

# Disparities in wound care:

social determinants of health, epigenetics, and  
the biochemical response to stress

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and

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# Disclosures:

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No relevant financial conflicts to disclose.



# Objectives

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1. Provide an overview of social determinants of health
2. Identify disparities in wound care
3. Describe the biochemical response to stress and its impact on wound healing
4. Explain the connection between epigenetics and stress



# Social Determinants of Health

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Factors other than the healthcare patients receive are driving outcomes; social determinants of health determine 80% of health outcomes.



# Social Determinants of Health

SDoH are conditions and environments in which people live

They affect a wide range of health, functioning, and quality-of-life outcomes and risks.



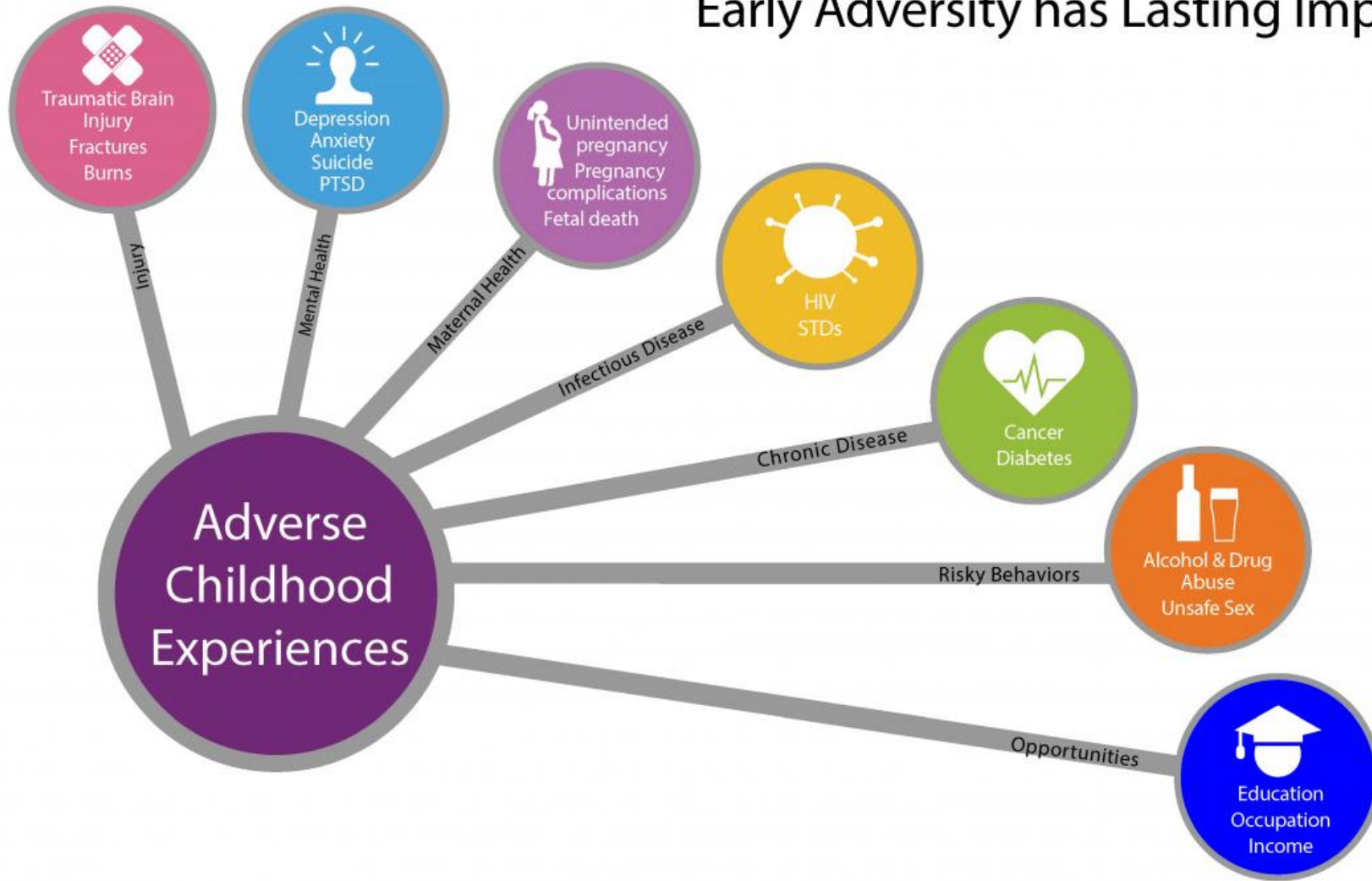
# Sources of disparities and care deserts

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- Economic stability
- Neighborhood and built environment
- Education access and quality
- Health care access and quality
- Social and community context



# Early Adversity has Lasting Impacts

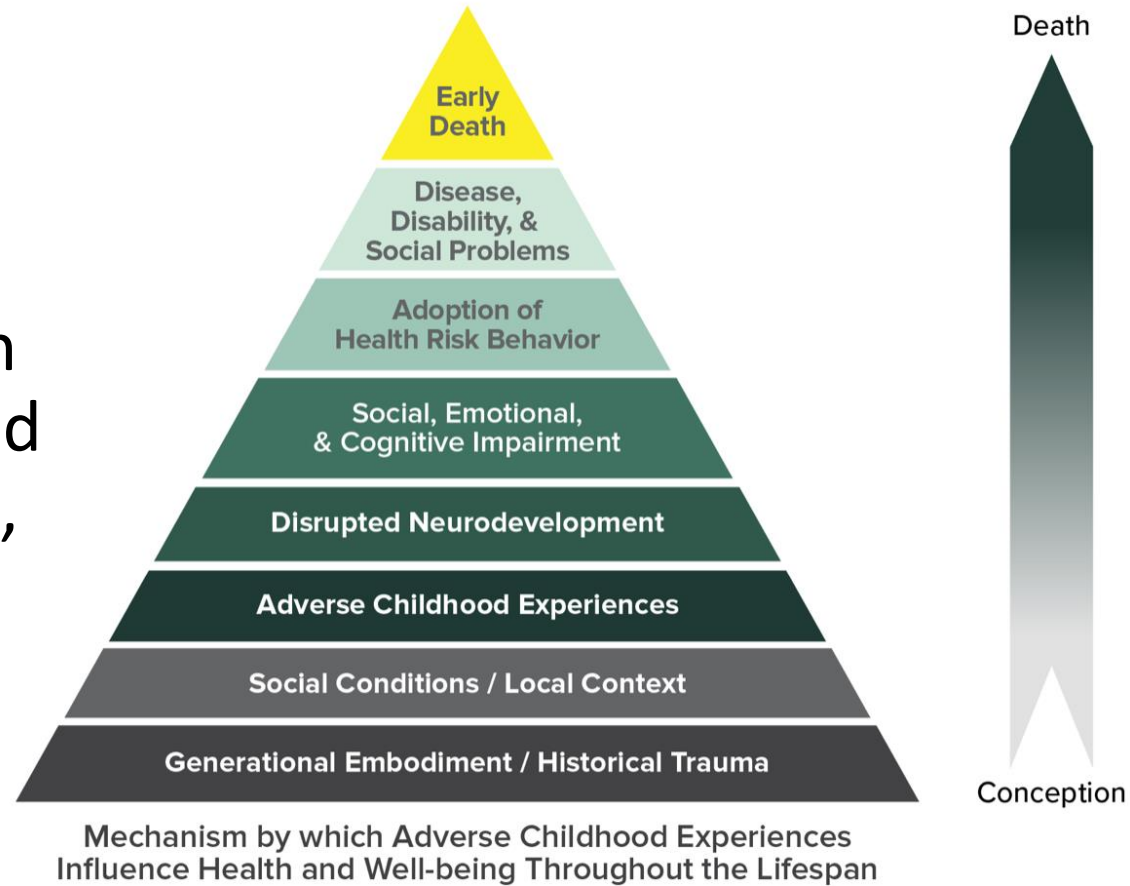


- ACEs are life stressors that have significant impact on future health outcomes
- Historical Trauma



# Adverse Childhood Events and Long-term Health Outcomes

- Exposure to ACEs predisposes children to not only social and emotional disorders, but also physical illness.





