Website: bit.ly/mahping

From Bench to Bedtime: Entraining Policy to Science

Day 3

Instructors: Lucy Lai, Brittany Bush, Mikaili Abdullah

Course Schedule

Day One

- What are circadian rhythms, and why do they matter?
- Autoinhibitory transcriptional networks allow for temporal gene regulation
- How environmental stimuli like light can “entrain” the circadian clock
- How the brain coordinates circadian rhythms in the periphery

Day Two

- How does circadian biology impact shift workers?
- Shift work as a historical phenomenon
- How to leverage circadian biology to improve health outcomes in shift workers
- Exploring the board ramifications of shift work

Day Three

- How our natural rhythms interact with societal demands
- The biological effects of policies such as Daylight Savings Time (DST)
- How future policies can be informed by circadian biology
- How to mitigate negative effects of circadian disruption

Learning Objectives

At the end of Day 3, students can ...

- ❏ discuss how chronotypes interact with health outcomes, and societal and work demands
- ❏ define daylight savings time and explain its cascading effects on behavior
- ❏ develop a plan to mitigate negative effects of circadian disruption
- ❏ appraise how future policies should be informed by circadian biology

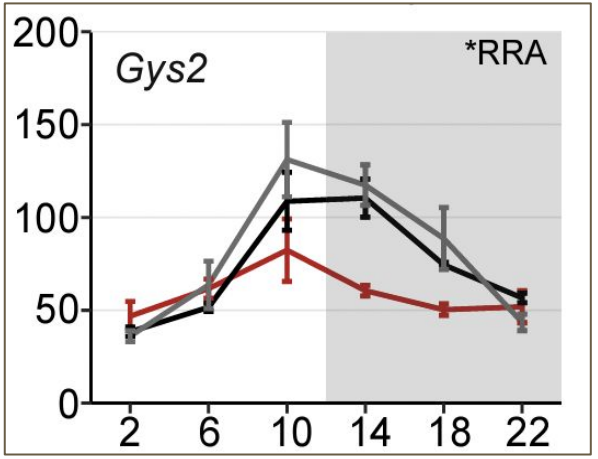
But first...

Addressing a few questions from Day 2

- What is it biochemically that makes daytime digestion so much more adaptive than nighttime digestion?
- Is healthy food also going to impact the metabolics as much as high-fat diet?
- Can peripheral cues train the master clock in absence of light?

Daytime digestion vs nighttime digestion, health interventions beyond TRE

- It’s not necessarily night vs day, but the segregation of disparate metabolic pathways
- If cells are producing mRNA for every pathway at once, each pathway is inherently less efficient
- Health benefits of TRE in mice are diminished if the mice are fed regular chow instead of a high-fat diet, even if the regular chow is ad libitum
- In human studies, diet interventions have similar efficacy to time-restricted eating in the short term



Can peripheral cues train the master clock in absence of light?

communications biology

ARTICLE

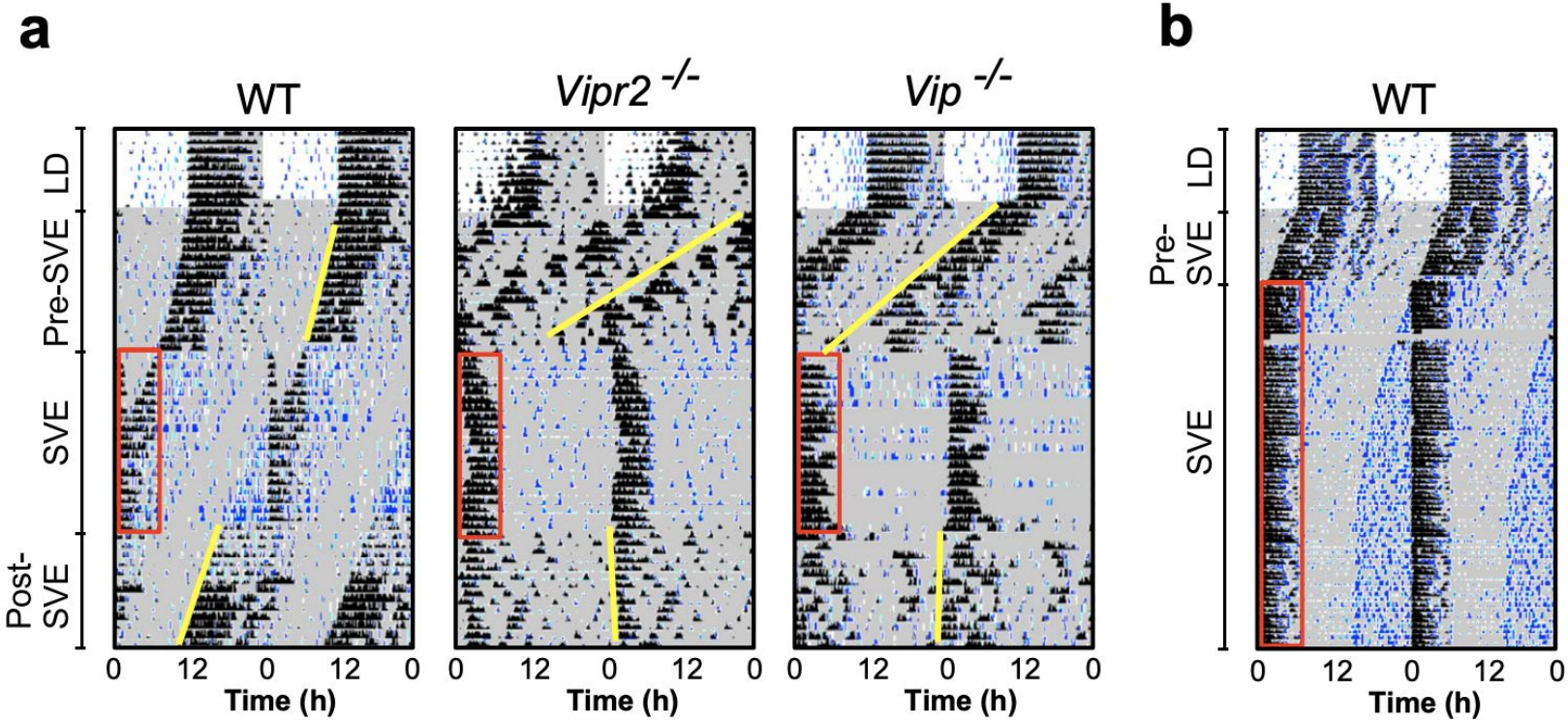
https://doi.org/10.1038/s42003-021-02239-2 OPEN

Check for updates

Timed daily exercise remodels circadian rhythms in mice

Alun Thomas Lloyd Hughes[1,2], Rayna Eve Samuels[1,6], Beatriz Baño-Otálora[1,6], Mino David Charles Belle[1,3], Sven Wegner[1], Clare Guilding[1,4], Rebecca Catrin Northeast[1], Andrew Stewart Irvine Loudon[1], John Gigg[1] & Hugh David Piggins[1,5]✉

In mice with disrupted SCN neuropeptide signaling, scheduled voluntary exercise (SVE) promotes SCN clock cell synchrony and robust 24h rhythms in behavior



Natural Rhythms Vs Society

- Previously, we learned that the body interacts with the environment allowing for entrainment of the biological clock.
- Environmental Influences:
  - Shift work
  - School start times
  - Daylight Savings Time
  - Traveling
  - Social Jetlag
- These environmental cues interact with the natural expression of our circadian rhythmicity.

Chronotypes

- The behavioral expression of our circadian rhythmicity.
  - Influenced by age, environment, genetics, and sex.
- Chronotypes are categorized into the following:
  - Morningness - “Lark”
  - Intermediate - “Finch”
  - Eveningness - “Owl”

Zavada, Andrei et al. “Comparison of the Munich Chronotype Questionnaire with the Horne-Ostberg's Morningness-Eveningness Score.” *Chronobiology international* vol. 22,2 (2005): 267-78.
Horne, J. A., & Östberg, O. (1976). A self-assessment questionnaire to determine morningness-eveningness in human circadian rhythms. *International Journal of Chronobiology, 4,* 97–110.

