基調講演 2

Old and New Challenges in Understanding the Social Determinants of Health

社会的健康決定要因の理解のための課題

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本基調講演では、社会的健康決定要因（Social Determinants of Health：以下 SDH）の健康影響のメカニズムについて理解を深めるうえで、克服すべき課題について、整理する。大きく分けて、われわれは 4 つの課題に直面している。第 1 の課題は、決定要因が様々の社会構造・レベルのものを含んでいるということである。第 2 の問題はそれと関連しているが、因果関係が複雑に入り組んでいることである。第 3 にメカニズムの解明をさらに難しくしているのが、要因同士の間が動的な関係にあり、全体として系（システム）を構築している点である。最後の課題は、どのように得られた知見を具体的な政策や行動に結び付けていくかである。

まず第 1 の課題である構造要因のレベルの問題について述べる。遺伝子・個人の行動や医学生物学的要因・感染症などの外的因子、さらには広い意味での「環境」要因など、健康を左右する要因には様々なレベルのものが存在し、どのレベルの要因の影響を明らかにしようとするかによって、設定される研究仮説やモデルが異なってくる。またあるレベルの要因の影響を検討するには、他のレベルの要因の分布も考慮しなくてはならない。これらの要因が最終的に健康に影響を与える共通プロセスとして、結局遺伝子への影響や生活習慣行動などの個人レベルの要因に帰着できるという考え方がある。これまでの疫学研究はこうした前提に基づいて、危険因子などの同定に寄与してきた。しかし、このアプローチだけでは健康決定要因をすべて説明しきれないし、集団全体としての特性や構造が個人の健康に影響を与えることもある。また政策的にも個人にすべてを帰することはできない。そこで集団レベルの影響を疫学研究に再度取り組む試みが過去 10 年以上にわたって進められてきた。国・州・職場・近隣などの影響を検討した研究が近年多く発表されている。集団レベルの要因はさらに、個人レベルの要因の影響修飾因子としても考えられる。さらに、集団に含まれる個人の状態が他の集団構成員に与える外部性影響もある（たとえば感染の伝播や、社会的規範の与える行動への影響など）。

第 2 の課題である、複雑な因果関係については、従来の単純な連鎖モデルや多変量線形回帰モデルなどで解析可能なものに留まらず、変数同士の内因性、特に観察されていない変数の影響や、時間依存性のある変数同士の影響、さらに共変数同士の直接・間接影響の分離をどう図るかなどが問題となる。近年これについては傾向スコア法や操作変数法、パネルデータを用いた動的解析などの新しい統計手法の試みや、Directed Acyclic Graph などを用いた視覚的な因果関係の検討などが進んでいる。

第 3 の動的な系の問題であるが、ある個人が環境の影響を受けるという一方的なものではなく、個人はある環境を選択して集まり、周辺の環境の影響を受けて行動を変容し、それがまた周囲の個

人に影響を与えて環境が変化するなど、双方向的・動的な関係にあることを、考慮しなくてはならない。こうした動的・双方向性は、従来の線形回帰分析や、それの延長であるマルチレベル分析だけでは適切に取り扱えない。非線形的なモデルも必要となる。またその結果、従来の単純な因果関係モデルでは想定していない、時間・空間が離れている事象同士の「思わぬ」影響なども考慮しなくてはならないだろう。

第 4 の政策・実践との関連については、良い回答はまだない。ひとつの試みとして筆者が注目しているシステム・アプローチについて簡単に紹介したい。まず系（システム）を構成する要素を網羅的に列挙し、その情報を集積する。そして既存の理論・情報に基づき、それらの構成要素の関連モデルを構築し、さまざまなシナリオのもとでシュミレーションを行うことで、どのようにシステムが変動するかを検討するのである。従来の疫学的モデルとの違いは、還元主義的に共変量を制御するのではなく、複雑な系そのものとして取り扱い、個人や集団の病気の発生などのアウトカムがどのように変動するのかを検討するところにある。ただし、システムアプローチにも欠点がある。複雑すぎるモデルは構築・解釈が難しいので、どこまでの要素を含むか、どのように系を組み立てるかが課題となる。またシュミレーションのための元のデータが得られるものばかりとは限らない。しかしシステムアプローチは、系の構成要素がなにか、それらがどのように連関しているのかを、明示的にモデル化することで、関係者の間での議論を透明で開かれたものに促進するというメリットがあることも触れておかなくてはならない。すべてはシステム（系）であり、様々な手法でこれに取り組むことができる。柔軟で開かれた思考でこの複雑な問題に取り組むことが求められており、そのうえでシステムアプローチが持つ意義は大きい。複雑な SDH に取り組むには、実践と評価、観察研究とシュミレーションなどが相互に連関しあいながら、SDH 政策に必要な知的情報とエビデンスを構築していくことが求められるのである。

キーワード： 教育、訓練、研究、社会経済的健康決定要因

Transcript

Old and New Challenges in Understanding the Social Determinants of Health

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First of all, I would like to thank the organizers for inviting me. I am delighted to be here. This is an outstanding project, as I indicated yesterday in terms of its breadth and its interdisciplinary areas that it's focused on, which are very key areas in understanding social determinants, in general, worldwide. I want to commend you on that.

What I'd like to do is try to give you an overview what I see as what are some of the main challenges and difficulties that we face in understanding the social determinants of health. These are not new challenges. In fact, they have been around for a long time, although now we have some new things that we can do about them, but there are other things that we still have no clear solutions to. But, I think, it's useful to step back and think about these issues at this point.

I am going to talk about four issues. One has to do with levels of organization/multilevel determinants. The second has to do with complex causal chains. The third has to do with dynamic relations and systems, that is the interrelations between individuals and environments and also interrelations between social and biologic processes. The fourth, which I will touch on a little more briefly, has to do with the connection to policy and more generally to action in public health, which is ultimately the goal of everything we do.

Starting with levels of organization, as I am sure, you all know because you work in this field, there are a number of ways in which levels of organization affect the formulation of research questions and the analyses that we do and the ways in which we understand the social determinants of health. The first is that factors or constructs relevant to health can be defined at different levels.

They can be defined at the levels of countries, at the levels of states, at the levels of neighborhoods, at the levels of families, at the levels of all sorts of different kinds of peer groups. Questions can be defined at different levels as well. We can ask questions about variability across people, but we can also ask questions about variability across other kinds of groups, and those questions are as important as questions about variability across individuals.