# ACEs and wound care

ACE chronic diseases associated with the development of wounds and poor self management of health:

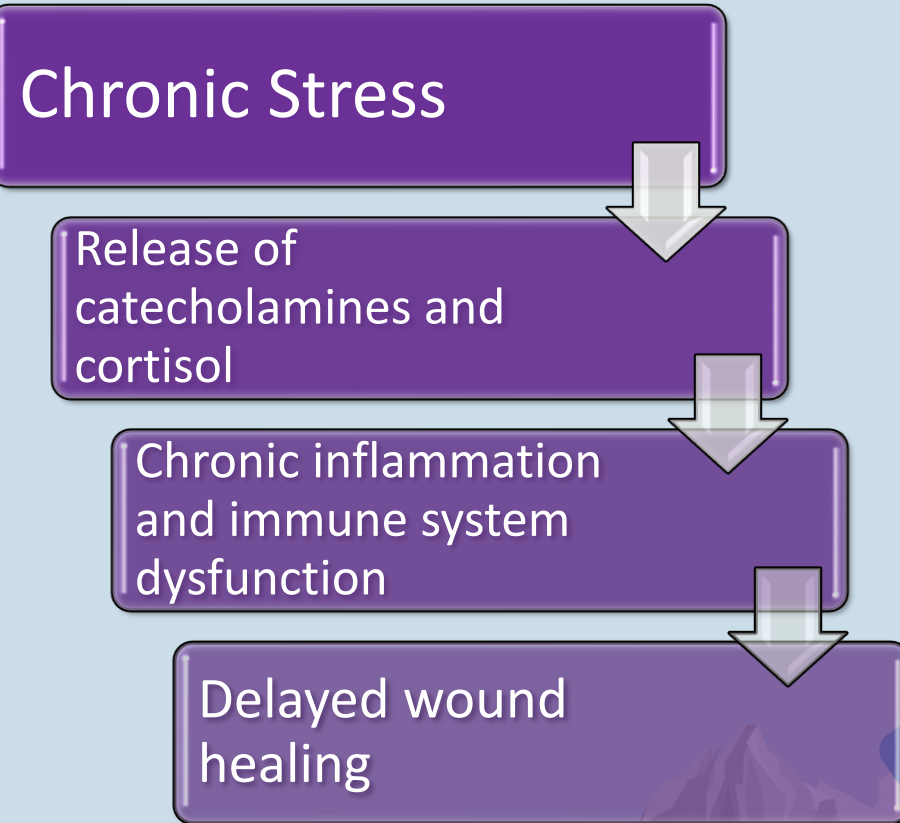
- ✓ Cancer
- ✓ Diabetes
- ✓ Obesity
- ✓ Fractures and burns
- ✓ Autoimmune diseases
- ✓ Depression and anxiety
- ✓ Drug and alcohol use



# Chronic Exposure to Stress

## Negative Outcomes:

- ✓ Risk taking behaviors
- ✓ Alterations in care
- ✓ Physiologic response to stress



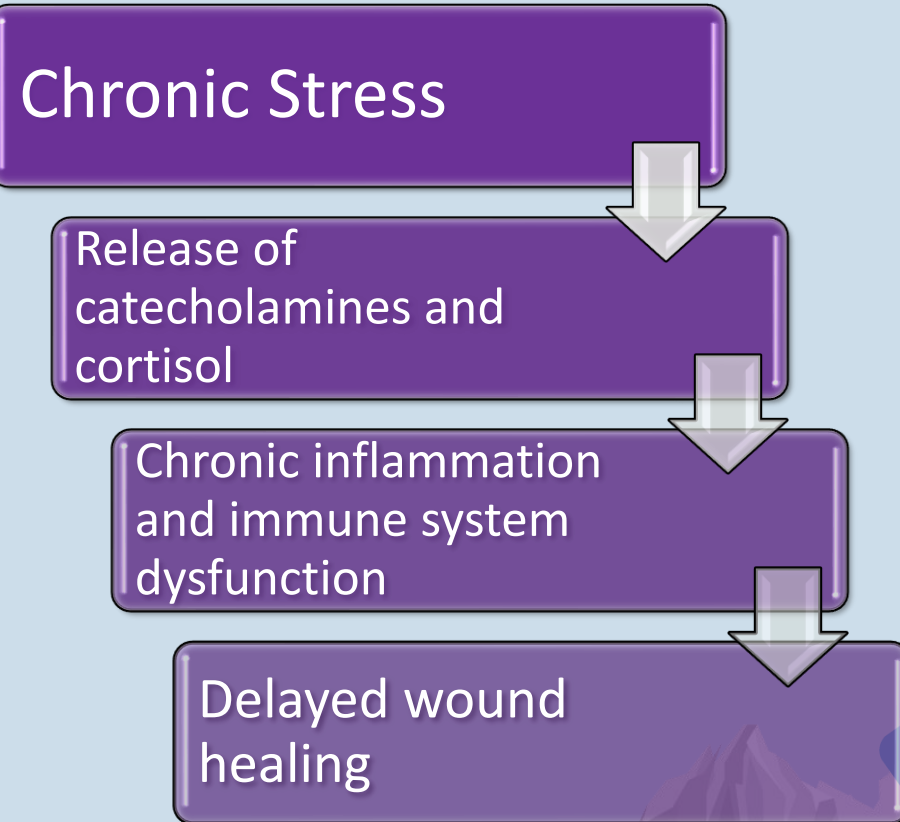
Source: Hannibal 2014; Preventing ACEs CDC, 2021; Maes 2011; Zunszain 2011



# Chronic Exposure to Stress

Short term stress:

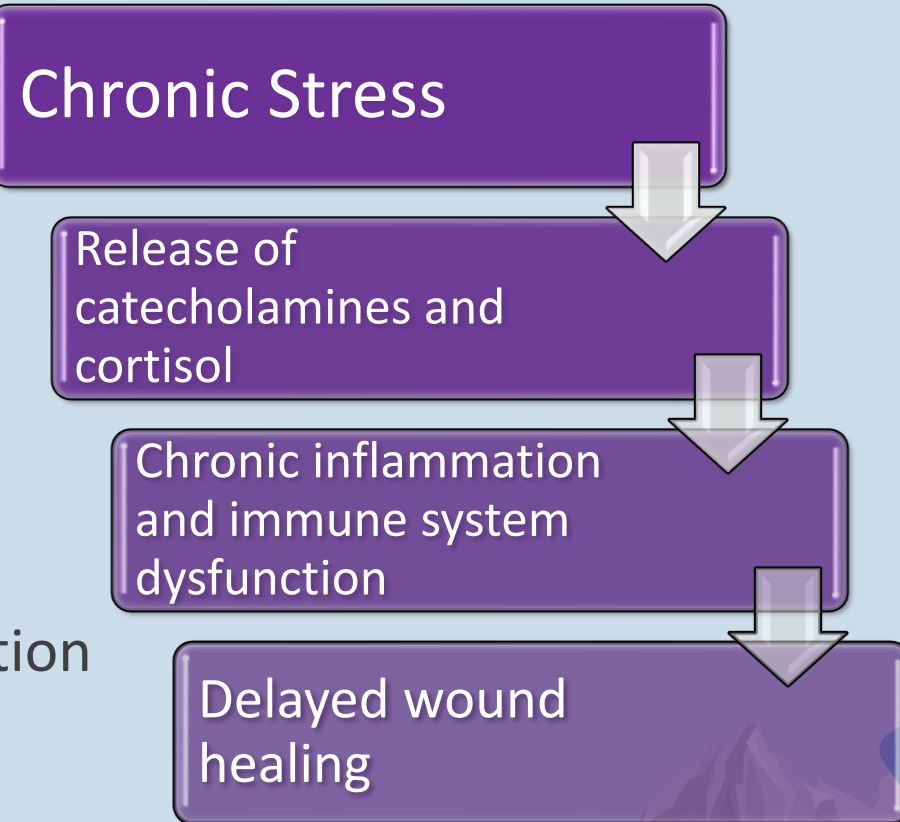
Cortisol initially anti-inflammatory agent / mobilizes glucose to use during the stress response