Chronotypes and Disease Risk

Morningness

- Associated with lower BMI
- Little to no expression change in clock genes
- Better sleep quality
- Better at following social and work time norms

Eveningness

- Associated with higher BMI
- Associated with Type 2 Diabetes prevalence and lack of glycemic control
- Poor sleep quality and increased sleep disturbance
- Changes in clock gene expression
- High association with anxiety and depression

Lemoine, Patrick et al. “Associations between morningness/eveningness and psychopathology: an epidemiological survey in three in-patient psychiatric clinics.” *Journal of psychiatric research* vol. 47,8 (2013)
Elizabeth Culnan, Jacqueline D. Kloss & Michael Grandner (2013) A prospective study of weight gain associated with chronotype among college freshmen, Chronobiology International
Takahashi, M., Tahara, Y., Tsubosaka, M. *et al.* Chronotype and social jetlag influence human circadian clock gene expression. *Sci Rep* **8,** 10152 (2018)

What chronotype are you?

Morningness

Eveningness

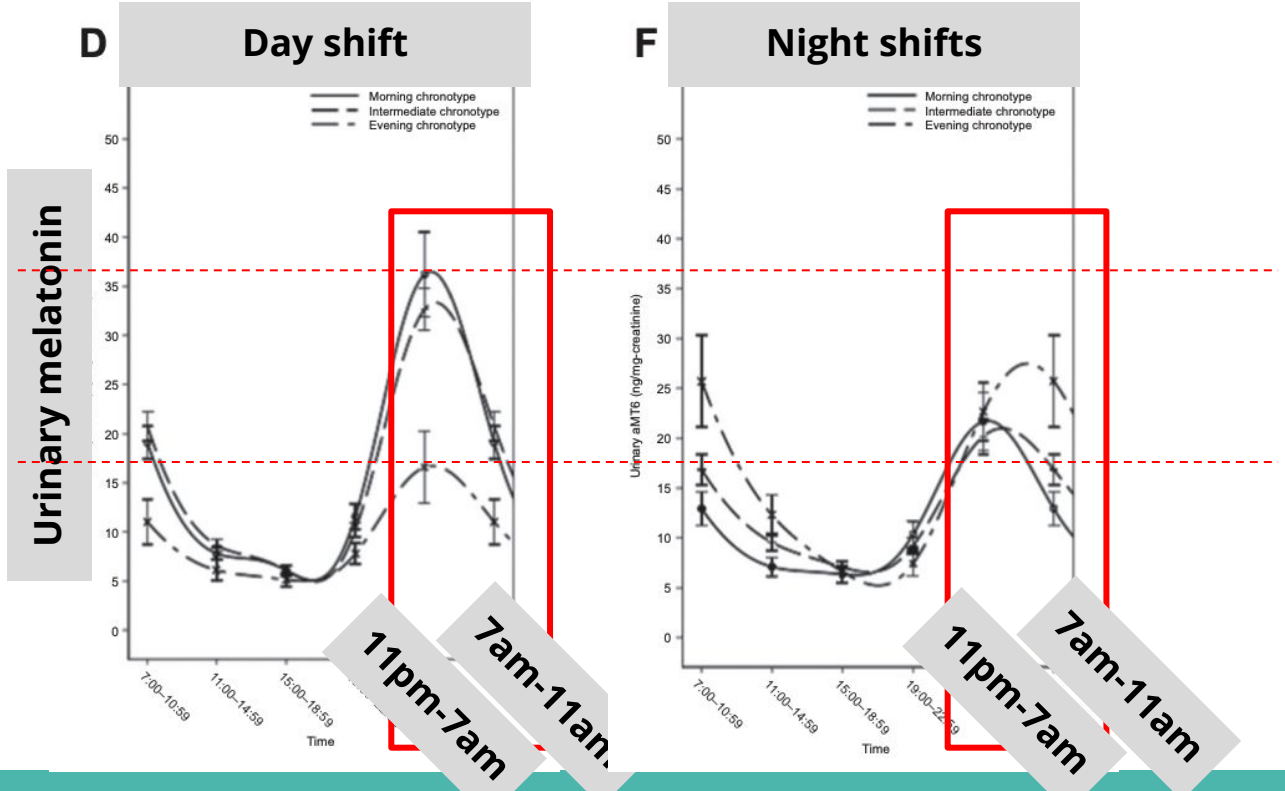
Intermediate

Do you think your chronotype matches your social behavior?

Shift work & chronotype

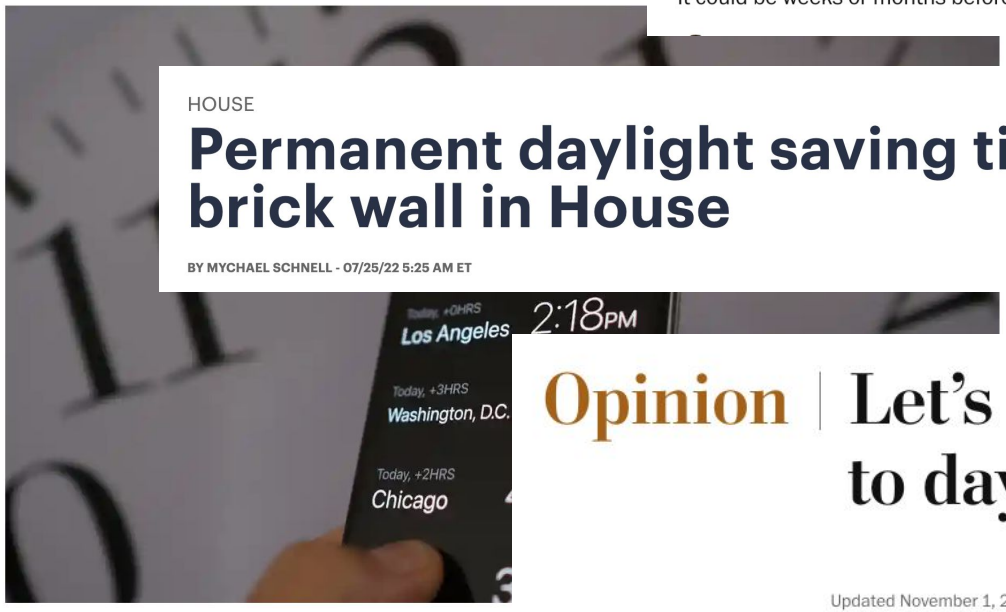
Razavi P, et. al., Shift Work, **Chronotype, and Melatonin Rhythm in Nurses.** Cancer Epidemiol Biomarkers Prev. 2019 Jul;28(7):1177-1186. PMID: 31142495

- Better alignment of shift-work type and chronotype may produce melatonin rhythms **more appropriately aligned with natural sleep-wake and dark-light schedules**



‘No more switching clocks’: Senate passes act to make daylight saving time permanent

Sunshine Protection Act needs approval from the signature of Joe Biden, to become law



Bill named the Sunshine Protection Act would ensure Americans no longer have to change their clocks twice a year. Photograph: Chris Delmas/AFP/Getty Images

Senate plan for permanent daylight saving time faces doubts in the House

It could be weeks or months before Democrats decide whether to tee up a vote, Rep. Frank Pallone Jr. says

HOUSE

Permanent daylight saving time hits brick wall in House

BY MYCHAEL SCHNELL - 07/25/22 5:25 AM ET

Opinion

Let’s say a permanent goodnight to daylight saving time

By Heather Turgeon and Julie Wright

Updated November 1, 2022 at 7:30 a.m. EDT | Published November 1, 2022 at 7:00 a.m. EDT

