UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE MEDICINA
PROGRAMA DE PÓS-GRADUAÇÃO EM EPIDEMIOLOGIA

DISSERTAÇÃO DE MESTRADO

ESTIMAÇÃO DE RISCO RELATIVO E RAZÃO DE PREVALÊNCIA COM DESFECHO BINÁRIO

Cecília de Leão Martins Papaléo

Orientador: Prof. Dr. Álvaro Vigo

Porto Alegre, Dezembro de 2009

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SUMÁRIO

RESUMO

O risco relativo (RR) e a razão de prevalência (RP) são medidas de associação que visam mensurar a relação de um desfecho binário e variáveis de exposição em estudos com delineamento coorte e transversal, respectivamente. Nos casos em que há variáveis de confusão ou um fator de exposição contínuo, a associação pode ser estimada através de métodos específicos, tais como regressão de Poisson, regressão log-binomial, análise estratificada e conversão de Zhang e Yu. A regressão logística tem sido extensivamente usada para estimar a razão de chances (RC), a qual muitas vezes é interpretada como RR ou RP. Quando a incidência/prevalência do desfecho não é < 10% a RC produz estimativas de RC próximas à RP e RR. Porém, se o desfecho for comum (≥ 10%), a RC superestima a RP e o RR. Este estudo tem como objetivo apresentar uma revisão em 10 revistas da área médica, para verificar a constância da utilização dos métodos que estimam a RP ou RR e a interpretação da RC como RP e RR. Foram selecionados um total de 333 artigos do ano de 2007 e 381 artigos de 2008 com desfecho binário. Entre os estudos de coorte e transversal, 76,2% aplicaram regressão logística e destes, 18,1% em 2007 e 14,7% em 2008 interpretaram a RC como RR ou RP. No caso desses estudos, seria aconselhável utilizar um modelo que estime diretamente essas medidas para evitar interpretação equivocadas. Uma vez que a regressão de Poisson com variância robusta e a regressão log-binomial são disponibilizadas em diversos pacotes estatísticos, não há mais motivos para não utilizá-los.

ABSTRACT

Relative Risk (RR) and Prevalence Ratio (PR) are association measures that aim to measure respectively the relation between an outcome binary and an exhibition variables in study of cohort and cross-sectional design. In the cases that there are confounding variables or a factor of e continuous exhibition, the association can be estimated by specific methods such as Poisson Regression, log-binomial regression stratified analyses and conversions proposed by Zhang & Yu. The logistic regression has been widely used to estimate Odds Ratio (OR) which, several times, is interpreted as RR or PR. When the incidence/prevalence of the outcome is not < 10% it produces estimation of OR similar to PR and RR. However, if the outcome is common (≥ 10%) the OR overestimates the PR and the RR. However, this study has the objective to present a review in 10 journals of Medicine to verify the constancy of the application of methods that estimate the PR or RR and the interpretation of OR as PR and RR. It was selected a sum of 333 articles from 2007 and 381 articles from 2008 that estimated OR to be RR or PR with binary outcome. Between cohort and cross-sectional studies, 76.2% applied logistic regression and, among these, 18.1% in 2007 and 14.7% in 2008 interpreted OR as PR and RR. In these studies should be used a model that estimate directly in order to avoid misinterpretations. Once the Poisson regression with robust variance and the log-binominal regression are available from many statistic packages, there is no reason to not use them.

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1. APRESENTAÇÃO

Este trabalho consiste na dissertação de mestrado intitulada **“Estimação de Risco Relativo e Razão de Prevalência com Desfecho Binário”**, apresentada ao Programa de Pós-Graduação em Epidemiologia da Universidade Federal do Rio Grande do Sul, em 18 de dezembro de 2009. O trabalho é apresentado em três partes, na ordem que segue:

1. Introdução, Revisão de Literatura e Objetivos
2. Artigo
3. Conclusões e Considerações Finais.

Documentos de apoio, incluindo o Projeto de Pesquisa, estão apresentados nos anexos.

2. INTRODUÇÃO

Os estudos do tipo transversal e coorte são utilizados com grande freqüência em investigações epidemiológicas e clínicas. Normalmente, estes estudos visam estimar a associação entre uma exposição e o desfecho binário. A razão de prevalências (RP) deve ser usada quando o delineamento é transversal, e o risco relativo (RR), quando delineamento é coorte (Fletcher, 2006; Huley, 2003; Rothman, 1986). Para ajustar RP ou RR para possíveis variáveis de confusão, análise estratificada ou modelos multivariáveis podem ser utilizados. A análise estratificada exige que a variável de exposição e as variáveis de confusão sejam categóricas, enquanto que, nos modelos multivariáveis estas variáveis podem ser categóricas e/ou contínuas. Entretanto, a análise estratificada torna-se complexa à medida que aumenta o número de variáveis de confusão, razão pela qual usualmente se utilizam modelos multivariáveis.

