SOLUTIONS

PRACTICAL 9: POPULATION AND INDIVIDUAL STRATEGIES FOR PREVENTION

SECTION 1: OBESITY

Question 1a

The graphs show that with increasing average BMI there is a higher proportion of the population who are overweight or obese (i.e. the prevalence is higher).

Question 1b

Either we could target the entire population for weight reduction or else focus on those at highest risk (those with BMI over a certain level.)

The advantage of focussing on the people at highest BMI is that they are at highest risk of developing diseases, and so this would be an efficient strategy. However, there is also a suggestion that the most extreme degree of variation is in part determined by where the majority lie. This suggests, furthermore, that moderate change by the population as a whole might greatly reduce the number of people with the most conspicuous, extreme characteristics. Finally, it is possible to show that when many individuals each receive a little benefit, the total benefit to the whole population may be large.

Question 1c

If one finds significant differences between populations, it suggests that some factor operating at community level is important: there may be a genetic explanation, or the explanation may be sought through an understanding of the behaviours and/or environment of the population. The latter two explanations would provide support to a population strategy: they suggest that the entire distribution of an exposure in a population can be shifted in a favourable (more healthy) direction if appropriate prevention policies are adopted.

SECTION 2: GENITAL HERPES AND HIV

Question 2a

The population attributable risk percent of HSV-2 in this population tells us what proportion (or percentage) of all HIV cases can be related to HSV-2 infection. This measure provides us with an indication of the public health burden of HIV, associated with HSV-2 infection.

The PAR% (or PAF) can be calculated in the following way:

$$\text{PAR\%} = [(R_t - R_o)/R_t] \times 100$$

$$= [(2.5\% - 1.7\%)/2.5\%] \times 100$$

$$= 32\%.$$

In other words, 32% of new cases of HIV in the population can be considered to be related to HSV-2 infection.

Question 2b

Relative risk measures the ratio of the incidence of disease (in this case HIV) in the exposed population compared with the unexposed population. For those who are HSV-2 infected, the relative risk of HIV infection is 6.1 (10.4%/1.7%). This is a large relative risk. However, this still tells us little about what proportion of all HIV cases could potentially be averted if HSV-2 could be prevented (or totally cured). Data on attributable risk, both at the individual and population levels are therefore of considerable value in identifying the potential impact of preventive strategies although a variety of assumptions in talking about preventable fractions or the proportion of risk or mortality which can be avoided are being made.

Question 2c

A variety of assumptions are implicit within calculation of attributable risk and population attributable risk. The first and most important is that the associations we observe are causative as opposed to simply being associated with one another. If we are to attribute a particular burden of ill-health or mortality, and to consider this as 'excess' disease over and above what would be present in the population concerned, we need to be sure this is the case. We also need to be sure that neither chance, nor bias or confounding could have accounted for the associations observed. The data presented in this example, reflect an unadjusted association between HSV-2 and HIV; therefore, we cannot exclude potential confounding e.g. alcohol consumption, number of sexual partners.

Furthermore, if we are to suggest that the entire fraction of disease (or mortality) experience which is associated with a particular exposure could be prevented by the institution of an appropriate programme, we are implicitly assuming that the programme in question will totally eliminate the disease in question. This is rarely the case as even the most effective

health promotion programmes are not 100% effective. In addition, at least some of the disease which is attributed to the exposure in question may in fact result from some other unidentified factor, which is confounded by the exposure we have examined. In this case, even if we remove the exposure of interest, some other factor will still be associated with the disease outcome in question.

SECTION 3: EVALUATION OF A CERVICAL CANCER SCREENING TOOL

Question 3a

	Reference test		
	Positive	**Negative**	
Diagnostic test			
Positive	a (71)	b (54)	a + b (125)
Negative	c (42)	d (118)	c + d (160)
Total	**a + c (113)**	**b + d (172)**	**a + b + c + d (285)**

The *proportion* of disease in the study population= (a+c) / (a+b+c+d) = 113/285 = **39.65%**

Question 3b

a. The *Sensitivity* of the test is the proportion of true positives correctly identified

   = a / (a+c)

   = 71 / (71 + 42) = **62.83%**

b. The *Specificity* of the test is the proportion of true negatives correctly identified

   = d / (b+d)

   = 118 / (54 + 118) = **68.60%**

c. The *PPV* is the likelihood that someone with a positive result has the disease

   = a / (a+b)

   = 71 / (71 + 54) = **56.80%**

d. The *NPV* is the likelihood that someone with a negative result does *not* have the disease

   = d / (c+d)

   = 118 / (42 + 118) = **73.75%**

Question 3c

An ideal test has high sensitivity (correctly identifies a high proportion of individuals with disease) and high specificity (gives few positive results in individuals without disease). The sensitivity and specificity of VIA in this setting is relatively low and the prevalence of CIN 2/3 is high. In this situation, around 40% of CIN 2/3 positive women would not be identified using VIA.