The third point which I think is key is that understanding variability at a given level may require a consideration of other levels. Even if we are interested in understanding differences across countries, we can't do a purely ecologic analysis because we have to consider the characteristics of the individuals who live in those countries.

Similarly, even if we are interested in understanding variation across individuals, we may need to consider features of the different groups to which individuals belong in understanding that variability. There is not a simple dichotomy between understanding variability across groups and across individuals and in fact we have to integrate both those things regardless of the level in which our questions are formulated.

This is a very, very schematic diagram outlining what the focus of public health inquiry has been over time beginning with a very holistic understanding of the environment – with environmental defined rather loosely, very broadly and not very specifically. With the advent of the germ theory, public health became interested in germs and microbes and the environment being important only and so far as it was conducive to the reproduction of the germ and the transmission of the germ.

Then with the interest in chronic diseases and the emergence of cardiovascular disease epidemiology, which has been a sort of paradigm of chronic disease epidemiology, I would say; the focus shifted to behavioral and biomedical characteristics; then with the genetic revolution, the focus on genes which vary of course from individual to individual, and more recently for those who are following the more genetic work, ideally, it's not just about variations in genes, but also potentially about mutations which are specific to each person. Each of us has different mutations that could lead to the same outcome.

Over the coyrse of this evolution the focus has become more and more individualized, focused on individual-level characteristics, so there is this idea of individualization of risk, where risk is becoming more and more defined as a purely individual-level characteristic. These person-specific mutations are really the ultimate expression of this individualization if you think about it. This has led to a focus on individual-level risk factors. The corollaries of this approach are that the true

causes of disease can be found exclusively at the level of individuals or the true causes of disease can be found exclusively in the behavioral and biological characteristics of individuals.

When populations are referred to, usually, they are thought of more as collections of individuals than things that have properties that are more than aggregates of individual-level attributes. Although I am sure most people in this group would understand the limitations of this paradigm, I think, it's still quite strong, I mean, a lot of the health research that's done still implicty accepts this paradigm.

The methodological correlate of course is methodological individualism where emphasis is on inferences about relationships between variables at individual level, and this is why we focus on individual-level variables, why there is a big emphasis on studies of individuals as the units of analysis and why ecologic studies are sort of considered as second-level studies because they are not useful for reasons which I am sure you are familiar with in drawing individual-level inferences. When group or population-level variables are used, they are used as proxies for unavailable individual-level data.

This paradigm, has this approach been useful? I would say, yes, absolutely, it's been useful. We've learned a lot of things from this paradigm, from this individualization risk. We've learned a lot about major behavioral and psychosocial risk factors for chronic and infectious diseases. We've learned about biomedical risk factors as well. But, there are also reasons why it's limited.

I think it's clear that we have lot of evidence that explanations are focused purely on individual-level factors really don't explain even variability across individuals fully and in fact interventions that focus on changing individual-level characteristics in order to exert some sort of health effect have been rather disappointing and a part of the reason may be they are purely individual-level focus.

Of course, the other limitation is that populations have attributes and structures which affect individuals within them. A lot of times our policy interventions or possible policy interventions are really at the level of populations, not at the level of individuals, which is why it's so important to understand these population level factors.

If you think about almost any research problem in health, you can very quickly see that there are multiple levels that are likely to be involved; levels both within individuals and the many different groups and contexts to which individuals belong.

Of course, all the levels are not going to be relevant to every single research question and it's imperative for the investigator to identify and be very specific and explicit about the levels that are likely to be relevant and that's part of our role as scientists to be able to extract what we think is most important. Of course people cvan disagree about this and that is the basis for scientific debate. Thinking conceptually about what levels are likely to be relevant to the problem that we are studying is going to be key.

There are numbers of ways in which people have talked about bringing back this group or population dimension and there are three principal ways. One is this group-level attributes as themselves important to health. Second is group-level attributes as modifiers of individual-level effects. The third is this notion that the outcome for one individual may influence outcomes for others in the same population.

This is a classic figure, which I am sure you've seen many times from the famous paper by Geoffrey Rose showing the shift in the distribution of blood pressure in different societies. This is a very nice example of group-level effects and factor that operates in the group-level that shifts the whole distribution. Then, if you focus just on within individual comparisons, you won't detect this.

Now, there are lots of recent examples of social epidemiology trying to isolate group and individual effects in a way that is somewhat analogous to Rose's distinction between the causes of incidence and the causes of cases (in which causes of incidence refers to group-level factors; causes of cases refers to factors that are related to intra-individual variability within a group). We've made a lot of progress in this sense.

The second way in which group-level factors can be brought back into our thinking about health consequences has to do with group-level variables as modifiers of individual-level effects.

I always like to show this very simple diagram. The purpose is to reflect how the number of sexual contacts that a person has affects the risk of a sexually transmitted disease/ The impact of the number of contacts, the relationship between number of contacts and risk of a primary infection is going to be different depending on the structure of contacts. So the structure of connections between people can modify the effect of the individual-level risk factor which is the number of sexual contacts.

There are a number of examples in social epidemiology, and I have put this hypothetical example here because I think we've been a little less successful at documenting these interactions (sometimes called "cross-level interactions"). I think people have attempted to look at them. Detecting them may be difficult for methodologic reasons; it's been more difficult to detect them and replicate them across studies. As an example we can also think of modification of income gradients by country-level policies.

You can think of modification of neighborhood effects by personal resources; neighborhood context doesn't affect everyone equally. If you think of gene environment interaction broadly, there's also this kind of cross-level effect, so population-level features may modify genetic effects on obesity. I think we still need to look for these

things. But, methodologically, it's a lot more complicated in terms of kind of samples that one needs to be able to do this.

There is a third way in which this group dimension enters into our studies that has to do with the idea that the outcome for one individual influences outcomes for others within the same population. This has been a mainstay of infectious disease epidemiology but only recently has it really trickled into other kinds of studies. Of course, transmission of norms or behavioral characteristics is one example.

This is, perhaps, a very famous recent example which was this paper published a few years ago in The New England Journal showing the relationship between a friend becoming obese and an index person becoming obese and lots of debate around what can be concluded from these analyses, whether it's true contagion. But, nevertheless, it shows that this idea has really come into chronic disease epidemiology and behavioral epidemiology as well.