Há ainda a razão de chances (RC), medida de associação que pode ser estimada pelo modelo de regressão logística (Rumel, 1986). Este método é bastante conhecido pelos pesquisadores e está disponível em diversos pacotes estatísticos, e por essas facilidades, também é habitualmente utilizado para estimar RC em estudos transversais e coorte, sendo, muitas vezes, interpretado como RP e RR (Coutinho *et al*, 2008; Francisco *et al*,2008; McNutt *et al*, 2003; Schiaffino *et al*, 2003). A estimativa pontual e intervalar da RC produzida por este modelo com o objetivo de estimar RP e RR pode tornar-se enviesada (Francisco *et al*, 2008). A RC produz uma estimativa afastada da RP e RR quando a variável de desfecho apresentar uma prevalência ou incidência comum, usualmente maior que 10% (Behrens, 2004; McNutt *et al*, 2003; Thompson, 1998; Zocchetti *et al*, 1997). Nesse caso, a RC produzirá medidas de associação superestimadas e, conseqüentemente, interpretação errônea (Thompson, 1998; Zocchetti *et al*, 1997). E mesmo que a estimativa pontual da RC seja idêntica ao RR e RP, não se pode ter a garantir de que o intervalo de confiança seja também o mesmo.

A discussão sobre este assunto surgiu quando Lee e Chia (1993) publicaram uma carta comentando sobre a RC e RR em estudos transversais. A partir disto, outras publicações ratificaram o tema e muitas destas sugeriram procedimentos para obter o RR e RP. Assim sendo, alguns métodos alternativos têm sido mais utilizados para estimar a medida de associação entre um desfecho dicotômico e um conjunto de preditores de estudos com delineamento coorte ou transversal, independente da

prevalência ou incidência do desfecho (Coutinho *et al*, 2008; Schiaffino *et al*, 2003). Estes métodos são os modelos de regressão de Poisson e log-binomial, análise estratificada e conversão de RC para RR proposta por Zhang & Yu (1998). Alguns estudos comparam esses métodos através de simulações e exemplos empíricos, porém, nem todos os autores concordam sobre qual é o método mais apropriado para estimar RP e RR.

Mesmo que atualmente estas técnicas tenham se tornado mais disponíveis, ainda há publicações que estimam RC através da regressão logística, interpretando como RP ou RR. Com o objetivo de aferir a freqüência com que os métodos de estimação da RP e RR vêm sendo utilizados em publicações de revistas epidemiológicas e clínicas, foi realizada uma seleção de artigos na base de dados de acesso público PubMed, considerando publicações de 10 revistas médicas dos anos de 2007 e 2008. O PubMed é uma base de pesquisa que abrange diversas áreas médicas e contém resumos e citações de periódicos. A sistemática de busca dos artigos foi criada através de um algoritmo no Pubmed, que restringiu a busca por descritores, ano de publicação e alguns limitadores importantes. Em cada artigo selecionado pela busca procurou-se encontrar o método utilizado para estimar as medidas de associação RP, RR e RC, o delineamento do estudo, a prevalência ou incidência do estudo e como foi interpretada a medida de associação. Com estes dados é possível identificar a constância com que as técnicas que estimam e interpretam RP e RR estão sendo utilizadas, bem como a maneira que a RC obtida regressão logística vem sendo interpretada, particularmente para delineamentos transversais e coorte.

3. REVISÃO DE LITERATURA

Muitas pesquisas epidemiológicas têm como objetivo central identificar associação entre fatores de risco ou de proteção e doenças ou medidas clínicas. A relação entre um fator de exposição e um desfecho pode ser expressa através de medidas que quantificam a magnitude dessa associação (Fletcher e Fletcher, 2006; Huley *et al*, 2003). O delineamento do estudo e o tipo das variáveis estudadas são aspectos que definem qual a medida de associação é a mais adequada para aferir esta relação.

No caso em que o delineamento é coorte ou experimental, a medida de associação é o risco relativo (RR), chamado também de razão de riscos. O RR é a razão das medidas de incidência de doenças em duas populações. Incidência é a proporção dos indivíduos em risco na população no início de um intervalo de tempo que se tornaram novos casos da doença até o fim do intervalo (Huley *et al*, 2003). O RR expressa a razão das probabilidades de ocorrência do desfecho entre os expostos em relação aos não expostos, isto é, representa o risco relativo de desenvolver o desfecho nos expostos em relação aos não expostos (Fletcher e Fletcher, 2006; Huley *et al*, 2003). Para o delineamento transversal, a associação entre as variáveis é dada pela razão de prevalência (RP), onde a medida de freqüência estimada é a prevalência pontual. Prevalência é a fração de um grupo de pessoas que possui uma condição ou desfecho clínico em um dado ponto do tempo. A interpretação da RP é similar ao do RR, considerando a prevalência ao invés da incidência. Para o delineamento caso-controle, não é possível estimar o risco diretamente, pois a incidência do desfecho entre os expostos e entre os não-expostos não é estimada (Rumel, 1986). Assim, a medida de associação entre fator de exposição e desfecho é a razão de chances (RC). A RC avalia a relação entre a chance de um indivíduo exposto possuir a condição de interesse, comparada à de um não exposto. Probabilidade compara o número de casos favoráveis com o de casos possíveis, enquanto que chance compara o número de casos favoráveis com o de casos desfavoráveis (Hulley *et al*, 2003).

