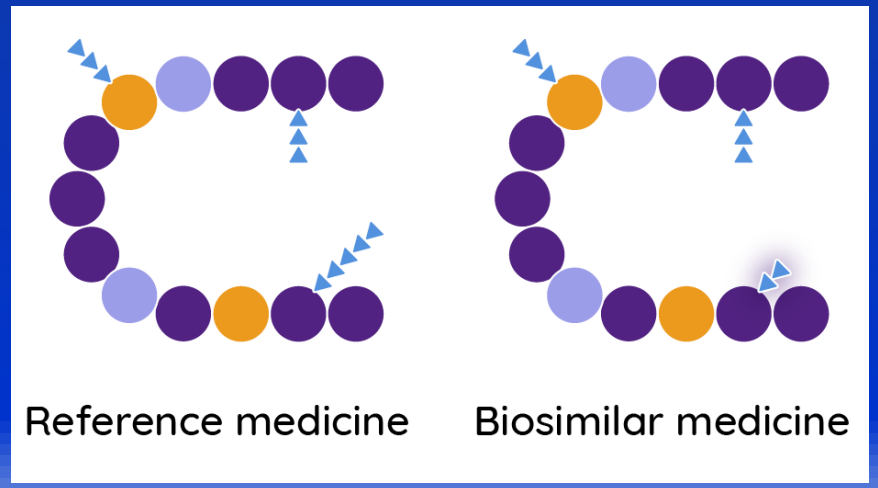
FDA Approvals Over Time

	Total new cancer drugs	Biosimilars	Supplemental indications	Total FDA approvals (all disease states)
2019	10 (as of 10/9/19)			30 (as of 10/9/19)
2018	19	6	38	59
2017	16	2		46
2016		(3 in non-oncology setting)		22
2105		1		45

The Cancer Letter 1/25/19
www.fda.gov/files/drugs

Biosimilar and Interchangeable Products

- Produced using biotechnology in a living system (microorganism, plant or animal cell)
  - Vaccines
  - Therapeutic agents:
    - filgrastim: growth factor used to prevent neutropenia with chemotherapy
  - Monoclonal antibodies:
    - rituximab: agent targeting surface protein (CD-20) on the surface of certain cancer cells

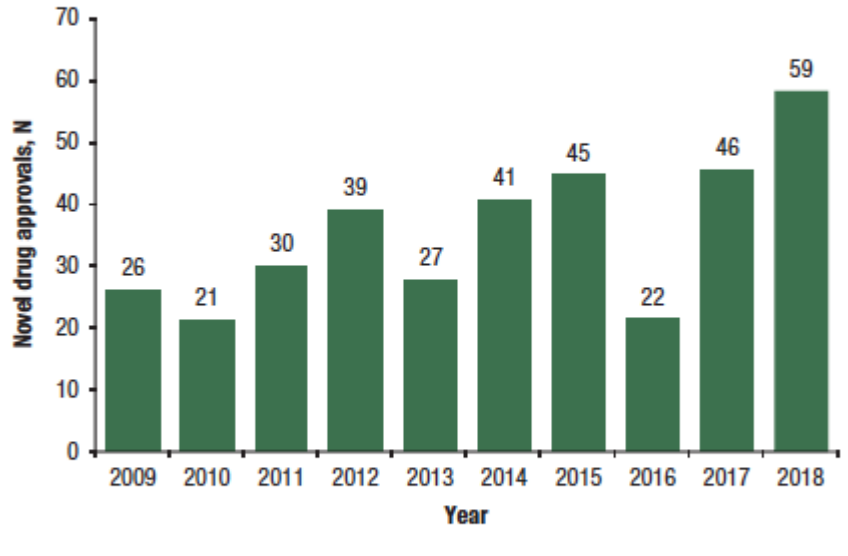


Across all disease states

2018 FDA approvals were highest since 1996

(when 53 new drugs were approved)

Figure Number of New Drugs Approved by the FDA, 2009-2018



Source: US Food and Drug Administration. Advancing health through innovation: 2018 new drug therapy approvals. January 2019. www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/DrugInnovation/UCM629290.pdf.