# Chronic Exposure to Stress

Long term stress:

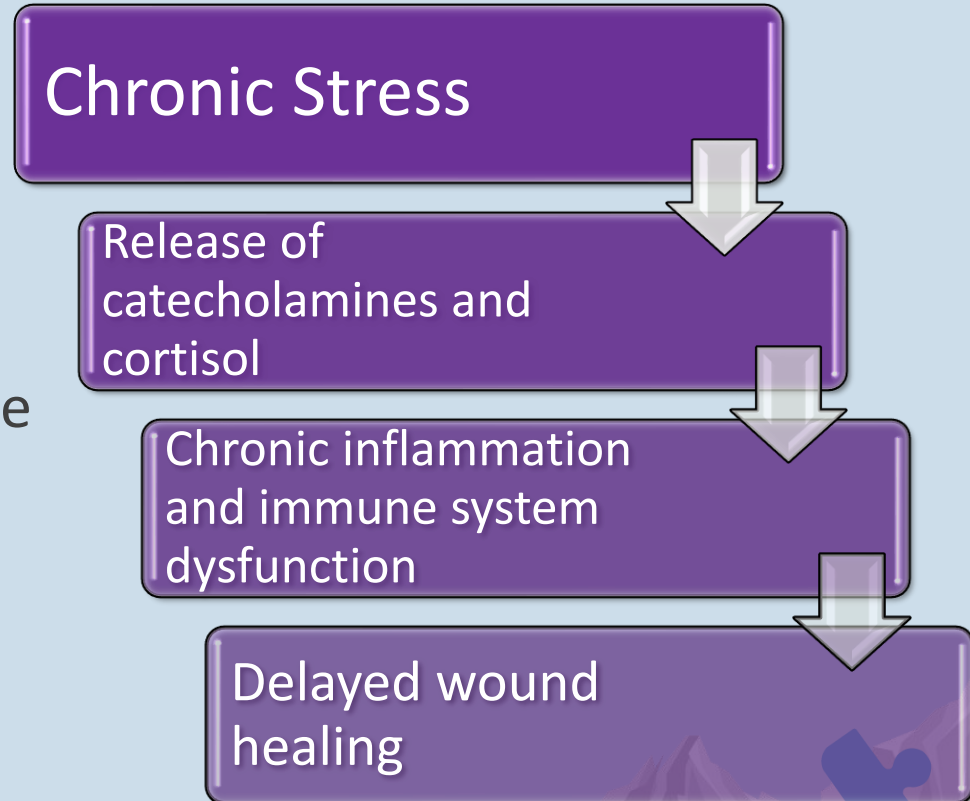
- pro-inflammatory  
(oxidative and nitrosative)
- free radical damage
- increased experience of pain
- cellular death/ aging/ tissue degradation



# Chronic Exposure to Stress

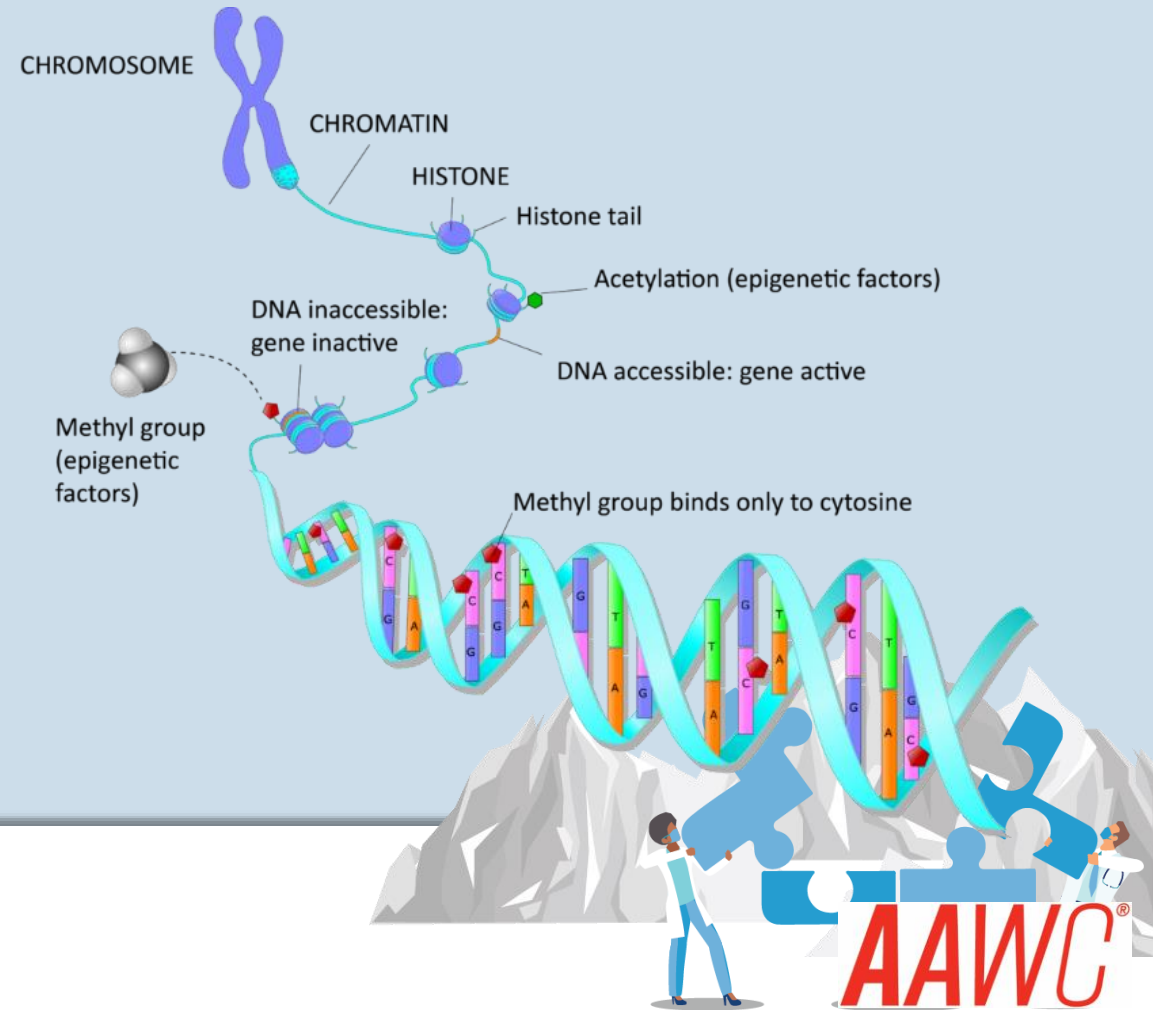
Chronic stress can lead to:

- Delayed wound healing
- Atherosclerotic vascular disease
  - Hypertension
  - Dyslipidemia
- Immune dysfunction



# Epigenetic changes, Historical trauma

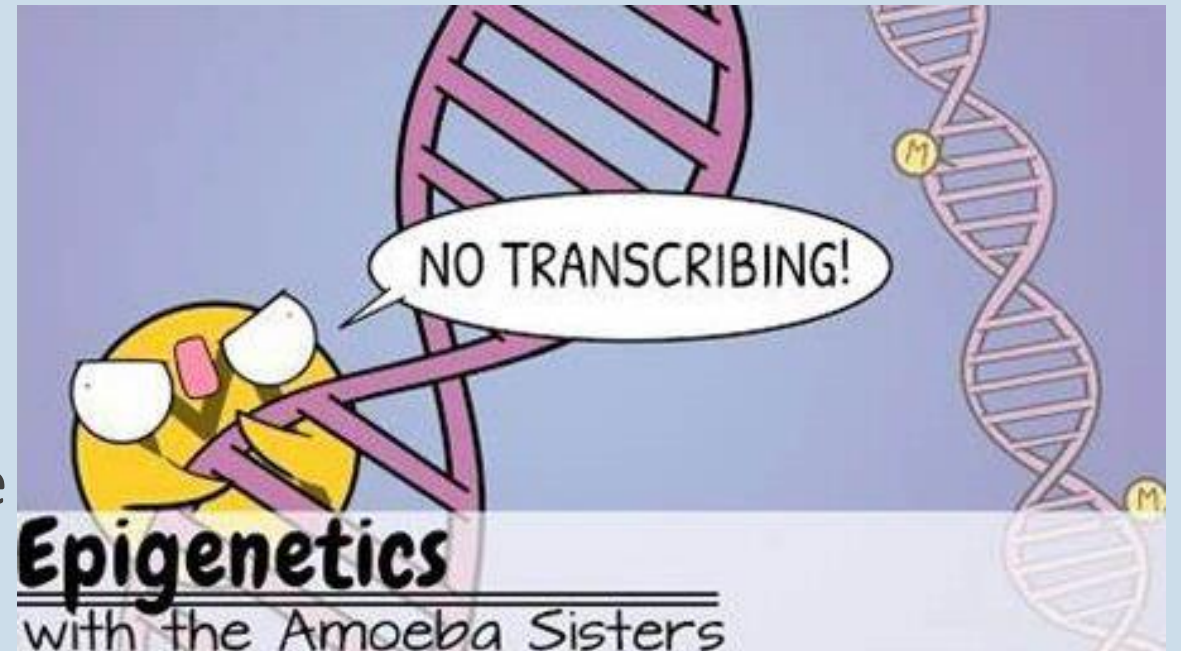
- Epi meaning “above” the genome
- Epigenetics = the study of changes in organisms caused by modification of gene expression rather than alteration of the genetic code itself



Source: Lang 2020; Ahmed 2017; Mossel 2020

# Epigenetic changes, Historical trauma

- Stress and neglect can change expression of DNA = epigenetic changes
- Stress (including ACEs) and environmental exposures contribute to epigenetic changes:
  - DNA hypo and hyper methylation
  - histone modification
  - telomere shortening.



# Epigenetic changes, Historical trauma

- Epi-genetic changes are heritable (eg dutch Hungerwinter of 1944-45)
  - October 1944 Germans blocked supply delivery including food to west Netherlands
  - Rations dwindled to 500-1000 k/cal/day = massive starvation including pregnant women
  - Increased incidence of obesity, diabetes, schizophrenia, and neural-tube defects found





# Epigenetic changes, Historical trauma

Epigenetic changes during pregnancy can be a biochemical source of generational trauma:

- ✓ chronic stress
- ✓ smoking
- ✓ food insecurity
- ✓ environmental exposures

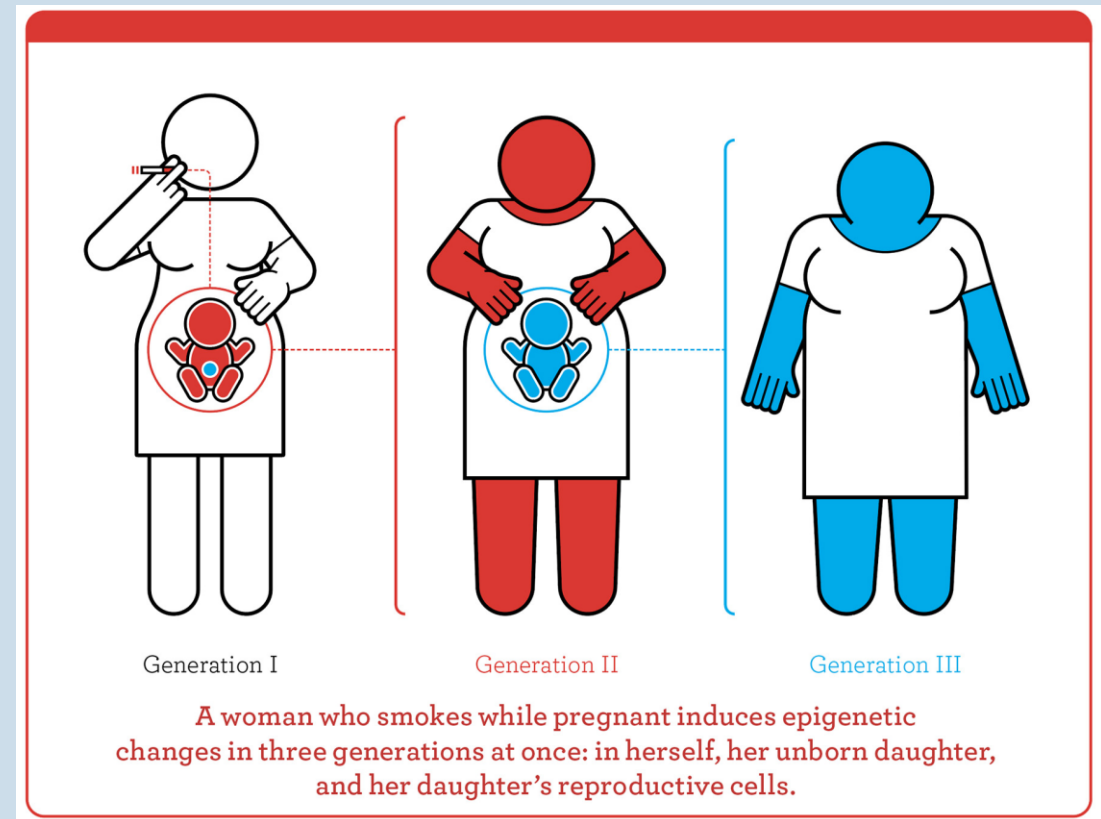
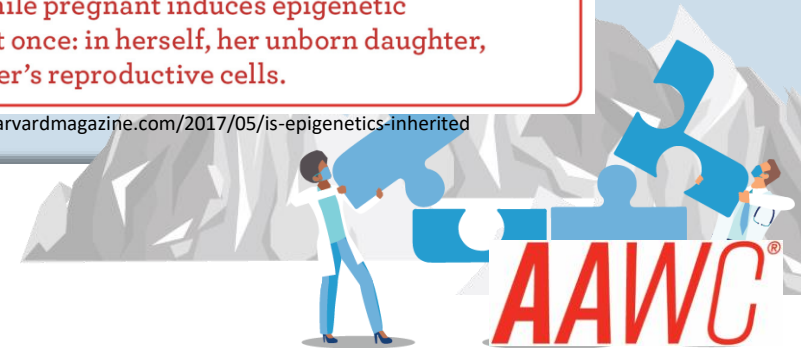