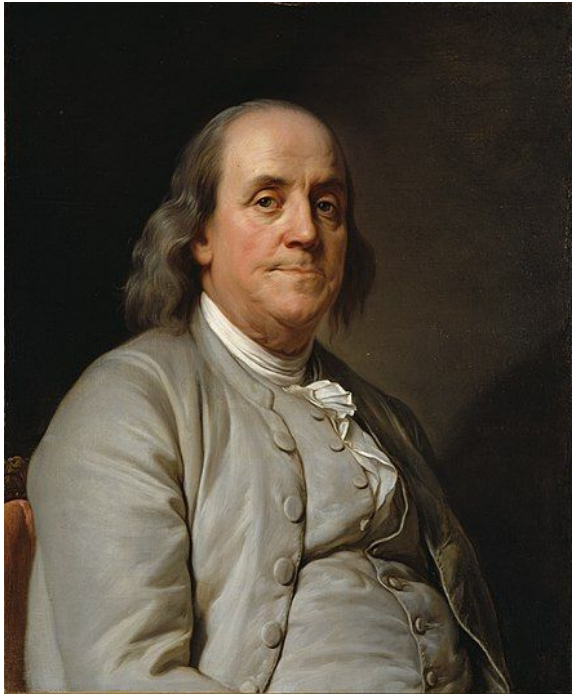
What is Daylight Savings Time?

Daylight Saving Time (DST) is to have darkness fall at a **later clock time during the spring and summer,** which gives people an **extra hour of daylight while the weather is warm.**

Some history about Daylight Savings Time

- The idea of of **aligning waking hours to daylight hours** to conserve candles was first proposed in 1784 by **Benjamin Franklin**.

“An immense sum! That the city of Paris might save every year, by the economy of using sunshine instead of candles.”



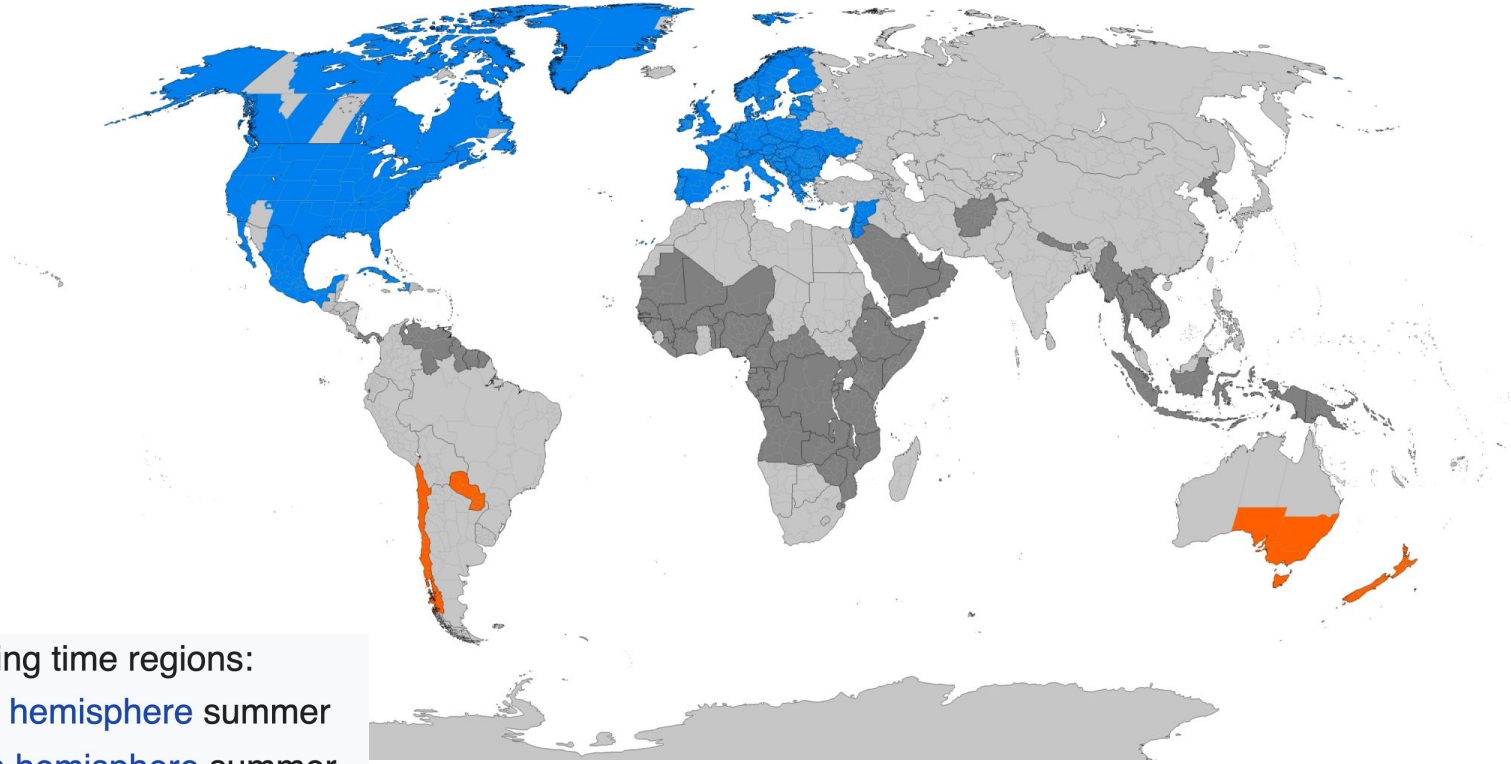
Some history about Daylight Savings Time

DST in the United States was first put to use during **World War I**

- In 1916, the German Empire set clocks ahead one hour in an effort to use **less power for lighting** and to **save fuel** for the war effort.
- In World War II, the US was on DST for more than **three years!**
- **Modern day:** According to a 2022 poll, **only 35% of Americans want to keep switching back and forth from ST to DST, and 59% wanted to see DST made permanent**

https://fivethirtyeight.com/features/do-americans-really-want-permanent-daylight-saving-time/

The use of DST around the world

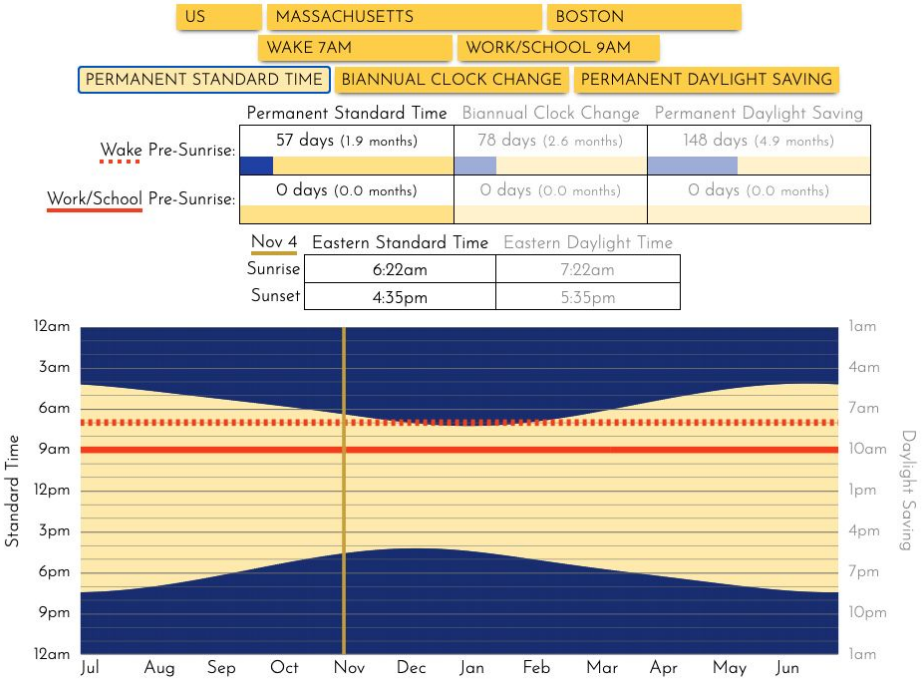


Daylight saving time regions:

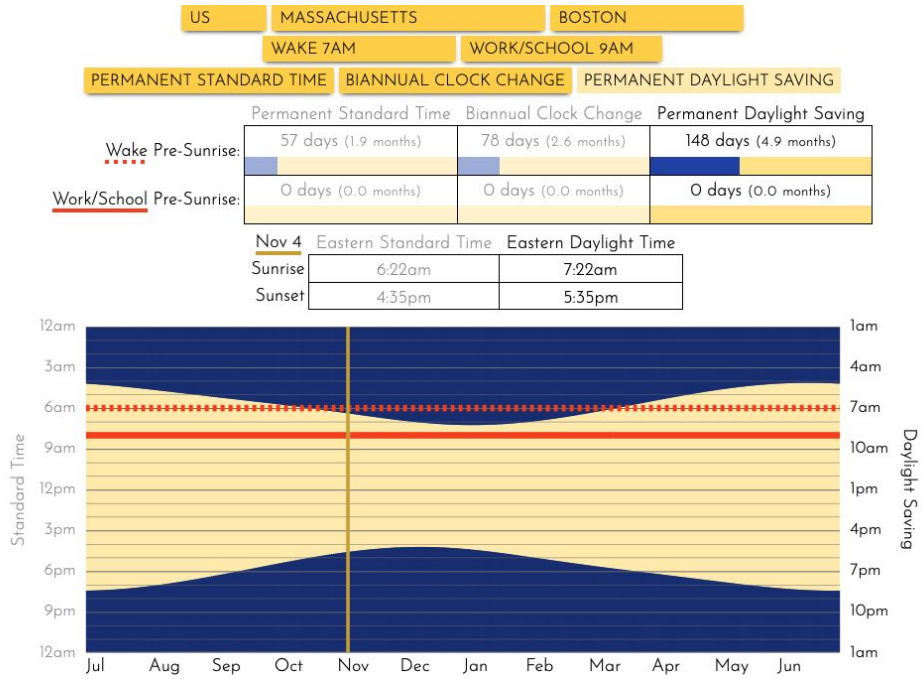
- Northern hemisphere summer
- Southern hemisphere summer
- Formerly used daylight saving
- Never used daylight saving

Go to website: bit.ly/mahping
Day 3 Links → “Save Standard Time”

Permanent Standard Time

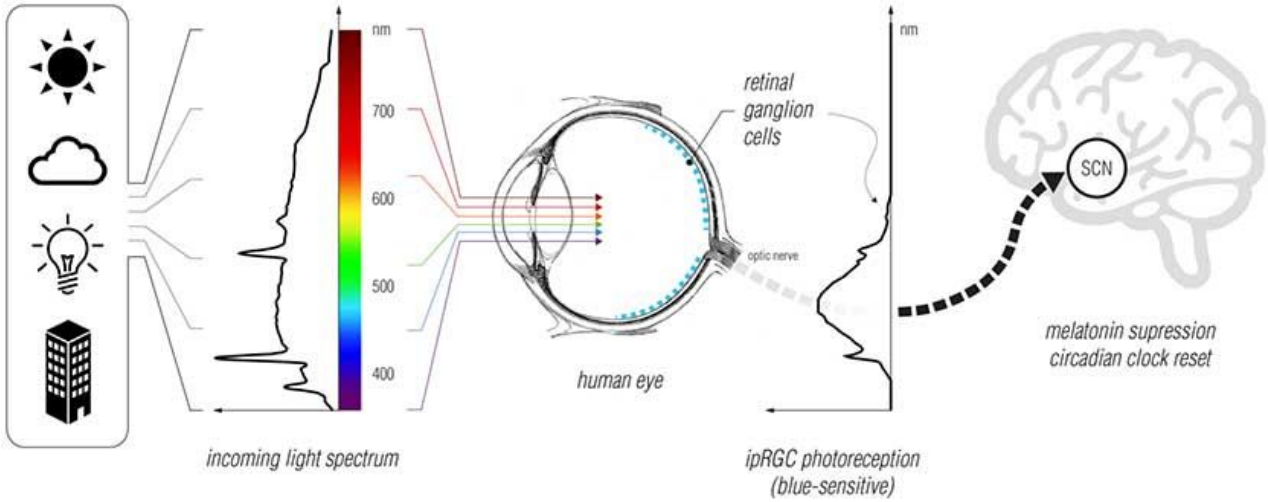


Permanent Daylight Savings Time

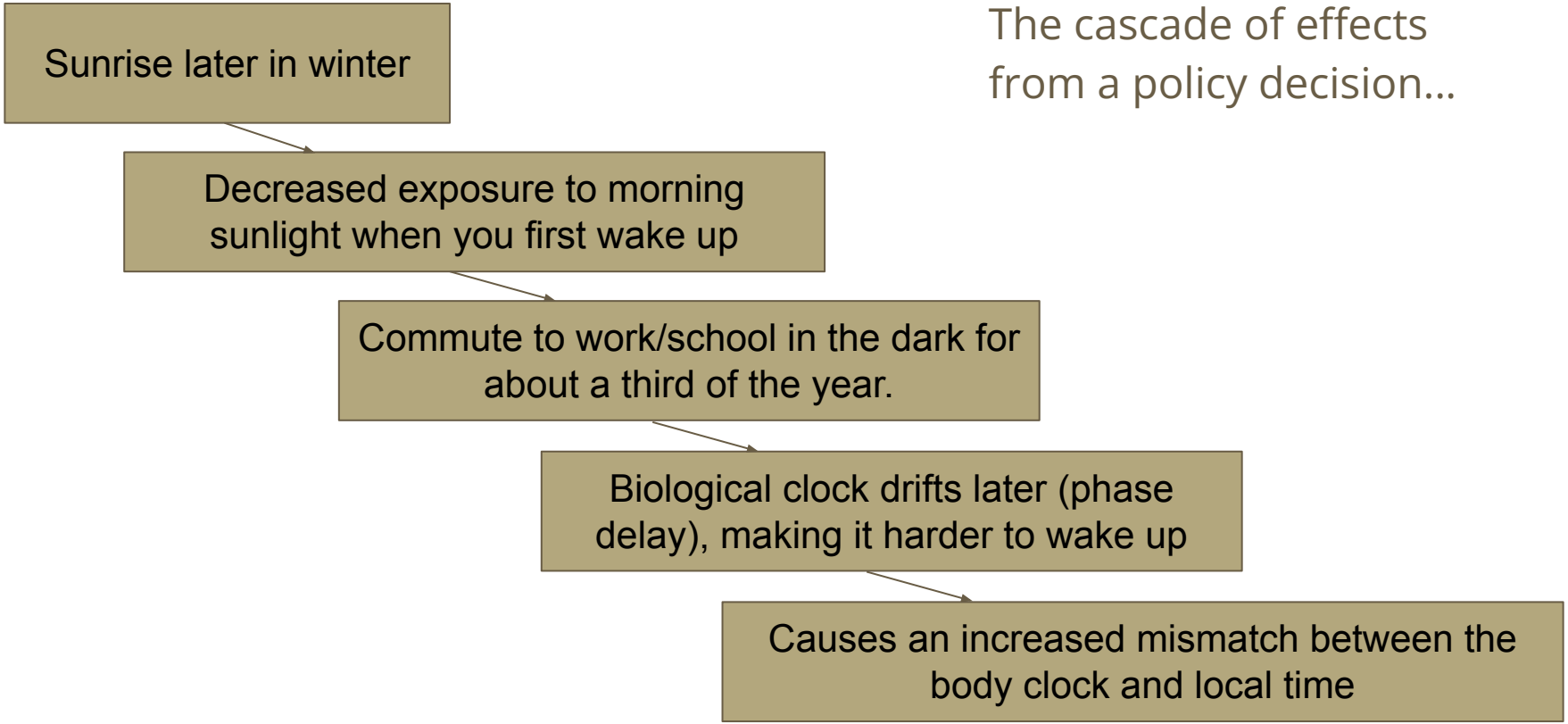


Review: morning light as a natural cue for wakefulness

- Morning light (short wavelength) *advances* the clock by triggering photoreceptors in your eye that suppress melatonin



Consequences of permanent DST



The cascade of effects from a policy decision...