However, acceptable levels depend on the nature of the disease and the consequences of false positives and negatives. The progression of CIN 2/3 to developing cervical cancer is very slow. It also is not a certainty that CIN 2/3 will lead to cervical cancer. This study was conducted in a resource-limited setting where access to lab facilities may be limited. VIA does not require a lab test and VIA positive women could be treated (by cryotherapy) at the same clinical visit. In the absence of resources, VIA may be appropriate economical alternative.

Question 3d

2 x 2 table using sensitivity of 62.83% and specificity of 68.60% to calculate true positives and true negatives in a sample of 285 women with a 10% prevalence of CIN 2/3:

	Colposcopy-directed biopsy (reference test)		
	CIN 2/3 (positive)	**Normal or CIN1 (negative))**	
Visual Inspection with acetic acid (VIA)			
Positive	**18**(=62.83%*29)	80 (=256 -176)	
Negative	11 (=29-18)	**176 (=69.8%*256)**	
Total	29 (prev 10%)	256 (=285 – 29)	**285**

PPV = a/(a+b) = 18/(18 + 80) = **18.37%**

NPV = d/(c+d) = **94.12%**

For most screening tests, the sensitivity and specificity of a test does not change. However, the PPV and NPV depend upon the prevalence of the disease. Sensitivity depends only on the numbers in the left-hand column of the table, and specificity depends only on the numbers in the right-hand column. When prevalence changes, the numbers in the left-hand

column change in proportion to the numbers in the right-hand column. The PPV and NPV of a test result depend on numbers in both columns and change if the prevalence changes. As the prevalence goes down, the PPV decreases and the NPV increases.

SECTION 4: UNIVERSAL SUICIDE SCREENING IN SCHOOLS

Question 4a

The CSS's sensitivity means that around 75% of adolescents who are actually at risk will be identified. The NPV is high, which means that most of the adolescents who screen negative are not at risk. A downside is the low PPV, which would result in many false positives.

Question 4b

Adopting the CSS may result in high rate of false positives, which could burden the schools' mental health resources. Over-stretching the already stretched mental health resources/school counselling systems etc. could limit the care available for students truly at risk. However, 'false positive' students may experience less severe but important mental health problems such as depression and anxiety and could benefit from help. In sum, schools that adopt the CSS should be prepared to manage the influx of mental health referrals. Schools would need to weigh this cost against the benefit of identifying those truly at risk.

SECTION 5: BIDI SMOKING AND MORTALITY IN INDIA (OPTIONAL DO IN YOUR OWN TIME)

Question 5a:
Odds Ratio = (20,910/20,090) / (13,760/29,240) = 2.21

Alternative formula (ad/bc): Odds Ratio = 20,910*29,240 / 13,760*20,090 = 2.21

Men who died in 2010-2013 years had 2.2 times higher odds of smoking bidis in the past five years than men who were still alive. Alternatively expressing the odds ratio in terms of the exposure, men who smoked bidis in the last five years had 2.2 times higher odds of death than men who did not smoke bidis in the last five years.

Question 5b:
Controls can be used to represent the exposure prevalence of the general population. The prevalence of smoking among the controls (survivors) is 13760 / 43000 = 32%.

It is assumed that the controls are representative of the general population. This may be problematic because these households were selected on the basis of having an adult death in the past years. If death is associated with SES, for example, controls may not be representative of SES in general population.

Question 5c:
The measure is Population Attributable Risk (PAF) %

Note: The formula for calculating PAF% from a relative risk (rate ratio, risk ratio. prevalence ratio or odds ratio) is given in the lecture notes. We can use the odds ratio from this case-control study as our relative risk (RR).

PAF = [p (RR-1)] / [p (RR-1)] +1

= [0.32*(2.2 – 1)] / [0.32*(2.2-1) + 1)]

= 27.7%

Approximately 28% of adult male mortality in India can be attributed to the smoking of bidis. Assuming a causal association 28% of adult male deaths in India would be prevented if bidi smoking were eliminated.