Photo: Buffum, J. Is Epigenetics Inherited? <https://www.harvardmagazine.com/2017/05/is-epigenetics-inherited>



# Epigenetics in action

Diabetes

Histone modifications

Macrophage phenotype changes

Inflammation

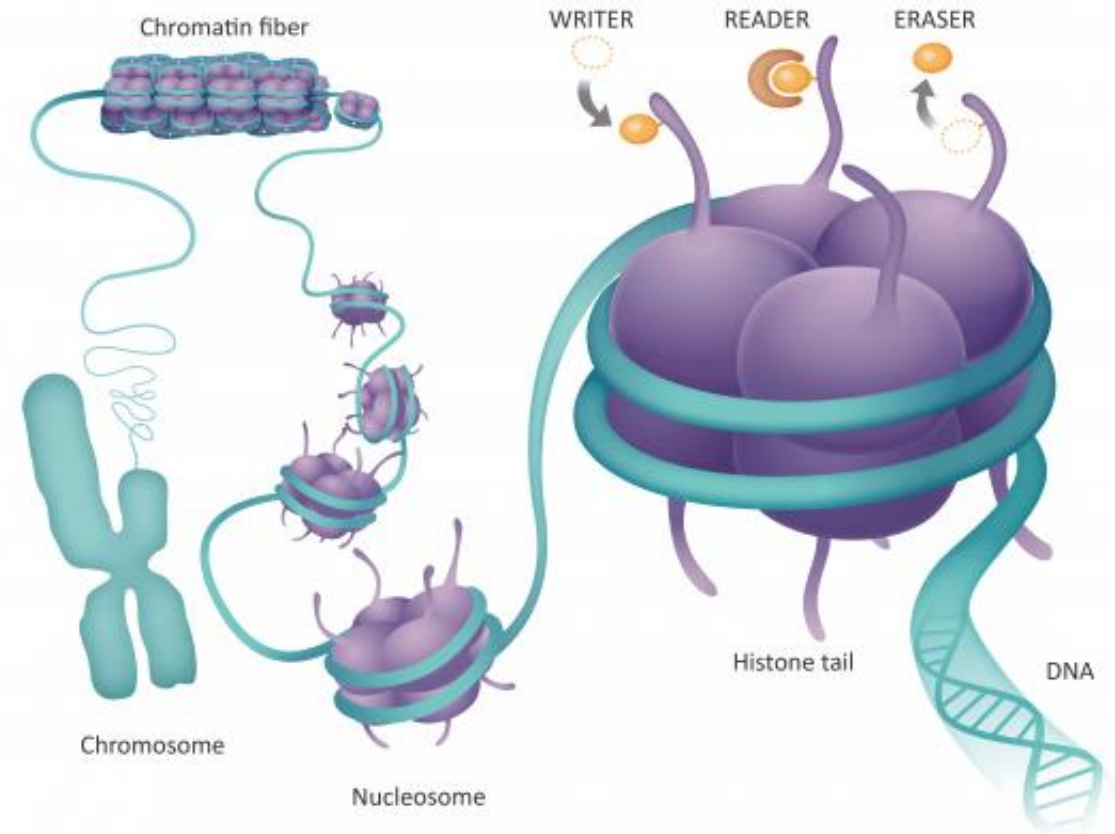


Photo: <https://www.oryzon.com/en/epigenetics/epigenetics>



The Potential Impact of Social Genomics on Wound Healing. *Adv Wound Care (New Rochelle)*. 2020;9(6):325-331. doi:10.1089/wound.2019.1095

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## Social genomics review

- Multiple studies: social influences impact stress and wound healing
- Social isolation impacts >200 genes
  - Downregulated antiviral response and production of antibodies
  - Upregulated inflammation cascade
- Social isolation - known correlation in delayed wound healing

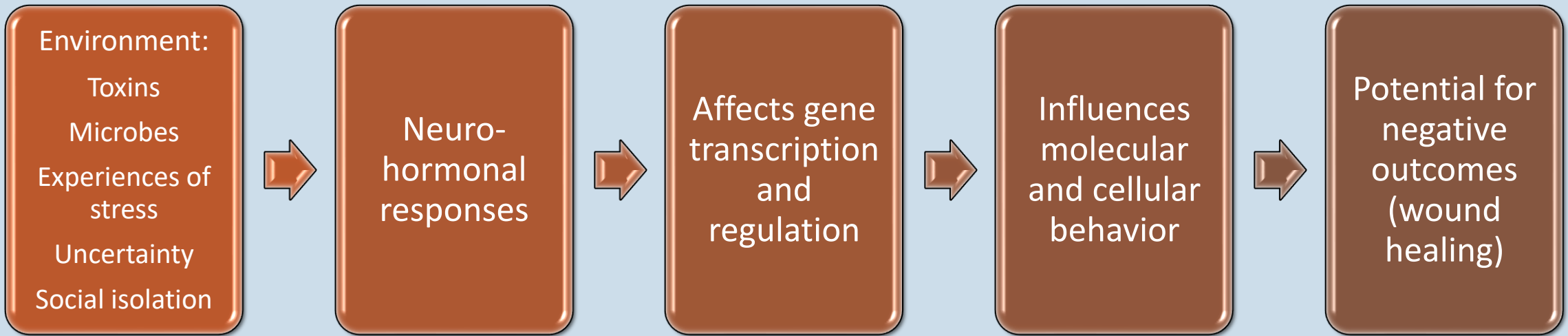


# Wound clinic visits and social interaction



- Wound clinic visit frequency influences rate of healing
- More frequent wound clinic visits associated with better healing





# Social modulation of gene expression



Happens in other species too!

- Bees – worker bees into scouts or guards based on hive needs
- Cichlids- switching sex



# Clinical Relevance – Wound Care

- Biochemical response to psychological stress in chronic wounds:
  - hypoxia
  - decreased cytokines
  - alterations in matrix metalloproteinases
  - alterations in immune response (increased infection)
  - decreased neutrophil infiltration
  - antimicrobial peptides which leads to increased rates of infection
  - microbiome alterations and biofilm promotion
  
- Eg: higher reported stress levels on the day of biopsy have been shown to have delayed healing.