Standard Time -> Daylight Savings Time Biannual Change

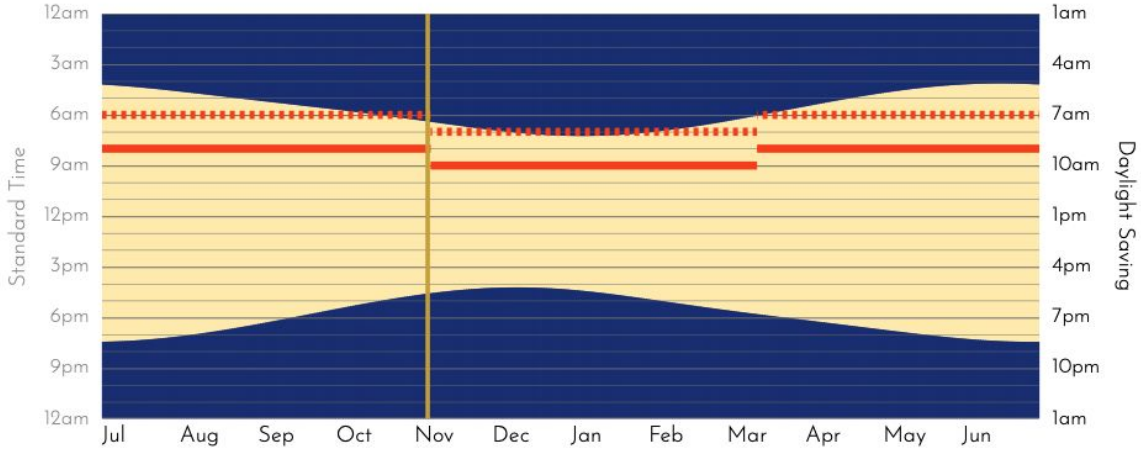
US | MASSACHUSETTS | BOSTON

WAKE 7AM | WORK/SCHOOL 9AM

PERMANENT STANDARD TIME | BIANNUAL CLOCK CHANGE | PERMANENT DAYLIGHT SAVING

	Permanent Standard Time	Biannual Clock Change	Permanent Daylight Saving
Wake Pre-Sunrise:	57 days (1.9 months)	78 days (2.6 months)	148 days (4.9 months)
Work/School Pre-Sunrise:	0 days (0.0 months)	0 days (0.0 months)	0 days (0.0 months)

Nov 4	Eastern Standard Time	Eastern Daylight Time
Sunrise	6:22am	7:22am
Sunset	4:35pm	5:35pm

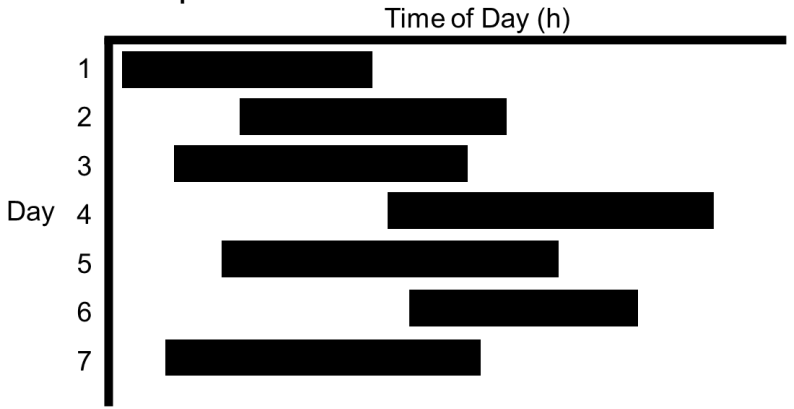


Group Activity:

Sketch a 7-day actogram of…

- **Scenario 1: “Fall Back” or the transition to Standard Time (November)**
- **Scenario 2: “Spring Forward” or the transition to Daylight Savings Time (March)**

Example:



Entering Standard Time (November)

Phase _____? (advance / delay)

Entering DST (March)

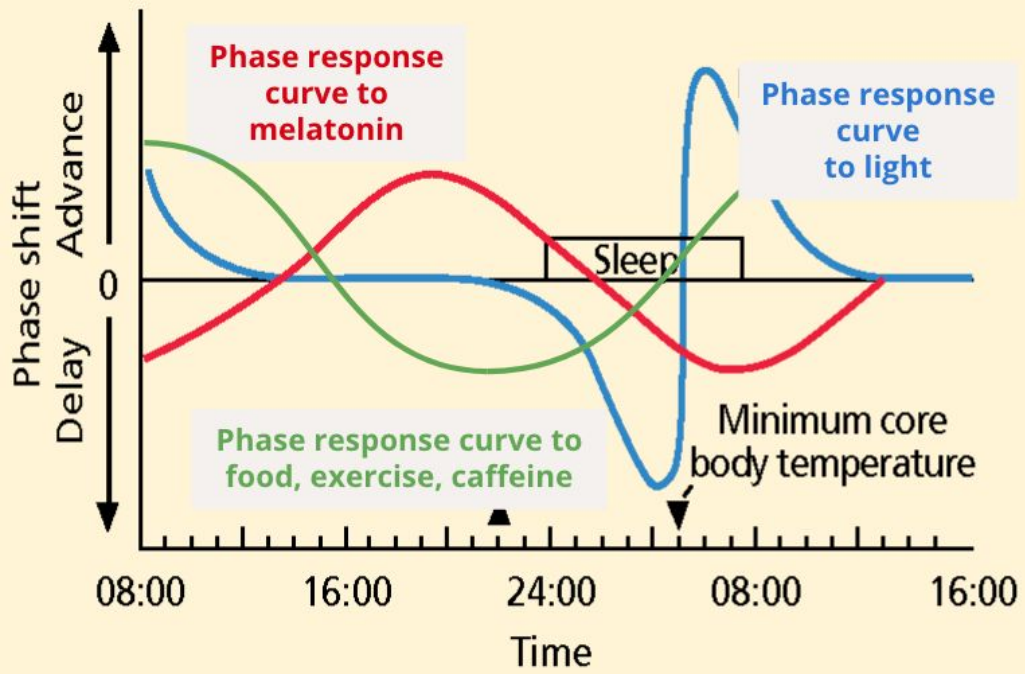
Phase _____? (advance / delay)

If the natural human circadian rhythm is >24hrs, which transition would naturally be easier for us?

Review activity: dealing with the biannual shift (or jet lag, or any circadian disruption!)

What are some behavioral changes you could make to adjust to...

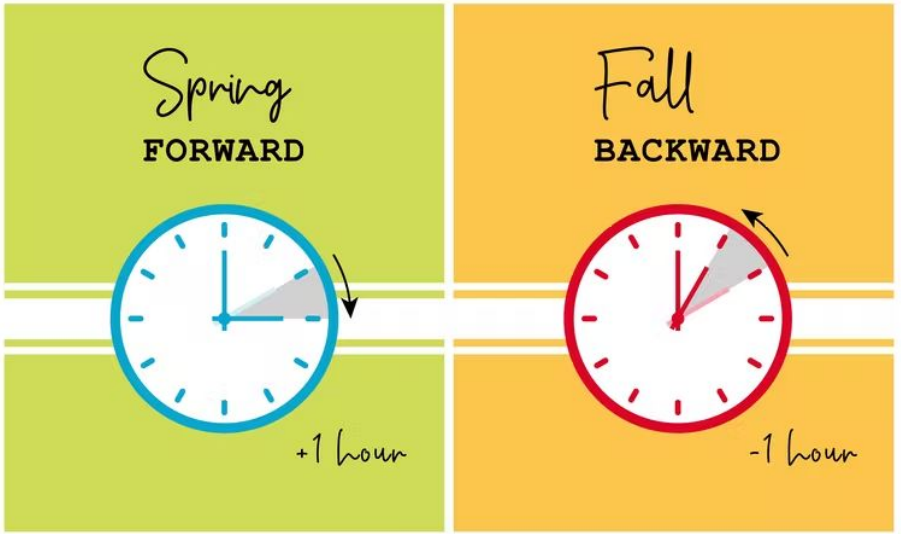
- the “Fall Back” phase delay in November (**on Sunday**)?!
- the “Spring Forward” phase advance in March?