I'll give you some examples of the ways in which we have brought the group-level dimension into epidemiologic analyses and more generally some of the implications of recognizing that we have processes operating at multiple levels resulting in the need for theories and conceptualizations that go across levels.

A major change is that we really need to be very specific for a particular and specific health outcome of what the levels that are relevant might be. I think one of the dangers with, for example, the advent of multilevel analysis is that it's very easy to add more variables to the existing study without thinking carefully about what are the specific hypotheses that we are testing and what are the processes.

There is a lot more room, I think, for theories that really articulate the levels of their interrelations and the multi-level processes, and that are specific to the particular thing that we are studying. The other implication has to do with study design and data collection obviously. I think everyone is quite aware that we really need studies in groups and individuals so that we can look at variability both within and between groups.

There are causes of cases and causes of rates in Rose's terminology, and important challenges related to measurement at various levels. We are relatively good at measuring things about individuals. We are not so good about measuring things about contexts. I think there has been a lot of advance in this area over the past few years, but there is still a lot of work to do because these are complex constructs, we saw the example of social capital for example, so measurement issues are really not trivial.

Then, of course, there are analytical methods and all I am going to say here is that it is about much more than multilevel analysis. One can address multilevel questions without doing multilevel analysis and in fact often that's the right thing to do. For some kinds of questions, you may need multilevel analysis. But, you may also need other kinds of methods, and I'm going to talk a little bit more about that.

The second big challenge has to do with the fact that by definition looking at the social determinants of health we are dealing with complex causal chains. I'd like to start with this quote by one of the fathers, I guess, of epidemiology, Wade Hampton Frost, who said "Epidemiology at any given moment is something more than the total of its established facts. It includes their orderly arrangement into chains of inference which extends more or less beyond the bounds of direct observation."

In understanding the social determinants of health, one of the challenges that we have is that we deal with very, very long causal chains because we are looking at very distal factors, factors that are very distal to the health outcome that we are looking at.

This presents a number of difficulties. This is a very simple (and I have put in quote "simple" because it's not so simple) causal chain showing the relationship between neighborhood resources and social features, individual economic resources, and how that could be related to cardiovascular disease through a single pathway in this case involving dietary choices.

There are some feedback arrows between neighborhoods and individual economic resources, between neighborhoods resources and dietary choices, for example, availability of healthy food might affect diet, but diet might affect what's sold in the neighborhood as well.

What do we usually do when we analyze this in most of our studies? Well, we do a regression model which basically does something like this. We breakdown and we cannot capture that structure into regression. We are ignoring all the feedbacks, but I'll talk more about later. But, essentially, we need to be able to interpret the results of this kind of analysis in light of this model that I showed you here.

I think what happens sometimes is that we forget this – we might start with this, but then very quickly we're drawn into this regression approach, and we completely forget how this fits into the rest of the picture and so this becomes reified It doesn't mean that this is wrong. It just means that you have to use it carefully and with intelligence and not let it takeover our thinking, which sometimes happens I think.

If you think more generally about higher level contexts and individual-level factors (and you can think of this as neighborhoods and people or workplaces and people or countries and neighborhoods, whatever levels you want to think about), we have the truly relevant group or context based on our theory (which is that circle with a "C" up there), but in fact we have difficulties even in defining that group. We have a shifted definition of the group, for example we don't have a perfect definition of what the relevant neighborhood context is.

In addition we have an imperfect measure of that

as well which is that "C" with the line over it. Then we have individual-level factors, which might be confounders or mediators, and we have omitted variables and mismeasured variables. We have a situation where we have contexts grossly underspecified compared to some of the individual level stuff, which we usually measured much better, not perfectly but probably much better than some of the context stuff.

We have individual-level confounders and mediators which have measurement error in them. We have big limitations of statistical adjustment in this context. Now, it doesn't mean that we can't learn anything from the standard approach, which involves statistical adjustment to regression. It just means that we may need to complement it with other kinds of things.

One of the issues with statistical adjustment is that sometimes we use it a little bit blindly, we just put everything in the model that someone might think might be a confounder. I think one of the good developments in epidemiologic thinking over the past few years has been the promotion of using directed acyclic graphs to help us think about what variables we should adjust for and to identify situations when statistical adjustment may create more problems than it solves.

This is just a simple slide where there are three examples illustrating the use of DAGS in trying to understand the impact of neighborhood violence on incident cardiovascular disease. These are some hypothesized relationships. The arrows indicate hypothesized causal relationships or exposure, for example, in the case of race, ethnicity, and neighborhood violence, it indicates that race/ethnicity results in differential exposure to neighborhood violence.

Depending on which of these diagrams is underlying your thinking, you would need to statistically control for different sets of variables. Here, if you wanted to isolate, identify the effect of violence on incident CVD, you have to control for these three. Here, you have to control just for these two, and in fact if you control for race, you might reduce your efficiency to estimate the effect, particularly if race is highly correlated with neighborhood violence.

Here, you have to control for three factors. One could come up with other kinds of examples and of course the impact adjusting for the wrong set of factors depends on how strong the relationships are in the data, it might not make much difference. But, thinking about this and clearly laying out the diagram that underlies your conceptual model, I think is very important.

Now, it's not going to solve other problems because anybody who has tried to do this realizes that if these diagrams can get very, very complicated, at which point they stop being useful, so it's not that easy, but nevertheless I think it's a useful tool. In particular, another example has to do with understanding mediation which is something that we're often very interested in doing.

For example, if you want to look at the impact of neighborhood violence on incident cardiovascular disease, and determine what components are or are not mediated through physical activity DAGS can be very hepful For example if you want to isolate this piece, the so-called "direct effect" and you control just for these two things, as would probably be the naive approach, and you forget this other variable, you may get the wrong answer.

If you don't control for this variable as well, you're going to get the wrong estimate for this. There are papers that discuss the reasons for this in more detail. If you're looking at mediation, you also have to think about the confounders of the mediator outcome relationship. This is another example of how these diagrams can be useful.

Another important situation in looking at social determinants has to do with the fact that some variables, may be both confounders and mediators at the same time. This is an example from looking at neighborhood effects on cardiovascular disease rates, so suppose these are measures of the neighborhood context, say, over the life course, and the Ls are a series of individual-level characteristics, suppose they are things like income and number of risk factors, and so we know that neighborhoods affect levels of these risk factors or we think they might, and that these levels of these risk factors may also, through other mechanisms, affect where a person lives later and so on.