32% of the 2019 new approvals were first-in-class agents

58% of the new approvals address rare or 'orphan' diseases

73% of new drug approvals were processed through expedited categories (fast track, breakthrough, priority review, or accelerated approval)

www.fda.gov/files/drugs/published/New-Drug-Therapy-Approvals-2018

2018:
You can
teach
an old dog
new tricks

What the FDA 'looks at' has also changed

- Metastasis-free survival
  - Overall survival: includes time with recurrent disease
  - Progression free survival: time period of stable disease
- Minimal residual disease
  - "what's left" after a course of therapy – mainly used in setting of leukemia or myeloma and based on sophisticated analysis of bone marrow biopsy results
- Disease and biology specific indications
  - 2017: FDA approved an agent based on common biomarker (pembrolizumab and PD-L1 expression)

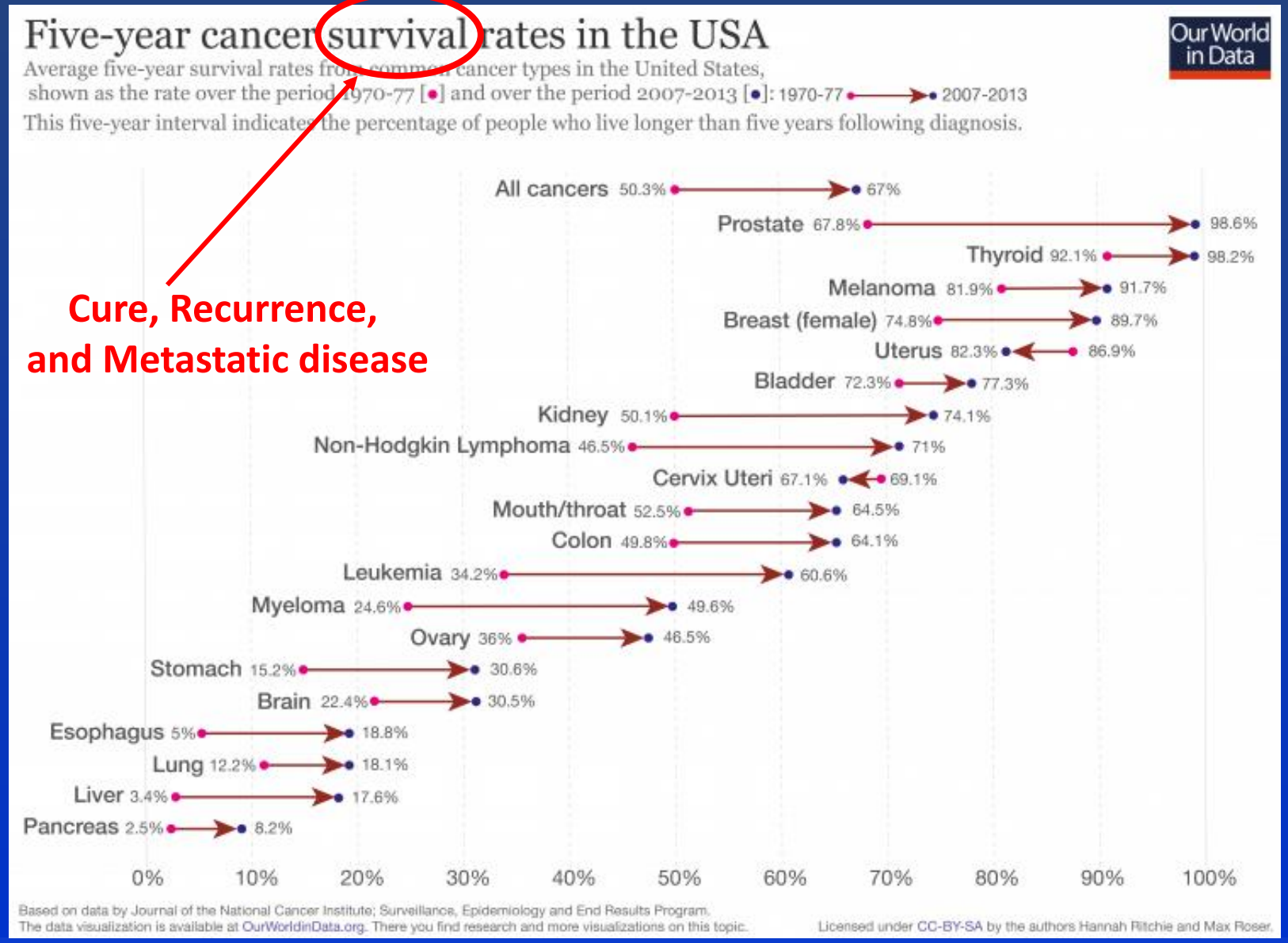
Impact of New Agents

- Side effect profile & Quality of life
  - Onset of side effects: Immediate, acute, sub-acute, late onset
  - Duration of side effects: short term, long term, permanent
  - More specific/less global
- Administration
  - IV, IM, SQ, self administered SQ, oral
- Financial toxicity
  - Increasingly complicated (co-pays, deductibles, co-insurance)
  - Real concerns of job loss, debt, bankruptcy

- *Generally* better tolerated