Has anyone been personally affected by the biannual clock change to and from DST?

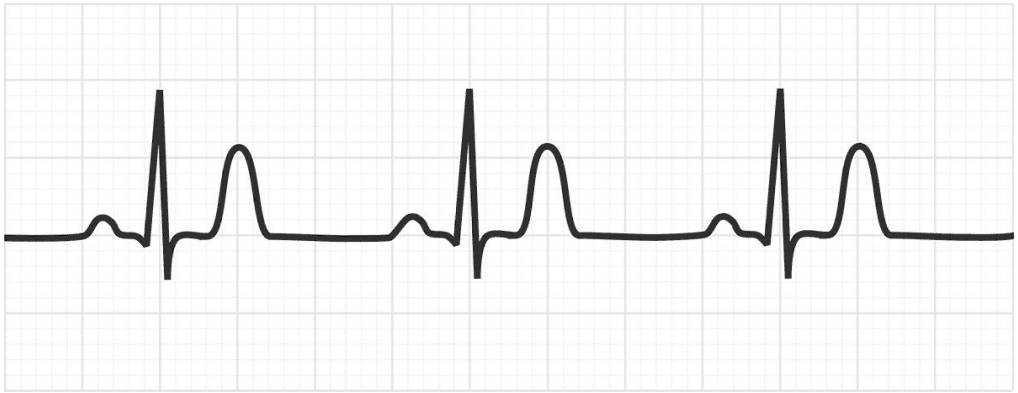
Clock changes and health outcomes

- The biannual clock change can increase many different health and safety risks.
  - Sleep
  - Diabetes risk
  - Cardiovascular health
  - Digestion
  - Psychiatric health
  - Traffic accidents



Effects of Time Shifting on Heart Attack Occurrence

- Assessed changes in admission of acute myocardial infarction between Jan 1, 2010 and Sep 15, 2013.
  - Accounts for four changes into DST (spring forward) and three changes into ST (fall back).
- Patient data collected from hospitals across the state of Michigan.
- The purpose was to investigate the differences in AMI admissions following the start of DST and ST.



Effects of Time Shifting on Heart Attack Occurrence

- The Monday following spring time changes was associated with a 24% increase in daily AMI counts.
- The Tuesday following fall changes was conversely associated with a 21% reduction.
- There was no significant difference for total weekly counts or any other weekdays.

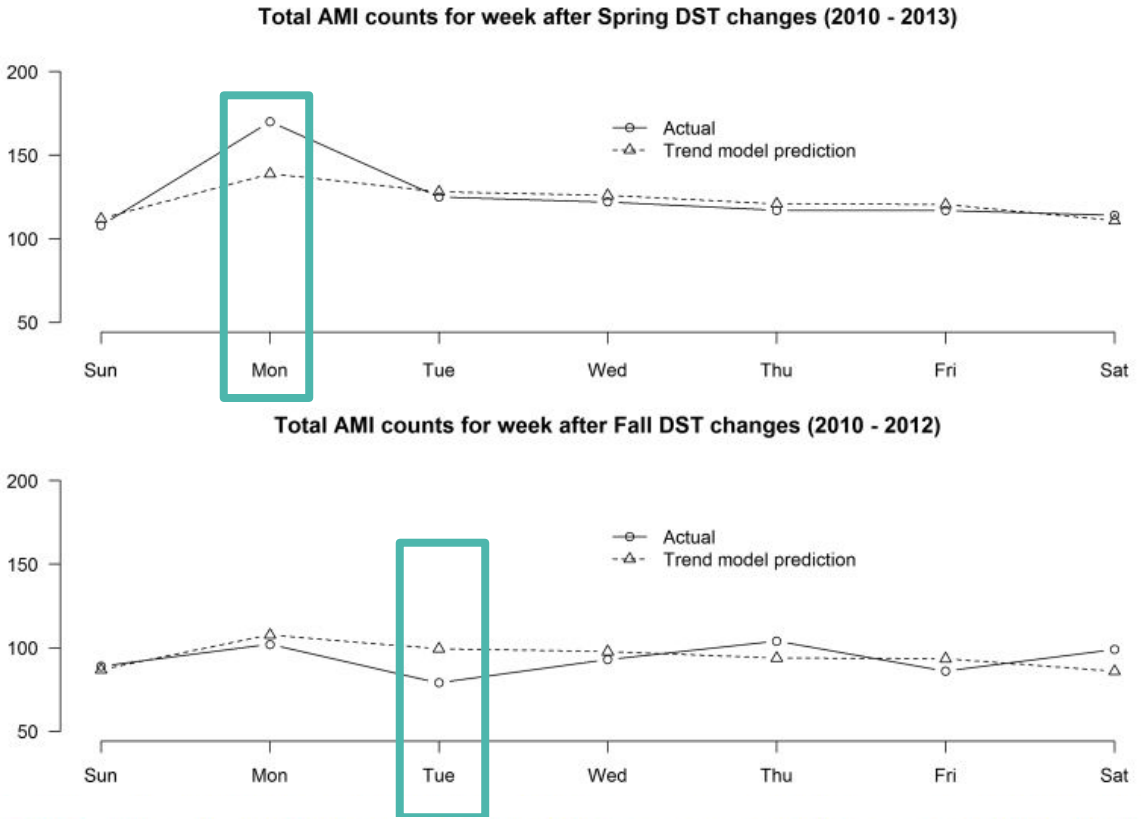
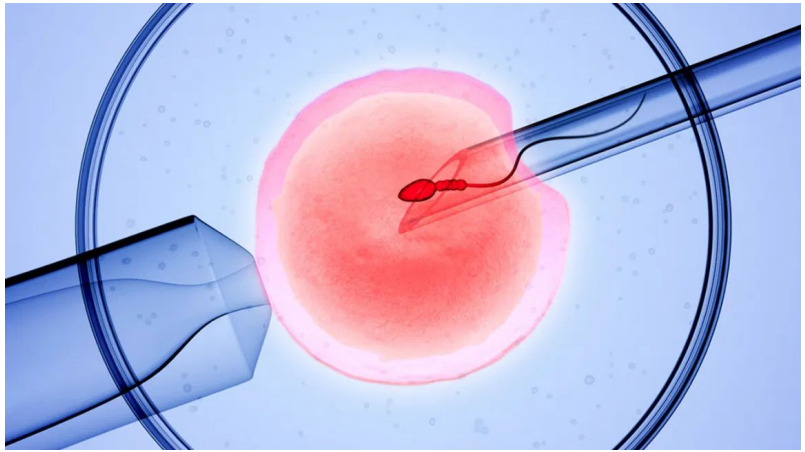


Figure 3 Actual and predicted acute myocardial infarction (AMI) counts for the weeks after the spring and fall daylight savings time (DST) time changes.