What happens is that these factors, this for example, is a confounder of this part of the neighborhood effect but is also a mediator of this part. Particularly, if you are looking at cumulative exposure to neighborhood conditions, these variables are confounders and mediators at the same time. This is a situation where if you control for that statistically, you have a problem.

There are statistical techniques that one can use, which are alternatives to the classic statistical adjustment for conditioning, marginal structure models for example and related techniques that one can use to better estimate the effect of interest, in this case the effect of the neighborhood exposure in the presence of time-dependent confounding.

Now, of course, you have to have the right data to do this, and in some situations, it may not make a big difference if these relationships are not very strong. It may or may not make a difference, but certainly thinking about it and at least particularly if you have this kind of data, using those techniques is important.

A number of methodologic approaches have been increasingly used to deal with some of the issues that I've just been talking about including the use of direct acyclic graphs; propensity score matching, which is a technique that many of you may be familiar with which is useful in doing sensitivity analyses to see how robust our results are to different methods of statistical control and also to avoid extrapolations to parts of the data where there is little overlap in the distributions; instrumental variables are another technique that increasingly used

– it's been used a lot by economists for a long time, and I think it's increasingly used now in epidemiology or at least attempted. Instrumental variables can be very useful to help identify causal effects and avoid some of issues related to residual confounding and reverse causation.But it's very hard to find instruments, and in fact you can look at these papers and see whether you are convinced that these instruments are good instruments or not. There is a paper called 'Instrumental Variables an Epidemiologist's Dream,' (by Miguel Hernan) which is a good title because it might be a dream. In addition there are appropriate methods to account for time-dependent confounding as I mentioned earlier.

The third big challenge, and probably one of the most difficult ones, has to do with the dynamic systems and the fact that almost anything that we are looking at is really a piece of a system. What do I mean by this?

Just to highlight this idea of old and new challenges, these are a couple of quotes from an epidemiologist called Reuel Stallones – who published very few papers actually but very insightful papers, at least in my view, and so you can see here what he said back in 1973, "The burden of disease on a human population is part of an environmental system and the interrelatedness of the components of the system cannot be understood by pursuing research whose rationale is to divide and isolate the components in ever greater detail."

"If we consider disease to be embedded in a complex network in which biologic, social, and physical factors all interact, then we are impelled to develop new models and adopt different analytic methods."

This concern has been around for a long time. In fact, if you think about it, it makes a lot of sense to think that in the case, for example, of individuals and environments and you can extrapolate this to social and biologic processes as well, individuals interact with their environment in the sense of there being feedbacks between individuals and their environment. Individuals interact with each other. They affect each other and individuals and environments adapt and change over time.

To give you a more concrete example, if you think of the processes that generate neighborhood differences in physical activity, one is that health is affected by features of the neighborhood, so availability of places to be physically active, say, promotes physical activity. Another is that people are sorted into neighborhoods based on individual attributes, so people with lower income and certain minority groups may tend to live in areas with less resources for a number of reasons.

This is what we've focused on separating in most of our work. We are really concerned about, can we separate the top from the bottom, can we really isolate the effect of the neighborhood context. But, in fact, there are lots of other things going on, so people may be selecting neighborhoods based on preferences for certain attributes, so physically active people may choose to live in neighborhoods with more resources; people may change their behavior and response to behavior of others, seeing more people walk may stimulate individuals to walk; neighborhoods change in response to the behavior of residents as well, so having more physically-active residents may increase the availability of recreational resources.

For the most part, because the tools that we have don't really allow us to incorporate these things, we really just focus on these two cases. The question is, are we getting the wrong answer or are we drawing the wrong conclusions about the impact of an intervention by ignoring some of these more dynamic relations. I think that's an open question, and it's a bit of a challenge for us. You can think about other examples, I'll show you a few that don't necessarily have to do with neighborhood effects.

The question is, well, can some other kinds of tools, dynamic models help us understand some of the key questions in social epidemiology, questions that are still persisting, and we haven't answered to everybody's satisfaction. I've put two question marks there, because I'm not sure of the answer to this question. I think the jury is still out. I think it's an interesting thing to explore, but we'll have to see how much it contributes. Let me run through, what I think that these tools can help us with.

The first has to do with place effects. If you think about how place affects health and you draw a model, you cpme up with a diagram that is not acyclic like a DAG but rather is cyclic and has feedbacks.

You can think that people's resources and preferences affect where they live, and this might be modulated by discrimination because discrimination processes may alter that relationship, and so people's resources and preferences affect their residential location and affect their composition of areas. This may affect the area material, social, and advocacy resources. There might be a feedback going on there because these features reinforce area composition because people with more resources, better off people will locate in areas with more resources creating a reinforcing cycle.

These area material, social, and advocacy resources can affect the location of health-related resources, and there might be some feedback here. The location of these resources could affect health behaviors, and there might be some feedback here going back as well. You can have some stress processes which modulate the relationship between location of resources and behaviors where they affect behaviors directly and all this may be related to health. You can start to see how this is looking like a system of relationships.

Thinking of another big question, an outstanding question has to do with how important genes, a question that social epidemiologist may have to grapple with. There is a genetic revolution that's taken over and lots of discussions about how important genes are to help disparities. Lets think a little bit about how genes might interplay with lots of other factors.

Let's suppose we identify some genetic factors linked to a predisposition to exercise Well, you have the ancestry of persons related to genes, and you have parental genes, which might be related to the genes of the offspring. But, there is also a culture, which is related to ancestry. There are also family norms, which are related to culture and parent's genes are important. Parents may also have some genes related to physical activity that might shape the family norms.

The family norms might interact with the genetic factors to modulate them. There is feedback between the family norms and the physical activity as well. Then, we have a situation where ancestry might be related to environments because of residential segregation, and genetic factors may also be related to environment selection and gene environment correlation.

In addition, people with the physical activity gene may choose environments which allow them to be more physically active. There might be feedbacks between environments and physical activity. In a situation like this, can we isolate the effect of genes? Probably, it's very, very difficult to do that using the methods that we use. You have not just the classic gene environment interaction but also correlations between genes and environments and feedbacks. In addition reductionist approaches that islotae the affect of the gens will just not work.