- Different side effect profile
- Less 'classic' febrile neutropenia
- Fewer hospitalizations
- More 'maintenance' therapy

- More therapies self administered at home
- Less 'chair' time in clinic
- Evolving education & follow-up

- Staff hired/devoted to address financial issues for both patient and clinic
- Financial counseling
- Aggressive research for grants, free-drug/drug replacement, etc..



Cure, Recurrence, and Metastatic disease

Patients are living longer with metastatic disease
(and yes, with better quality of life)

- Colon cancer:
  - Median survival 1990: 14 months 2019: 30 months
- Breast cancer:
  - Median survival ER+ 1990: 32 months 2019: 57+ months
  - Median survival ER- 1990: 14 months 2019: 33 months
- Lung cancer (non-small cell):
  - Median survival: 1990: <6 months 2019: 24+ months
- Melanoma
  - Median survival: 1990: 6-9 months 2019: 36 months (34% are alive at 5 years)
- Myeloma:
  - Median survival 1990: 3 years 2019: 6+ years

Current and Post-treatment Statistics

- 2019: 16.9 million people living with active cancer or a history of cancer
  - Roughly 5% of the total US population
  - 64% of survivors are ≥65 years old
- 2029: expected to grow to an estimated 21.7 million people
- By 2040, roughly 75% of survivors will be ≥65 years old

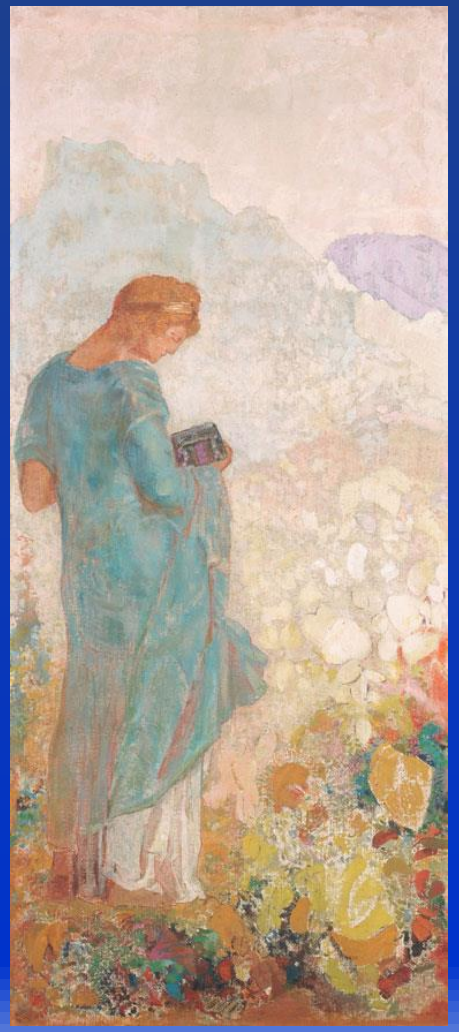
https://cancercontrol.cancer.gov › ocs › statistics › statistics