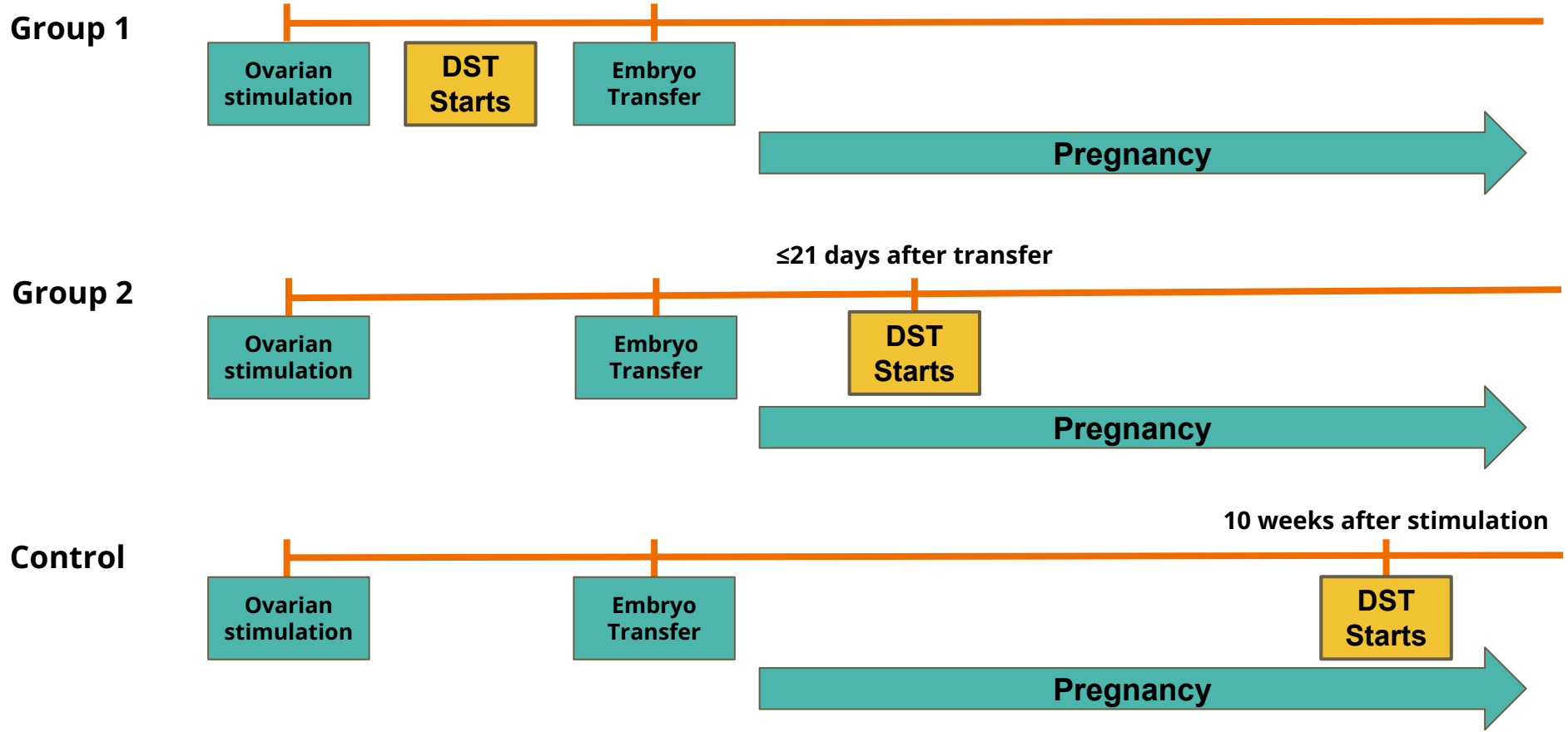
Sandhu A, Seth M, Gurm HS. Daylight savings time and myocardial infarction. Open Heart 2014;1:e000019. doi:10.1136/openhrt-2013- 000019

DST effects on IVF Pregnancy

- Retrospective study of 1,654 women who underwent in vitro fertilization (IVF).
- Data analyzed was collected between 2009 and 2012.
- Purpose was to investigate the impact of DST on IVF outcomes.



DST effects on IVF Pregnancy



DST effects on IVF Pregnancy

Table 2. Rates of pregnancy and spontaneous pregnancy loss compared by season and across age groups.

	Spring				
	Group 1[1] (n = 294)	Group 2[2] (n = 274)	Control[3] (n = 255)	TOTAL (n = 823)	*p*-value
Pregnancy Rate	40.1% (n = 118)	40.5% (n = 111)	43.9% (n = 112)	41.4% (n = 341)	0.622
Age <40 only	41.4% (n = 99)	44.5% (n = 97)	44.0% (n = 91)	43.2% (n = 287)	0.777
Age 40+ only	34.5% (n = 19)	25.0% (n = 14)	43.8% (n = 21)	34.0% (n = 54)	0.131
Pregnancy Loss	10.2% (12/118)	24.3% (27/111)[4]	12.5% (14/112)	15.5% (53/341)	0.007
Age <40 only	8.1% (8/99)	19.6% (19/97)[5]	7.7% (7/91)	11.8% (34/287)	0.015
Age 40+ only	21.1% (4/19)	57.1% (8/14)	33.3% (7/21)	35.2% (19/54)	0.098
	Fall				
	Group 1[1] (n = 253)	Group 2[2] (n = 287)	Control[3] (n = 291)	TOTAL (n = 831)	*p* value
Pregnancy Rate	40.7% (n = 103)	45.3% (n = 130)	40.5% (n = 118)	42.2% (n = 351)	0.431
Age < 40 only	41.8% (n = 87)	46.7% (n = 113)	42.4% (n = 98)	43.8% (n = 298)	0.514
Age 40+ only	35.6% (n = 16)	37.8% (n = 17)	33.3% (n = 20)	35.3% (n = 53)	0.894
Pregnancy Loss	17.5% (18/103)	16.2% (21/130)	17.8% (21/118)	17.1% (60/351)	0.936
Age < 40 only	13.8% (12/87)	13.3% (15/113)	15.3% (15/98)	14.1% (42/298)	0.910
Age 40+ only	37.5% (6/16)	35.3% (6/17)	30.0% (6/20)	34.0% (18/53)	0.886

- Pregnancy loss following IVF increased during DST
  - Embryo transfer before spring forward experienced a significantly higher rate of pregnancy loss at 24.3%.
  - Embryo transfer 10 weeks before DST resulted in 12.5% pregnancy loss.

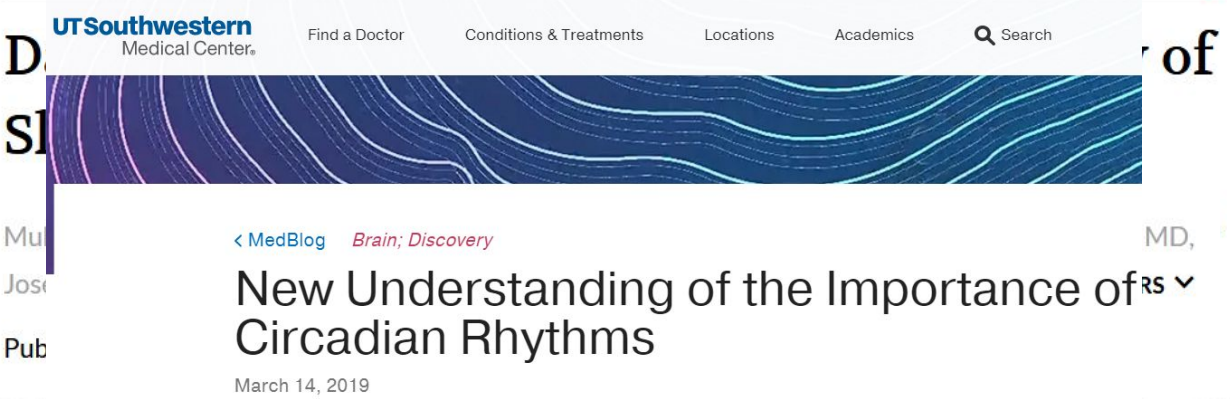
Constance Liu, Joseph A. Politch, Evan Cullerton, Kathryn Go, Samuel Pang & Wendy Kuohung. 2017. Impact of daylight savings time on spontaneous pregnancy loss in in vitro fertilization patients.Chronobiology International