Question 5d:

The assumptions are that the association between smoking and adult mortality is causal, i.e. that there is no confounding or bias in the calculation of the relative risk and the study population is representative of India as a whole. Given the limitations discussed in (4b) this may not be true.

In addition, the PAF% calculated here does not take into account the impact of bidi on population mortality via passive smoking.

SECTION 6: POPULATION SCREENING FOR PROSTATE CANCER (OPTIONAL: DO IN YOUR OWN TIME)

Question 6a

The study results indicate a significant 27% relative reduction in prostate cancer mortality due to PSA screening. The rate ratio of 1.57 for incidence indicates a 57% increased incidence of prostate cancer in the screening group compared to the control group. The authors estimate that close to half (41%) of men who screened positive would not have been diagnosed with prostate cancer in their lifetime (over-diagnosis). Over-diagnosis results in patients undergoing unnecessary treatment, which could lead to treatment complications & side effects.

Question 6b

The main benefit of using RCTs to evaluate screening is that you can say with more certainty if a reduction in disease is attributable to the screening. Trials are also capable of providing evidence on the harms of the screening (over-diagnosis and false positives), although seldom do so (1). One approach to figuring out over-diagnosis is to use the excess incidence (the difference between incidence with screening and incidence without screening) as an estimate (2). Another approach uses statistical modelling of the lead time or the natural history of the disease to produce an over-diagnosis estimate.

Some drawbacks to using trials to evaluate screening are: they are expensive, usually require a long follow up time (problems with loss to follow up), over-diagnosis & overtreatment can strain resources, potential problems with generalizability of results to other settings (external validity).

SECTION 7: DOSE-RESPONSE CURVES (OPTIONAL: DO IN YOUR OWN TIME)
Question 7

a) Exposure increases without adverse effects until a particular level of exposure is reached. Example: an increase in intra-ocular (inside the eye) pressure is not dangerous until it exceeds certain levels: at those levels, the incidence of glaucoma (increased pressure in the eye, eventually leading to loss of sight) rises rapidly. In this case, keeping pressures below a certain level is desirable, but there is little point in being much below the danger level.

At the same time, however, one must recognise that the level at which adverse effects become manifest is derived from whole populations: among individuals, some will have adverse outcomes at lower than this level and some will be well despite being above this level.

b) This shows a linear dose-response relationship (more accurately described here as an exposure-response relationship). The greater the exposure, the greater the risk: there is even an increased risk at very low exposure levels. Example: cigarette smoking and increased risk of lung cancer. Even with the small amounts of tobacco smoke associated with passive smoking, there is an increased risk of lung cancer. There is no such thing as a safe exposure level. Total removal of the hazard would require an end to all exposure; shifting people's exposures towards lower levels will invariably bring beneficial effects, so this should be the public health objective.

c) A curved relationship of exposure to risk is usually a more accurate description than the oversimplified linear exposure-response relationship. Example: the incidence of Down's syndrome increases over the whole range of maternal age, but the slope is shallow below the age of around 30 years. Thereafter, the risk of having a baby born with Down's syndrome begins to increase and it may be desirable to screen all women over this age. In Britain, screening used to be promoted only among those aged 37 years. With the presence of a safer, cheaper and more reliable screening test, this policy has changed to include screening for all pregnancies.

There are two influences on prevention: the high risk faced by particular individuals (those aged 37 and above), and the low risk faced by most, for whom screening seems to not be worth the cost and risk of side effects at present.

d) This is more complex. It fits in with the lay view that ‘moderation is good; extremes bad’. It shows a wide band of exposures over which the exposure carries no increased risk of disease. Example: for a given body size, there are a wide range of weights which may carry no increased risk of disease. At the extremes of low weight and high weight, however, there may be associated disease hazards. A policy which sought to decrease body weight for the entire population might shift some people into the extreme range associated with increased levels of mortality. For this pattern of dose-response, there are problems inherent in shifting entire populations by too large a degree in either direction.

References

1. Heleno B, Thomsen MF, Rodrigues DS, Jorgensen KJ, Brodersen J. Quantification of harms in cancer screening trials: literature review. *BMJ* (Clinical research ed). 2013;347:f5334.

2. Etzioni R, Gulati R, Mallinger L, Mandelblatt J. Influence of study features and methods on overdiagnosis estimates in breast and prostate cancer screening. *Annals of internal medicine*. 2013;158(11):831-8.