Cancer Survivorship

- "Survivorship" defined as period of time from diagnosis to death
  - Coined 1985 essay by Dr. Fitzhugh Mullan
- Language of cancer continues to evolve over time
  - Studies suggest that patients embrace different terms over the course of their treatment
- *War* is a common metaphor but is increasingly less universally accepted
- Patient, warrior, ninja, hero, fighter, thriver, veteran…
  - No single term is universally accepted
  - Different patient groups embrace or promote different terms

Growing Demographic with Unique Needs: cancer as a chronic disease

- Metastatic disease versus adjuvant setting
- Surveillance
- Work force/financial
- Interpersonal relationships



Potentially Five Generations in Contemporary Oncology Practices

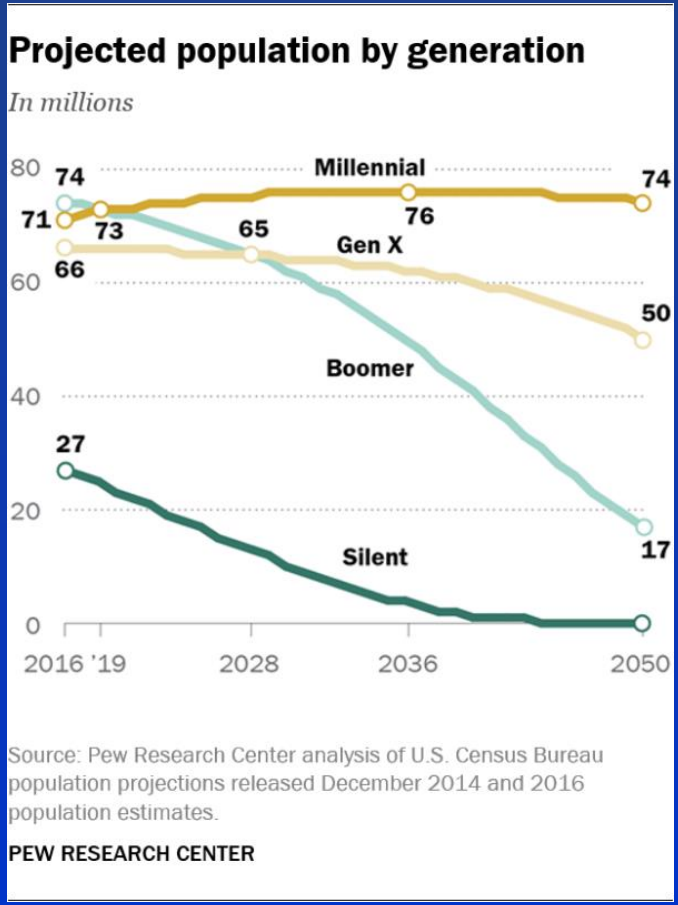
Traditionalists/Silent Generation (1928 – 1945) ages 74-91 in 2019

Baby Boomers (1946 – 1964) ages 55-73 in 2019

Generation X (1965 – 1980) ages 39-54 in 2019

Millennials (1981 – 1996) ages 23-38 in 2019

Generation Z (1997 – 2012) ages 22-7 in 2019



https://www.pewresearch.org/fact-tank/2019/01/17/where-millennials-end-and-generation-z-begins/ft_19-01-17_defininggenerations_generationzdominates/