The last example, I am going to show you, has to do with lifecourse processes. We are interested in lifecourse things in epidemiology, and we know there is a lot of evidence that early life factors affect health.

Parental socioeconomic circumstances may be related to offspring health and to offspring education, and these things may also relate to the peer characteristics which may also feedback to health and educational achievement. These factors may also affect the offspring socioeconomic circumstances as an adult and their health as an adult, and in turn there are some bidirectional relationships, say, between income and health. This also affects the future generation.

Again, we have a situation where we have feedbacks, where we have things happened a long time ago affecting things happening much later on. Some of the key features of the three examples that I showed you are that you have feedbacks and adaptations over time, as well as dependencies between units and interactions between units leading to effectsdistant in space and time and things that would have been difficult to predict. This results in what are called emergent patterns, but they don't emerge magically. It's a function of these relationships that are not easily reducible to independent effects as we usually think of them.

Complex systems have, by definition, factors of multiple levels. They have heterogeneous and interdependent units. They have recursive relationships and feedback loops, endogeneity is part of everything and, in fact, it's an objective of study, not just a nuisance that prevents causal inference. There are these effects that might not be the classic linear relationship. This results in things that might be unanticipated or might result in effects that are distant in space and time. This might be intergenerational effects, for example.

If you think about it, this is pretty typical probably of most of the things that we study. The question is: Are we missing something by not thinking about it this way. One consequence of these dynamic relations is what Sterman in a paper of American Journal of Public Health referred to as policy resistance, which is when the interventions are defeated by the system's response to the intervention itself or when obvious solutions fail or even worsen the situation.

If you think about what some of our advances in disease prevention have done to health inequalities, they've actually increased, for example. This may have something to do with these dynamics that are going on. This is another quote also from many years ago from a famous system's person, Forrester, "In the complex system… causes are usually found, not in prior events, but in the structure and policies of the system." I think this makes a lot of sense to researchers in health disparities or social determinants but we don't analyze our data this way. The question is: Is there something that we could do differently.

In the biology world, systems biology, there is a long tradition of think consistent thinking. This is a quote from system's biologist. "A systems approach does not investigate individual genes or proteins one at a time, rather it investigates the behavior and relationships of all the elements in a particular biological system while it's functioning." You can paraphrase that thinking of population health so "would not investigate individual risk factors or individuals one at a time, but rather behavior and relationships of multiple factors and multiple elements in a particular population system.

How to do this? That's the question, right? It's really a paradigm shift. A systems approach really begins thinking about the components of the system, and then develops a formal model, a stimulation model, and there are different kinds of models to explore the functioning of the system and to obtain predictions under specific perturbations, and then also draw conclusions about the drivers of patterns and the plausible impact of some interventions.

There are a number of different modeling approaches, which I don't have time to get into. I'm going to talk about one example that I'll refer to in more detail in tomorrow's symposium to make it more concrete. Here, I'm going to just talk about it generally. But, what are some of the benefits of adopting this kind of paradigm?

The first and the most important to me is that it really forces to think differently in terms of formulating conceptual models. It really forces to think about processes again, which we've forgotten a little bit because we are so

wrapped up in isolating independent effects that we've forgotten that these associations merely reflect a small piece of what is really a system. Just forcing us to think about the processes in a dynamic way, I think is very good for the field.

Probably, this is the most important thing. Just like multilevel analyses, stimulated people to think about levels regardless of whether they actually need to use the technique of multilevel analysis or not which ultimately may or may not be necessary. The increasing availability sysyems tools can help us think dynamically again.

There are tools that we can draw from systems, simulation modeling tools that allows to make thought experiments in the context of systems accounting for these feedback loops. Another nice feature of these tools is that they allow us to integrate data from different sources, which we don't really do that much of in the social determinants world. We have all these different studies. Sometimes, they replicate, a lot of times they don't, but we never really put stuff together.

This systems' modeling provides a framework in which you can put in different kinds of data, even qualitative data, together with various kinds of relationships that are relevant to the models, for example, some of the models that I've showed you. Another really important feature together with the dynamic conceptual model thinking piece is identifying gaps and data needs because when we start to try to develop these models, we realize how ignorant we are about many things that are probably pretty important, so identifying data needs is another really big thing. These are couple of examples of models that we have started to try to explore, and I will talk about one of these tomorrow.

Now, what are some of the caveats in adopting some of these dynamic modeling approaches? Well, there are very good reasons why reductionism has been so successful, and that's very important to keep in mind because, like I said, we'll have to see in what circumstances these approaches yield added value– I don't think we should abandon what we are doing, by any means.

The other big challenge with these models is that sometimes people think, well, this is a model that we just put everything in, and that's really not the case. You really have to abstract what are the key dynamic relationships. It's a different form of abstraction. Just like reductionism, it simplifies but does it in a different way. That's why I emphasize the notion of intelligent abstraction because you can't put everything in because if you do, then you will have something that's very difficult to evaluate.

There is also a tension between building a model that predicts perfectly versus a model that just allows you to do some very, very basic thought experiments or proof of principle types of things. I think the latter is probably going to be the more useful aspect of these models, if they turn out to be useful.

These models have many assumptions because you have to model processes about which we often have very little data. It's an arduous process, takes a long time, lots of work. Communication is difficult because these models are complicated, so if we adopt them we are going to need ways to communicate them clearly, so people can replicate them.

Another question is when do these things yield real insight, when does it make a difference. Because obviously sometimes what you get out of the models is exactly what you put into it, so the question is when do you learn something new. These questions are really things to be answered.

In fact you can think about everything as a system, and systems can be studied using a variety of approaches. The key thing is that sometimes focusing on a single methodologic approach can constrain the way we think about things, can constrain even the kinds of questions that we ask.

I think we have become used to asking questions almost purely about independent effects because of our reliance on regression. In fact, you can think of observation, systems model, and experimentations, as three kinds of sources of evidence. We are very used to the fact that observation leads to experiments and experiments lead to new observations, but there are also feedbacks between observations and systems modeling, and systems model can also suggest new experiments, and the results of experiments can feedback into the modeling.

Because we are dealing with complex systems, we need a whole range of different kinds of evidence for social epidemiology. I think it's naive to think that any one single approach is going to yield the answers that we need. I am going to emphasize among the many methods that you are already familiar with, action based on best available evidence, and there may be situations where we have to act based on what we know and that in itself can be a source of learning information and lead to new observations, to new models and to new experiments, so action as a way of generating knowledge as well.