# Disparities in wound care:

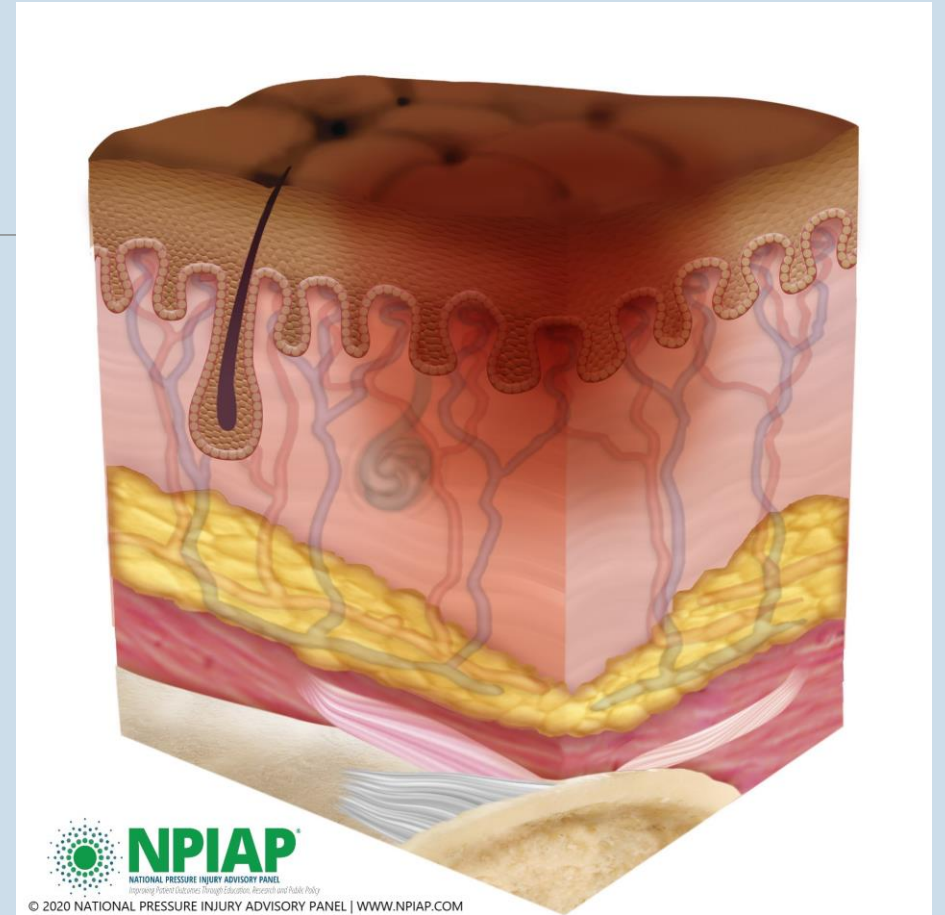
- skin color
- age
- geography (rural vs urban)
- highly resourced vs low resources
- insured/under-insured/un-insured
- limb loss inequalities
- access to wound care clinicians, tools, advanced therapies, & products



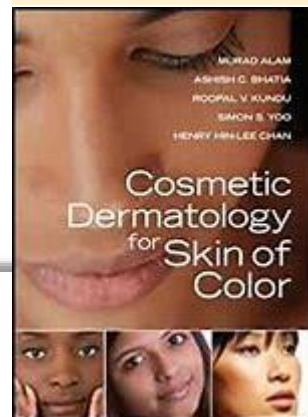
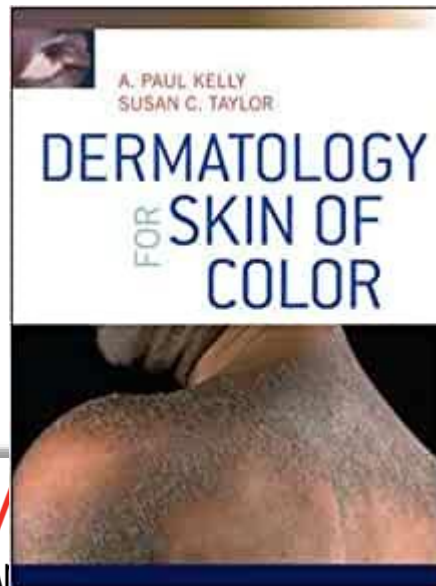
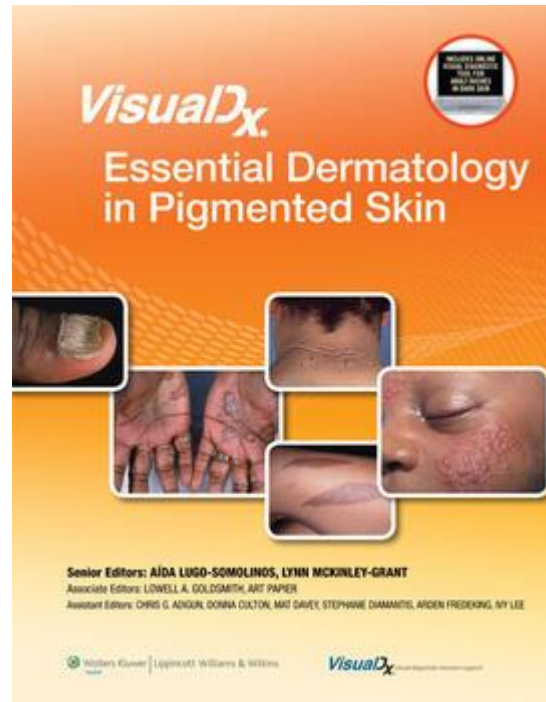


# Racial/ethnic disparities

- Investigative needs on the differences in skin biomechanics in racial/ethnic groups
- Differences have been found: viscoelasticity, hydration, etc.
- Disparities in co-morbid disease states and healing have also been found



# Disparate care for other dermatologic care



- Black and Hispanic populations have reduced access to outpatient dermatologic care
- 75% of counties with majority Black and Hispanic populations have zero dermatologists
- Black and Hispanic patients more likely than white patients to utilize EDs for dermatologic care

Sources: Hooper 2022; Vaidya 2018; Abokwidir 2015



Racial and ethnic differences in hospital admissions for cellulitis in the United States: A cross-sectional analysis [published online ahead of print, 2022 Aug 27]. J Am Acad Dermatol. 2022;S0190-9622(22)02613-5. doi:10.1016/j.jaad.2022.08.038



Examined hospital admissions vs discharged

- 378,350 admissions (24.3%)
- 1,118,791 discharges (75.7%)

Admitted patients were more likely to be:

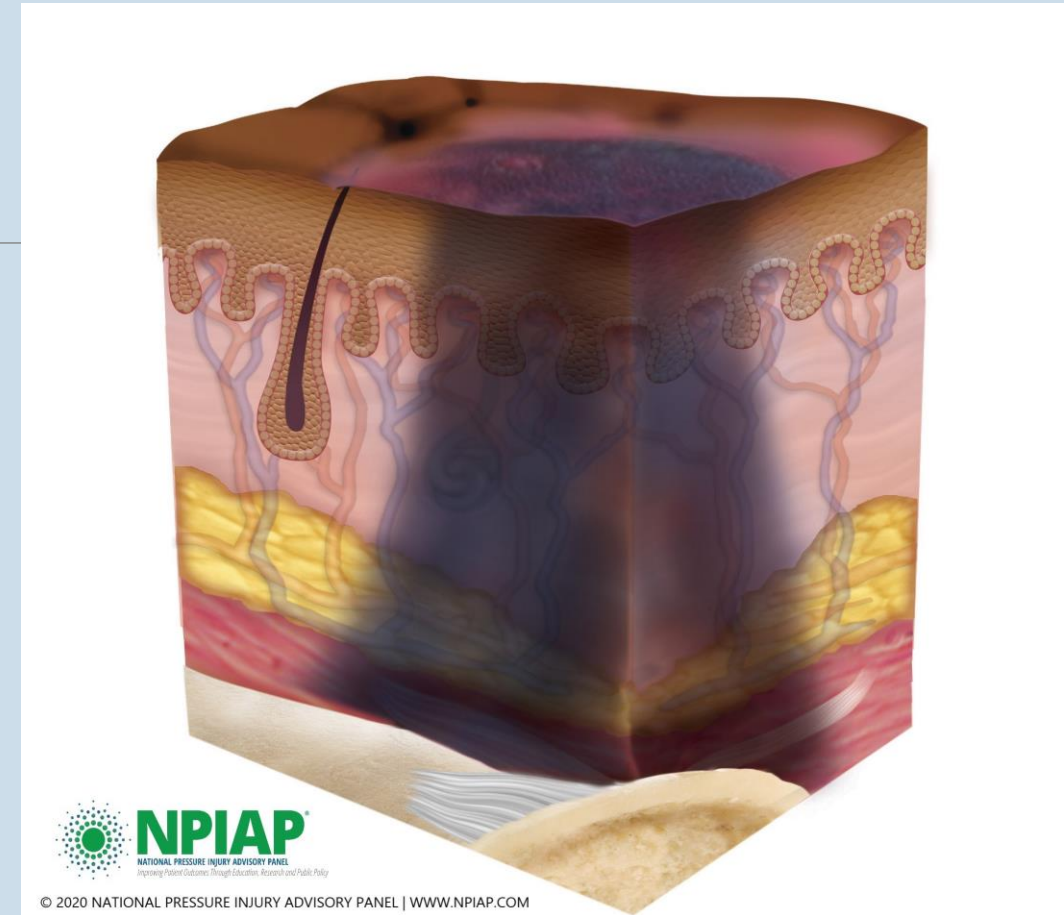
- White
- Older (>65 years)
- Urban teaching hospitals
- Have Medicare