- **24%** higher risk of heart attacks
- **6%** spike in fatal car accidents
- **8%** increase in stroke risk
- **11%** spike in depressive episodes

The week after shifting into DST

https://www.nm.org/healthbeat/healthy-tips/

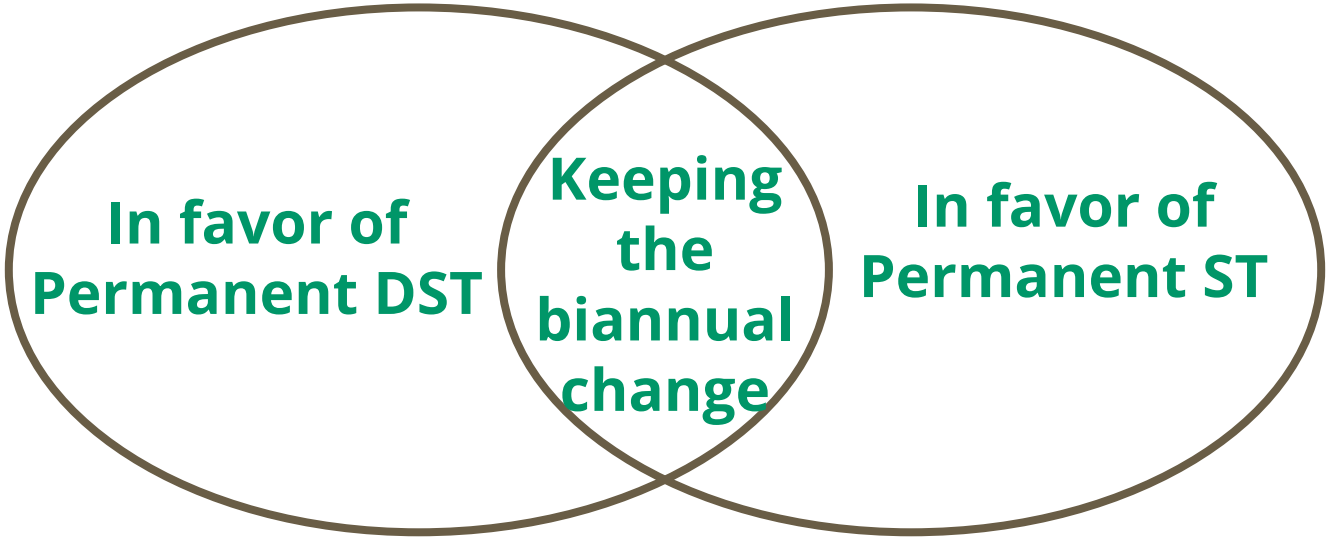
DST Position of Circadian Biologists



The choice of DST is political and therefore can be changed. If we want to improve human health, we should

disorders, and motor vehicle crashes. Although chronic effects of remaining in daylight saving time year-round have not been well studied, daylight saving time is less aligned with human circadian biology—which, due to the impacts of the delayed natural light/dark cycle on human activity, could result in circadian misalignment, which has been associated in some studies with increased cardiovascular disease risk, metabolic syndrome and other health risks. It is, therefore, the position of the American Academy of Sleep Medicine that these seasonal time changes should be abolished in favor of a fixed, national, year-round standard time.

DST or ST?



You might consider the following factors:

- Consequences of a clock change 2x/year
- Consequences of delayed morning light (later sunrises)
- Consequences of less light in the evenings (earlier sunsets)
- Consequences on the economy

Design an Experiment

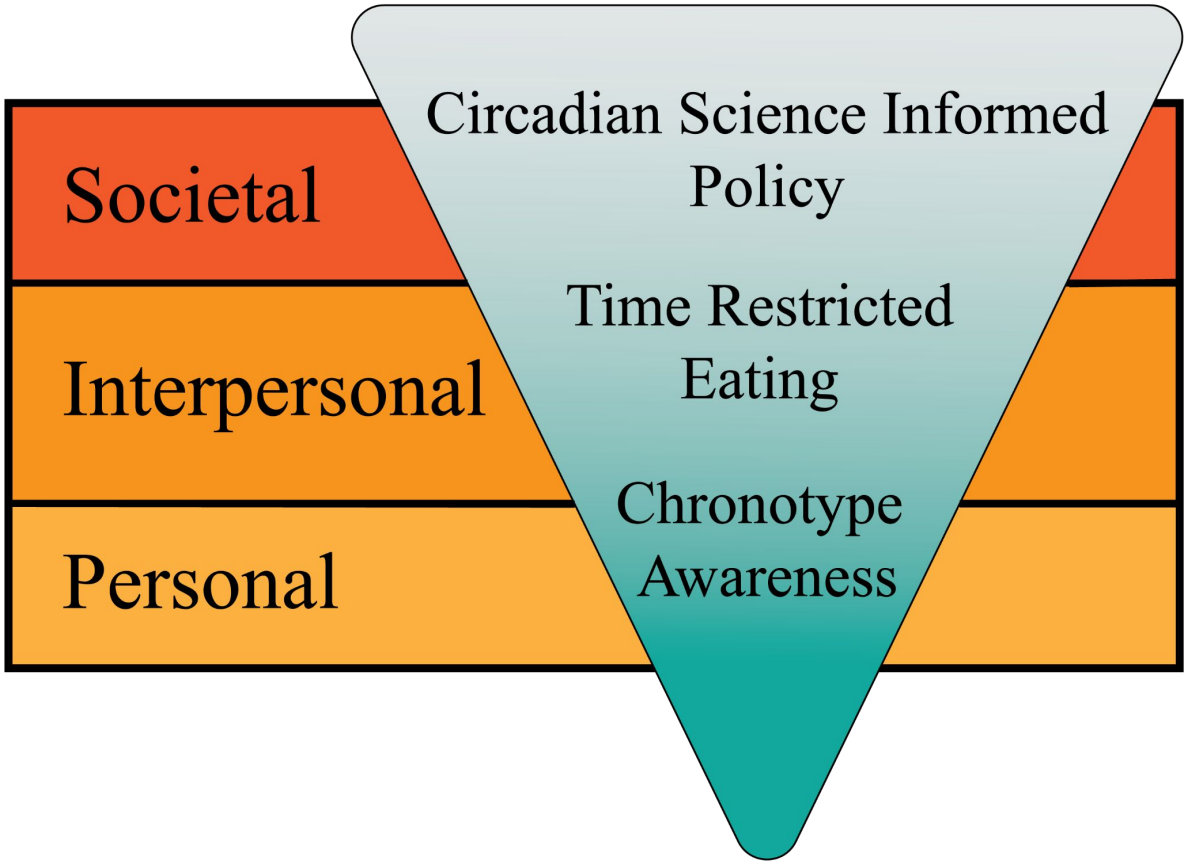
There are not many studies testing the effects of Permanent DST versus Permanent ST, and although scientists are in favor of permanent ST, the public does not fully agree.

To help determine which is better for overall health, we want you all to break into groups and design an experiment investigating how **permanent DST**, **permanent ST**, or **switching between DST and ST** would affect circadian biology in a specific organ system.

- How would they change expression of circadian proteins and hormone release (melatonin, CRY, PER, BMAL1, CLOCK)?
- Be sure to state your hypothesis and your research question.
- **BONUS:** Incorporate the role of chronotype in your study.

***There is no budget and no experimental limitations.**

Ways to Mitigate Negative Effects of Circadian Disruption



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- How environmental stimuli like light can “entrain” the circadian clock
- How the brain coordinates circadian rhythms in the periphery

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- How does circadian biology impact shift workers?
- Shift work as a historical phenomenon
- How to leverage circadian biology to improve health outcomes in shift workers
- Exploring the board ramifications of shift work

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