To finish up, I think the challenges that we face in the social determinants of health have to do really with the object that we study, and it has to do with individuals and populations, social and biologic factors, distal causes and mechanisms, and knowledge and action. I think the fact that we are at the interface of these things is what makes our field so challenging but also at least from my perspective so interesting, not just intellectually interesting, but also relevant for policy. Thank you very much for your attention.

Old and New Challenges in Understanding the Social Determinants of Health

Ana V. Diez Roux
Center for Social Epidemiology and Population Health
University of Michigan

Four challenges

- Levels of organization/multilevel determinants
- Complex causal chains
- Dynamic relations and systems
  - Interrelations between individuals and environments
  - Interrelations between social and biologic processes
- Connection to policy/action

Levels of organization

Levels of organization

- Factors (constructs) relevant to health can be defined at different levels
- Questions can be defined at different levels
- Understanding variability at a given level may require consideration of other levels

Holistic and "environmental" factors

↓

Germs

↓

Behaviors and biomedical characteristics

↓

Genes

↓

Person-specific mutations

Individualization of risk

- Individual-level risk factors
  - Behaviors
  - Biologic characteristics
  - Genes
- True causes of disease can be found exclusively at the level of individuals
- True causes of disease can be found exclusively in the behavioral/biological
- Populations as collections of individuals

Examples in social epidemiology

- Country-level income inequality and health
  - Kondo et al BMJ 2009
- State-level social capital and health
  - Kim and Kawachi Ann Epidemiol 2007
- Workplace factors and health
  - Suzuki et al BMC Public Health 2010
- Neighborhood health effects
  - Auchincloss et al 2010

2. Group-level variables as modifiers of individual-level effects

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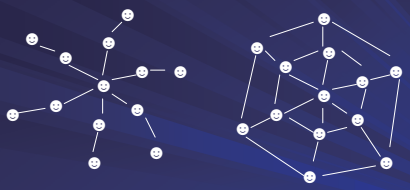


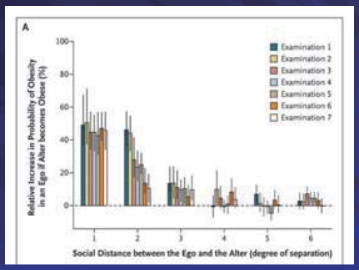
Hypothetical examples in social epidemiology

- Modification of income gradients by country-level policies
- Modification of neighborhood effects by personal resources
- Population-level features (e.g. availability of processed energy dense foods, transportation structures that detract from walking) as modifiers of gene effects on obesity

3. Outcome for one individual influences outcomes for others within the same population

- Contagion: Infectious diseases
- Transmission of norms: Behavioral characteristics

Social networks and obesity



Fowler and Christakis NEJM 2007

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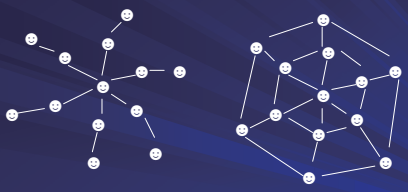

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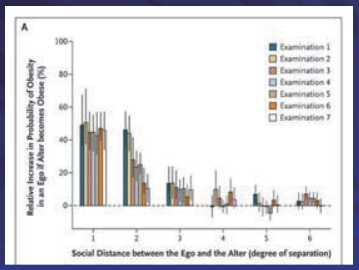

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KEYNOTE 2

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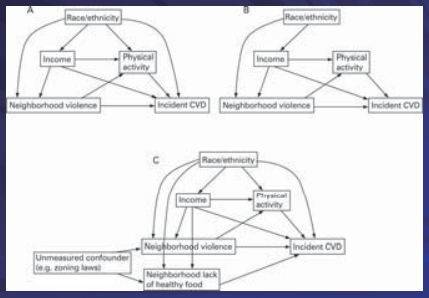
Using directed acyclic graphs to identify variables that need to be controlled for in estimating neighbourhood health effects.



Fleischer, N L et al. J Epidemiol Community Health 2008;62:842-846

JECH

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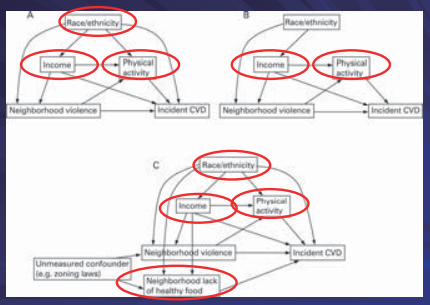

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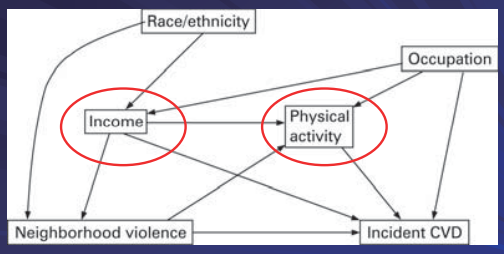
Using directed acyclic graphs to identify the unintended consequences of estimating "direct" effects by conditioning on a mediator.



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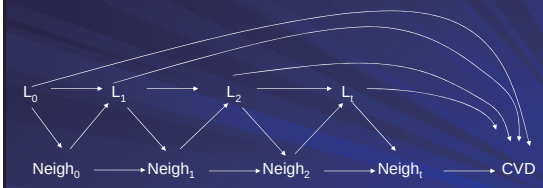
Time-dependent confounding



L_0: Age, race, gender, education

L_t: Income, BMI, smoking, physical activity

Recent methodologic approaches

- Use of DAGS
  - Richairdi et al JECH 2008
  - Fleischer and Diez Roux JECH 2008
- Propensity score matching
  - Quesnel-Valle Soc Sci Med 2010
- Instrumental variables
  - Behncke Health Economics 2011
  - Fisch Am J Public Health 2010
- Appropriate methods to account for time-dependent confounding
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Dynamic systems

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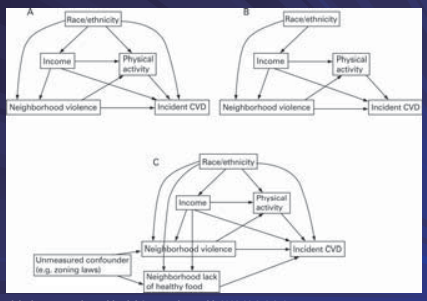