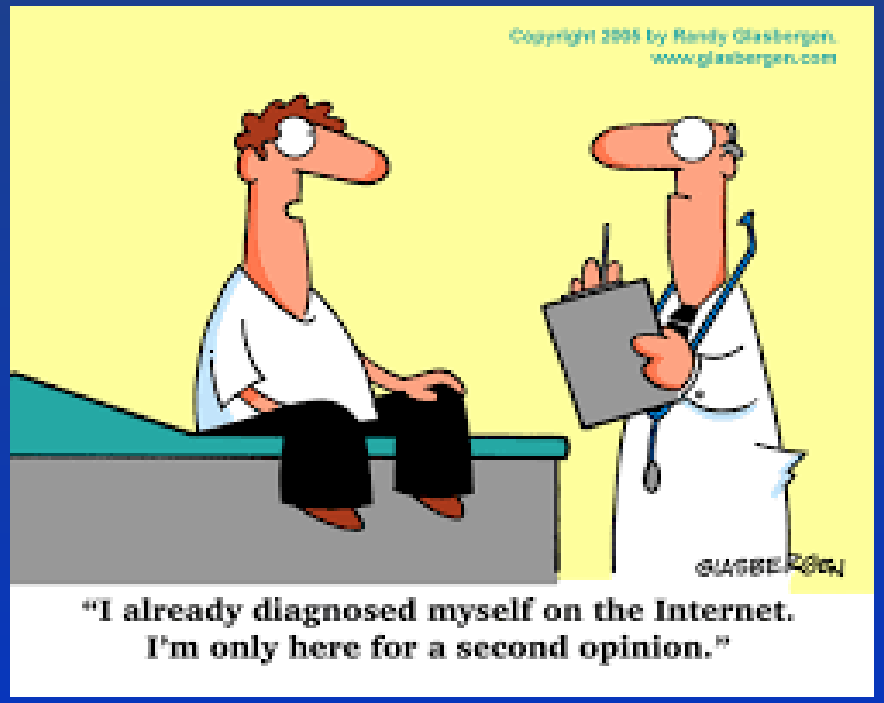
https://www.pewsocialtrends.org/essay/millennial-life-how-young-adulthood-today-compares-with-prior-generations/psdt_02-14-19_generations-00-09/

Influences on Generations

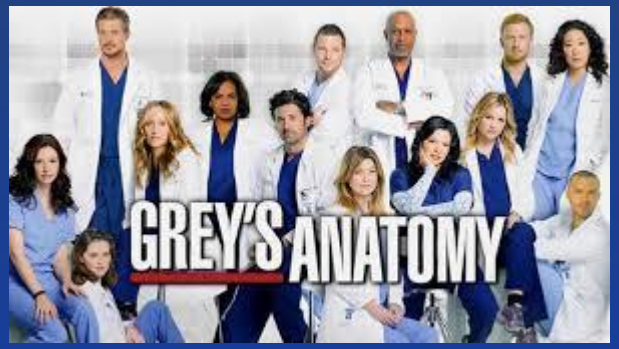
	World Events	Technology	Other key features
Traditionalists (ages 74-91)	WWII	Radio, print media, early T.V., "adapted" to technology	Stability and security
Baby Boomers (ages 55-73)	Vietnam War, sexual revolution	T.V., radio, print media "acquired" technology	Personal growth, high divorce/remarriage rates
Generation X (ages 39-54)	Fall of Berlin Wall, Iron Hostage Crisis, Operation Dessert Storm	T.V., VCR, rapidly evolving digital "assimilated"	Smaller generation, more formal education, flexible
Millennials (ages 23-38)	9/11, immigration, great recession	Digital is "integral" to life	Less formal education, politically liberal, lower marriage/fertility rates
Generation Z (ages 22-7)	Post 9/11	Digital from birth	Anticipated to be highly educated

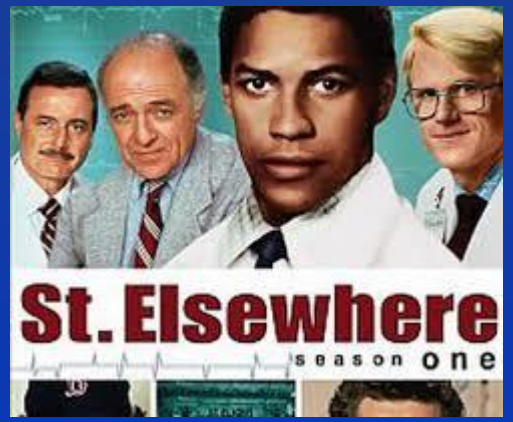
Patient Expectations Vary According to Generation

- Higher patient satisfaction has been linked with patient age across several studies, several sub-specialities, and several countries
  - Life experience versus expectations versus patient/physician interaction
- Expectation, integration, and acceptance of technology varies
  - Appointment reminders
  - On-line appointments versus phone
  - Access to medical records and providers
- "Shared appointments" are being trialed in some settings (non-oncology)
- Expected and delivered care
  - Patient prepping



"I already diagnosed myself on the Internet.
I'm only here for a second opinion."