Black & Hispanic patients had higher odds of being discharged



# Racial/ethnic disparities

- Visual cues for pressure injury identification may be insufficient in darkly pigmented skin
- Disparities in pressure injury prevalence, incidence, severity, and healing



# Evidence Based Practice vs. Insurance Base Practice

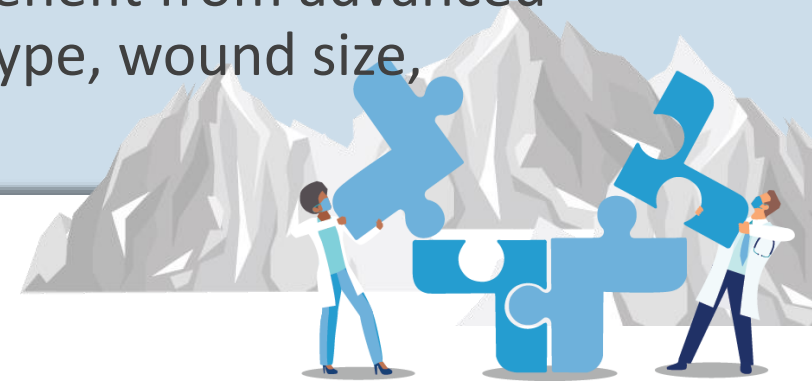
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## Disparate care based on insurance coverage

### Un-insured v. under-insured

- Un-insured in 2020: 8.6% or 28 million people
- Under-insured: 2020 estimates are that 28% of Americans are underinsured
  - Delay or avoid health care because of costs at twice the rate of people who are insured but not underinsured

Insurance based practice: Patients that would medically benefit from advanced therapy use but insurance has limited use due to wound type, wound size, co-morbid dx etc.



# Wound Research Gaps

Exclusion criteria present commonly excludes real world patient situations:

- diagnoses outside of venous and diabetic ulcers
- exposed structures
- Large or small wounds
- peripheral vascular disease
- elevated A1C/ uncontrolled diabetes
- autoimmune disorders
- noncompliance
- poor nutrition



Disparities and stress

Chronic stress response and health behavior changes

Physiologic, biochemical, epigenetic changes

Development of chronic disease and poor self care behaviors

Wound development and Delayed wound healing



# One Health

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- Movement in healthcare to not only treat and support the patient during acute illness, but to create a Culture of Health that prevents illness through supporting access to structural drivers of health like safe housing, food, education, and healthcare including mental healthcare.
- The health of our patients and ourselves is influenced by so much more than what we are able to address during an office visit or inpatient stay.





# Case 1

## 55 YEAR OLD FEMALE WITH PAD, PROTEIN S DEFICIENCY, AND DVT

- couldn't afford copay for warfarin
- developed recurrent DVT
- Cerebral vascular attack
- Now with primarily palliative wound to left leg
- Presented to clinic taping together OTC non-adherent dressings and pieces of old 2 layer compression wraps because she ran out of dressings
- Increased drainage from poor bioburden management, daily dressing changes



# Case 2 – reverse case

77 YEAR OLD, CYCLING 1 HOUR DAILY

HAD UNWITNESSED FALL, AND WAS FOUND UNCONSCIOUS

PRESENTATION TO WOUND CENTER:

- UNDERMINING TO BOTH WOUNDS
- EXPOSED MUSCLE TO KNEE
- PALPABLE TENDONS TO HAND



# Case 2- at 4 week follow up

**HAND COMPLETELY EPITHELIALIZED, KNEE IS NEARLY**

## **POSITIVE SOCIAL DETERMINANTS OF HEALTH**

**Lack of psychiatric issues**

**adherence to plan of care**

**Transportation to wound center for advanced therapies 3x/week**

**Good nutrition**

**Caucasian, middle class, exercises regularly**

**Very few comorbidities**

**Great insurance!**

**Advanced therapies immediately used**

**Able to be seen in the wound center**



# Case Study #3 – Stage IV Pressure Injury

## Rural vs Urban

### Both have Private Insurance

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#### PATIENT RURAL

65 Year old White Male

Spinal Cord Injury related to fall from roof

Strong Family Support

- Wife continues to work outside of the home at local convenience store
- Adult Children live near-by and helping
  - Daughter is a LPN

Plan of Care

- Home Health
- Packing site with Silver Alginate
- Cover with Absorbent dressing

#### PATIENT URBAN

69 Year old Hispanic Male

Spinal Cord Injury related to MVA

Strong Family Support

- Wife is a Registered Nurse – Oncology
- Adult Children live out of state
- Family friend lives next door and helps out

Plan of Care

- Home Health
- Negative Pressure Therapy



# Case Study #4

## Residual of the Tuskegee Experiment

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42 Year Old Black Male

- ESRD – Dialysis
- Diabetic - A1c = 6.9
- ABI = 0.6

Non-healing Diabetic foot ulcer to right foot – over a year

Treatments attempted

Fem-pop to improve perfusion

Bioengineered Skin substitutes

Total Contact Casting

Standard of Care – debridement, cleansing, topicals etc.



# Case Study #5

## Social Interactions and Unconscious Bias

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25 Year Old Black Female

Married for 5 years

Gravida 3 - Para – 1 A – 2 (Spontaneous/Hydatidiform mole)

1. Reporting of feeling extremely tired and eating ice
2. Availability of the Provider with issues
3. Addressing and inclusion of Spouse



# Conclusions

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Many opportunities for further research and process improvement in how and where we deliver care.



Photo retrieved from Resilient Wisconsin: ACE. <https://www.dhs.wisconsin.gov/resilient/aces.htm>



# Conclusions

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Social determinants of health contribute to the development of  
conditions associated with wounds  
AND  
limits successful healing outcomes





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# Where does our role in the facilitation of the health of our patients end?