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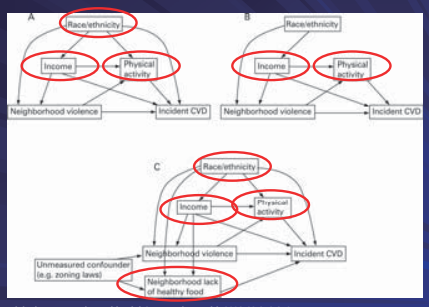

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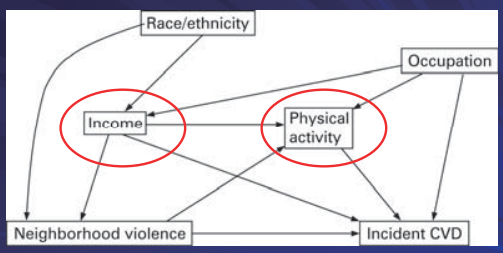

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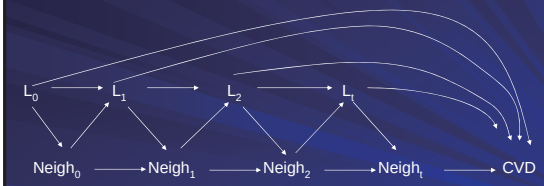

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Dynamic systems

"…the burden of disease on a human population is part of an environmental system and the interrelatedness of the components of the system cannot be understood by pursuing research whose rationale is to divide and isolate the components in ever greater detail."

" If we consider disease to be embedded in a complex network in which biologic, social, and physical factors all interact, then we are impelled to develop new models and adopt different analytic methods.."

R. Stallones, 1973

Bi-directional relations between individuals and environments in the causation of disease

- individuals interact with their environment
- individuals interact with each other
- individuals and environments adapt and change over time.

Neighborhoods and physical activity

General Process	Example neighborhood differences in physical activity
I. Health is affected by features of neighborhood	Availability of places to be physically active promotes physical activity
II. Persons are sorted into neighborhoods based on individual attributes	Persons of lower income and minorities live in neighborhoods with less resources

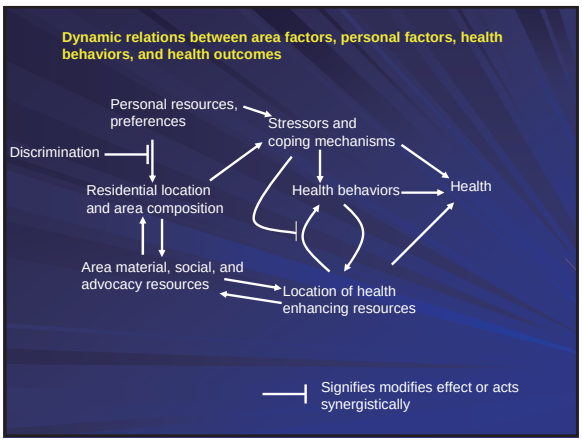
General process	Example neighborhood differences in physical activity
III. Persons select neighborhoods based on preferences for certain attributes	Physically active persons choose to live in neighborhoods with more PA resources
IV. People change their behavior in response to the behavior of others around them	Seeing more people walk in the neighborhood stimulates individuals to walk
V. Neighborhoods change in response to the behavior of residents	The presence of more physically active residents increases the availability of recreational resources

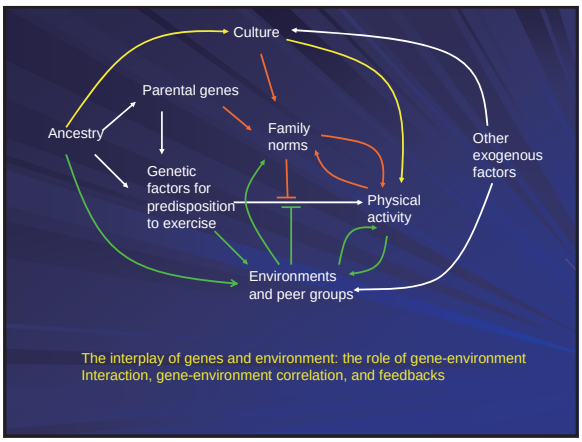
The focus of regression approaches……

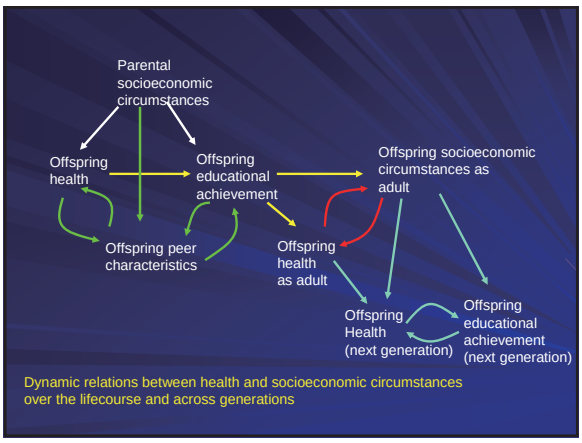
General Process	Example neighborhood differences in physical activity
I. Health is affected by features of neighborhood	Availability of places to be physically active and promotes physical activity
II. Persons are sorted into neighborhoods based on individual attributes	Persons of lower income and minorities live in neighborhoods with less resources

Can dynamic models help us understand key questions in social epidemiology??

- Place effects
- Genes and Environments
- Lifecourse







Processes resulting in health inequalities/disparities

- Feedbacks (positive or negative), adaptation over time
- Dependencies across units, interaction between units
- Effects distant in space and time
- Emergent patterns not easily reducible to "independent effects"

Five features of complex

- Factors at multiple levels
- Heterogeneous and interdependent units
- Recursive relationships and feedback loops
  - endogeneity
- Non-linear effects
- Unanticipated effects and effects very distant in time and location

Policy resistance

"the tendency for interventions to be defeated by the system's response to the intervention itself"

"obvious solutions fail or even worsen the situation"

Sterman, AJPH 2006

KEYNOTE 2

In the complex system…causes are usually found, not in prior events, but in the structure and policies of the system…"

Forrester 1969

What is a "systems" approach?