74% of Americans have a positive view of medical doctors
57% of Americans feel doctors usually care about their patient's best interests

-Pew Research Center, 8/2/19

70% of patients read on-line reviews
50% of patients used online information to choose a physician
Gen X and Millenials are more likely to use on-line reviews
Evolving data on management of on-line sites

-Medical Economics , 8/8/19

Quality Initiatives in Oncology

- Assessing outcomes is challenging
  - Tremendous variation on individual levels
- Assessing adherence to practice guidelines is easier
- Standardization of care
- Clinical Pathways – championed by UPMC in early 2000's
  - Algorithms and pathways based on evidence, specialist input, and consensus
  - Generally 80% of patients fall into algorithm pattern
- National guideline and accreditation bodies
  - NCCN, CoC, NAPBC, others
- Future: reimbursement based on compliance with guidelines

Physician Expectations Vary According to Generation

- Approximately 54% of practicing oncologists are ≥65 years old
- Changes in training programs impact expectation
  - 2003: 80 hour work week limitations
  - Younger physicians are trained in nuanced collaboration with more team/shared care
- Electronic medical records and tech impacts patient flow and physician style
  - "See and type", voice recognition, scribes
- Majority of oncology positions are employed – private practice is increasingly uncommon
  - Recruiting private practice complicated by lower interest in the business aspect
- Early career physicians tend to favor positions with greater flexibility

Medical Oncology Recertification Process

"work in progress"

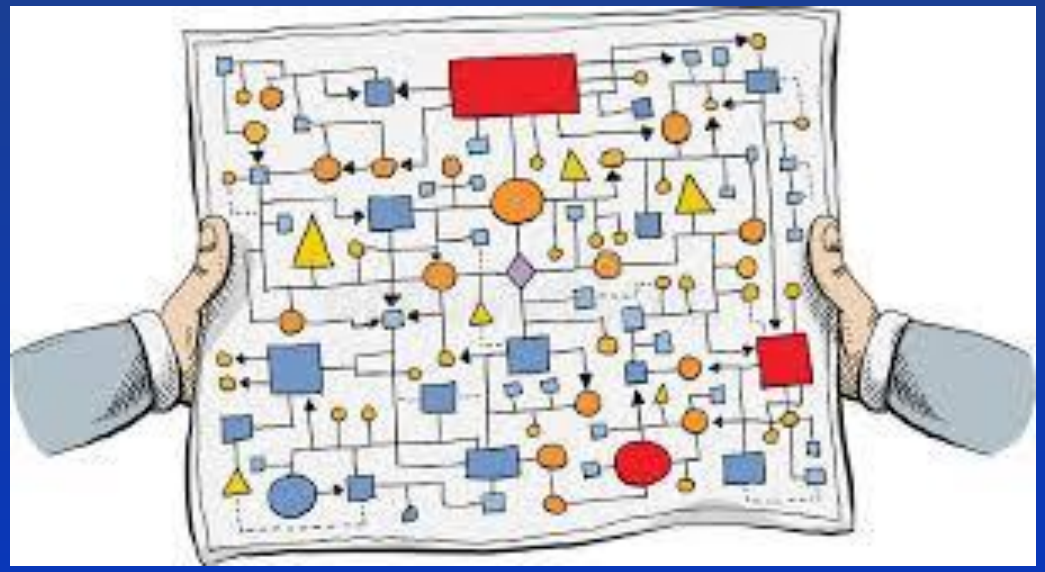
- Earn 100 MOC points every 5 years and complete MOC test

-or-

- Two year assessment option (shorter version of the MOC)

-or-

- Cross your fingers and hope they make it easier before you need to prove you're keeping up



“It was the best of times, ~~it was the worst of times,~~
It was the age of wisdom, it as the age of foolishness,
It was the epoch of belief, it was the epoch of incredulity,
It was the season of light, ~~it was the season of darkness,~~
It was the spring of hope, ~~it was the winter of despair.~~”

-Charles Dickens, A Tale of Two Cities