# References

1. Medicaid's Role in Addressing Social Determinants of Health. Robert Wood Johnson Foundation. Published 2019 Feb 1. Retrieved 11/17/21 from <https://www.rwjf.org/en/library/research/2019/02/medicaid-s-role-in-addressing-social-determinants-of-health.html>
2. Preventing Adverse Childhood Events. Center for Disease Control and Prevention. Last reviewed 4/6/21. Retrieved 11/16/21 from <https://www.cdc.gov/violenceprevention/aces/fastfact.html>
3. Lang J, McKie J, Smith H, et al. Adverse childhood experiences, epigenetics and telomere length variation in childhood and beyond: a systematic review of the literature. *Eur Child Adolesc Psychiatry*. 2020;29(10):1329-1338. doi:10.1007/s00787-019-01329-1
4. Dube SR, Fairweather D, Pearson WS, Felitti VJ, Anda RF, Croft JB. Cumulative childhood stress and autoimmune diseases in adults. *Psychosom Med*. 2009;71(2):243-250. doi:10.1097/PSY.0b013e3181907888
5. Ports KA, Holman DM, Guinn AS, et al. Adverse Childhood Experiences and the Presence of Cancer Risk Factors in Adulthood: A Scoping Review of the Literature From 2005 to 2015. *J Pediatr Nurs*. 2019;44:81-96. doi:10.1016/j.pedn.2018.10.009
6. Cunningham TJ, Ford ES, Croft JB, Merrick MT, Rolle IV, Giles WH. Sex-specific relationships between adverse childhood experiences and chronic obstructive pulmonary disease in five states. *Int J Chron Obstruct Pulmon Dis*. 2014;9:1033-1042. Published 2014 Sep 26. doi:10.2147/COPD.S68226
7. Dong M, Giles WH, Felitti VJ, et al. Insights into causal pathways for ischemic heart disease: adverse childhood experiences study. *Circulation*. 2004;110(13):1761-1766. doi:10.1161/01.CIR.0000143074.54995.7F
8. Hannibal KE, Bishop MD. Chronic stress, cortisol dysfunction, and pain: a psychoneuroendocrine rationale for stress management in pain rehabilitation. *Phys Ther*. 2014;94(12):1816-1825. doi:10.2522/ptj.20130597
9. Maes M, Galecki P, Chang YS, Berk M. A review on the oxidative and nitrosative stress (O&NS) pathways in major depression and their possible contribution to the (neuro)degenerative processes in that illness. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35:676-692.
10. Zunszain PA, Anacker C, Cattaneo A, et al. Glucocorticoids, cytokines and brain abnormalities in depression. *Prog Neuropsychopharmacol Biol Psychiatry*. 2011;35:722-729.
11. Ahmed M, de Winther MPJ, Van den Bossche J. Epigenetic mechanisms of macrophage activation in type 2 diabetes. *Immunobiology*. 2017;222(10):937-943. doi:10.1016/j.imbio.2016.08.011
12. Mossel DM, Moganti K, Riabov V, et al. Epigenetic Regulation of S100A9 and S100A12 Expression in Monocyte-Macrophage System in Hyperglycemic Conditions. *Front Immunol*. 2020;11:1071. Published 2020 Jun 2. doi:10.3389/fimmu.2020.01071
13. Gouin JP, Kiecolt-Glaser JK. The impact of psychological stress on wound healing: methods and mechanisms. *Immunol Allergy Clin North Am*. 2011;31(1):81-93. doi:10.1016/j.iac.2010.09.010
14. Kim JH, Ruegger PR, Lebig EG, et al. High Levels of Oxidative Stress Create a Microenvironment That Significantly Decreases the Diversity of the Microbiota in Diabetic Chronic Wounds and Promotes Biofilm Formation. *Front Cell Infect Microbiol*. 2020;10:259. Published 2020 Jun 3. doi:10.3389/fcimb.2020.00259
15. Regueira Y, Fargo JD, Tiller D, et al. Comparison of Skin Biomechanics and Skin Color in Puerto Rican and Non-Puerto Rican Women. *P R Health Sci J*. 2019;38(3):170-175.
16. Sullivan R. A 5-year retrospective study of descriptors associated with identification of stage I and suspected deep tissue pressure ulcers in persons with darkly pigmented skin. *Wounds*. 2014;26(12):351-359.
17. Healthy People 2030, U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. Retrieved [date graphic was accessed], from <https://health.gov/healthypeople/objectives-and-data/social-determinants-health>
18. Centers for Disease Control and Prevention. (2021). Violence prevention: The ACE pyramid (adapted by RYSE Youth Center). <https://www.cdc.gov/violenceprevention/aces/about.html>
19. Bates-Jensen BM, Anber K, Chen MM, et al. Natural History of Pressure Injury Among Ethnically/Racially Diverse Nursing Home Residents: The Pressure Ulcer Detection Study. *J Gerontol Nurs*. 2021;47(3):37-46. doi:10.3928/00989134-20210210-03
20. Bliss DZ, Gurvich O, Savik K, et al. Racial and ethnic disparities in the healing of pressure ulcers present at nursing home admission. *Arch Gerontol Geriatr*. 2017;72:187-194. doi:10.1016/j.archger.2017.06.009
21. Zheng NS, Shung DL, Kerby EH. Racial and ethnic differences in hospital admissions for cellulitis in the United States: A cross-sectional analysis [published online ahead of print, 2022 Aug 27]. *J Am Acad Dermatol*. 2022;S0190-9622(22)02613-5. doi:10.1016/j.jaad.2022.08.038
22. Fayne RA, Borda LJ, Egger AN, Tomic-Canic M. The Potential Impact of Social Genomics on Wound Healing. *Adv Wound Care (New Rochelle)*. 2020;9(6):325-331. doi:10.1089/wound.2019.1095
23. Yao, B., Cheng, Y., Wang, Z. et al. DNA N6-methyladenine is dynamically regulated in the mouse brain following environmental stress. *Nat Commun* 8, 1122 (2017). <https://doi.org/10.1038/s41467-017-01195-y>
24. Keisler-Starkey, K & Bunch, L. Health Insurance: Coverage in the United States: 2020. United States Census Bureau. Sept 2021. Retrieved 9/6/22 from <https://www.census.gov/library/publications/2021/demo/p60-274.html>
25. Inzerro, A. Incremental Steps Helpful but Not Enough to End Underinsurance Issue, Panelists Say. *American Journal of Managed Care*. April, 2022. Retrieved 9/6/22 from <https://www.ajmc.com/view/incremental-steps-helpful-but-not-enough-to-end-underinsurance-issue-panelists-say>
26. Gauthier T, Chen W. Modulation of Macrophage Immunometabolism: A New Approach to Fight Infections. *Front Immunol*. 2022;13:780839. Published 2022 Jan 26. doi:10.3389/fimmu.2022.780839
27. Koehly LM, Persky S, Philip Shaw, et al. Social and behavioral science at the forefront of genomics: Discovery, translation, and health equity. *Soc Sci Med*. 2021;271:112450. doi:10.1016/j.socscimed.2019.112450
28. Cole SW, Hawkey LC, Arevalo JM, Cacioppo JT. Transcript origin analysis identifies antigen-presenting cells as primary targets of socially regulated gene expression in leukocytes. *Proc Natl Acad Sci U S A*. 2011;108(7):3080-3085. doi:10.1073/pnas.1014218108
29. Carter MJ, Fife CE. Clinic visit frequency in wound care matters: data from the US wound registry. *J Wound Care*. 2017;26(Sup1):S4-S10. doi:10.12968/jowc.2017.26.Sup1.S4
30. Warriner RA 3rd, Wilcox JR, Carter MJ, Stewart DG. More frequent visits to wound care clinics result in faster times to close diabetic foot and venous leg ulcers. *Adv Skin Wound Care*. 2012;25(11):494-501. doi:10.1097/01.ASW.0000422629.03053.06
31. Hooper J, Shao K, Feng H. Racial/Ethnic Health Disparities in Dermatology in the United States Part 1: Overview of Contributing Factors and Management Strategies. *J Am Acad Dermatol*. 2022.
32. Vaidya T, Zubritsky L, Alikhan A, Housholder A. Socioeconomic and geographic barriers to dermatology care in urban and rural US populations. *J Am Acad Dermatol*. 2018;78(2):406-408.5.
33. Abokwidir M, Davis SA, Fleischer AB, Pichardo-Geisinger RO. Use of the emergency department for dermatologic care in the United States by ethnic group. *J Dermatolog Treat*. 2015;26(4):392-394.
34. LH Lumey, Aryeh D Stein, Henry S Kahn, Karin M van der Pal-de Bruin, GJ Blauw, Patricia A Zybert, Ezra S Susser, Cohort Profile: The Dutch Hunger Winter Families Study, *International Journal of Epidemiology*, Volume 36, Issue 6, December 2007, Pages 1196-1204, <https://doi.org/10.1093/ije/dym126>



# Thank you!

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# Questions?

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