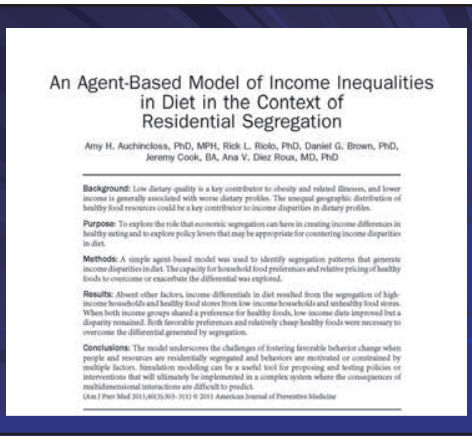
- A systems approach "…does not investigate individual genes or proteins one at a time, as has been the highly successful mode of biology for the past 30 years. Rather, it investigates the behavior and relationships of all the elements in a particular biological system while it is functioning."
  - Ideker et al 2001
- A "systems" approach to the study of health would not investigate individual risk factors (or individuals) one at a time, rather it would investigate the behavior and relationships of multiple factors and multiple elements in a particular population system while it is functioning .

A "systems" approach

- Define the components of the system and compile information on them: dynamic conceptual models
- Develop a formal model in order to:
  - Explore the functioning of the system
  - Obtain predictions under specific perturbations
- Draw conclusions regarding drivers of patterns and plausible impact of interventions

Benefits

- Dynamic conceptual models
  - Force investigators to think about processes: from describing associations to modeling the processes that generate them
  - Explicitly account for the interrelatedness of people and environments
    - relative importance of these reciprocal and dynamic relationships
- Tools
  - Thought experiments and evaluate the effects of hypothetical interventions in the context of SYSTEMS
  - Under conditions different from those observed in real world
  - Accounting for feed back loops and adaptation of people and environments over time
- Data
  - Integrates various sources of data
  - Identifies gaps and data needs



An Agent-Based Model of Income Inequalities in Diet in the Context of Residential Segregation

Amy H. Auchincloss, PhD, MPH, Rick L. Riolo, PhD, Daniel G. Brown, PhD, Jeremy Cook, BA, Ana V. Diez Roux, MD, PhD

Background: Low dietary quality is a key contributor to obesity and related illnesses, and lower income is generally associated with worse dietary profiles. The unequal geographic distribution of healthy food resources could be a key contributor to income disparities in dietary profiles.

Purpose: To explore the role that economic segregation can have in creating income differences in healthy eating and to explore policy levers that may be appropriate for countering income disparities in diet.

Methods: A simple agent-based model was used to identify segregation patterns that generate income disparities in diet. The capacity for household food preferences and relative pricing of healthy foods to overcome or exacerbate the differential was explored.

Results: Absent other factors, income differentials in diet resulted from the segregation of high-income households and healthy food stores from low-income households and unhealthy food stores. When both income groups shared a preference for healthy foods, low-income diets improved but a disparity remained. Both favorable preferences and relatively cheap healthy foods were necessary to overcome the differential generated by segregation.

Conclusions: The model underscores the challenges of fostering favorable behavior change when people and resources are residentially segregated and behaviors are motivated or constrained by multiple factors. Simulation modeling can be a useful tool for proposing and testing policies or interventions that will ultimately be implemented in a complex system where the consequences of multidimensional interactions are difficult to predict.

(Am J Prev Med 2011;40(3):303–311) © 2011 American Journal of Preventive Medicine

A Spatial Agent-Based Model for the Simulation of Adults' Daily Walking Within a City

Yong Yang, PhD, Ana V. Diez Roux, PhD, MD, Amy H. Auchincloss, PhD, Daniel A. Rodriguez, PhD, Daniel G. Brown, PhD

Abstract: Environmental effects on walking behavior have received attention in recent years because of the potential for policy interventions to increase population levels of walking. Most epidemiologic studies describe associations of walking behavior with environmental features. These analyses ignore the dynamic processes that shape walking behaviors. A spatial agent-based model (ABM) was developed to simulate people's walking behaviors within a city. Each individual was assigned properties such as age, SES, walking ability, attitude toward walking and a home location. Individuals perform different activities on a regular basis such as traveling for work, for basic needs, and for leisure. Whether an individual walks and the amount she or he walks is a function of distance to different activities and her/his walking ability and attitude toward walking. An individual's attitude toward walking evolves over time as a function of past experiences, walking of others along the walking route, limits on distances walked per day, and attitudes toward walking of the other individuals within her/his social network. The model was calibrated and used to examine the contributions of land use and safety to socioeconomic differences in walking. With further refinement and validation, ABMs may help to better understand the determinants of walking and identify the most promising interventions to increase walking.

(Am J Prev Med 2011;40(3):353–361) © 2011 American Journal of Preventive Medicine

Caveats…

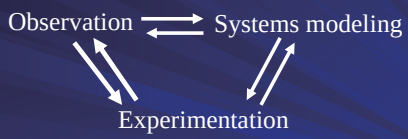
- There are reasons why reductionism has been so successful!!
- Keeping it simple but relevant…
  - Boundaries and level of detail (intelligent abstraction)
  - Thought experiments/proof of principle vs. prediction
- Assumptions, Where is the data?
  - Often lack data on fundamental processes
- Arduous process….
- Transparency and communication
- Real insight/WHEN DOES IT MAKE A DIFFERENCE???

Systems thinking

- Rethink questions: no longer about partitioning
- Think more creatively and broadly about the complex problems that we study
- Broaden range of questions, address questions using a variety of approaches

- Everything is a "system"
- "Systems" can be investigated using a variety of approaches
- Methods can constrain our thinking

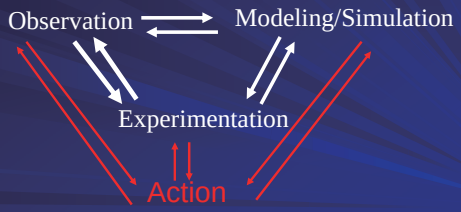
Knowledge generation and evidence for policy



Types of evidence

- Rigorous observational studies
- Experiments
- Qualitative studies
- Simulation/systems approaches
- Action based on "best available evidence" and systematic evaluation of this action

Knowledge generation and evidence for policy



KEYNOTE 2


The social determinants of health
Individuals AND Populations
Social AND biologic factors
Distal causes AND mechanisms
Knowledge AND action