A relação entre um fator exposição e um desfecho dicotômico na população, está representada pela Tabela 1, abaixo:

Tabela 1- Distribuição de probabilidade conjunta de exposição ao fator de risco e presença do desfecho em uma população.

Exposição	Desfecho		Total
	Presente	Ausente	
Fator presente	a	b	a+b
Fator ausente	c	d	c+d
Total	a+c	b+d	n

Fonte: Fletcher e Fletcher, 2006; Huley *et al*, 2003.

onde,

a = número de indivíduos expostos ao fator com o desfecho;

b = número de indivíduos expostos ao fator sem o desfecho;

c = número de indivíduos não expostos ao fator com o desfecho;

d = número de indivíduos não expostos sem o desfecho.

Através dessa tabela, podemos apresentar definições da RC, RR, e da RP, na população, no caso de termos somente um preditor dicotômico, pelas fórmulas a seguir:

$$RR = RP = \frac{\frac{a}{(a+b)}}{\frac{c}{(c+d)}} \qquad RC = \frac{\frac{a/(a+c)}{c/(a+c)}}{\frac{b/(b+d)}{d/(b+d)}} = \frac{ad}{bc}$$

No entanto, quando houver pelo menos uma variável de confusão ou o fator de risco é uma variável contínua, essas fórmulas não podem ser aplicadas. A RC pode ser estimada pelo modelo de regressão logística com resposta binária. Neste modelo a variável dependente (desfecho) Y é dicotômica e assume valor 1 se o evento de interesse ocorre e 0 se o evento de interesse não ocorre. A associação entre o desfecho e as covariáveis é definida pela equação:

$$P(Y=1|\underset{\sim}{x}) = \frac{e^{\beta' \underset{\sim}{x}}}{1+e^{\beta' \underset{\sim}{x}}} = \frac{e^{\beta_0+\beta_1 x_1+...+\beta_k x_k}}{1+e^{\beta' \underset{\sim}{x}}}$$

onde $\underset{\sim}{x} = [x_1,...,x_k]'$ são as variáveis preditoras e coeficientes $\beta = [\beta_0, \beta_1,..., \beta_k]'$ são parâmetros desconhecidos estimados a partir dos dados observados. Se o modelo não

contempla termos de interações, a quantidade $e^{\beta_i}, \forall = 1,2,...k$, representa a razão de chances de ocorrência do desfecho associada ao acréscimo de uma unidade no preditor x_i, ajustada pelos demais preditores no modelo.

As estimativas da RP e RR podem ser obtidas por métodos alternativos que vem sendo discutidos na literatura epidemiológica e que estão se tornando cada vez mais usuais, métodos estes que serão apresentados nas seções seguintes. Estes métodos são os modelos de regressão de Poisson e log-binomial, análise estratificada e conversão de RC em RR proposta por Zhang & Yu. Porém, a regressão logística ainda é a alternativa freqüentemente utilizada para estimar RP e RR. Estudos de simulação, descritos nas próximas seções, comparam os resultados do RR obtido por métodos alternativos, e da RC obtida pela regressão logística, com diferentes prevalências do desfecho. Não há unanimidade na definição de evento comum, podendo variar a prevalência acima de 5% até acima de 30%. No entanto, na grande maioria das publicações, define-se desfecho comum quando a prevalência for acima de 10% (Nijem *et al*, 2005; McNutt *et al*, 2003; Thompson *et al*, 1998; Zhang & Yu, 1998; Zocchetti *et al*, 1997).

Estes estudos mostram que, se a prevalência do desfecho for comum, o valor da RC é diferente do RR e RP, sendo inadequado interpretá-la como RP ou RR (Axelson *et al*, 1994; Greenland, 2004; Nijem *et al*, 2005; McNutt *et al*, 2003; Thompson *et al*, 1998; Zhang & Yu, 1998; Zocchetti *et al*, 1997). Se o fator do estudo for de risco, a RC é superestimada, e se o fator for de proteção, a RC é subestimada. A Tabela 2 apresenta um exemplo hipotético que expressa a diferença entre as duas medidas de associação para diferentes prevalências ou incidências do desfecho, considerando um fator de risco.

Tabela 2 - Comparação entre risco relativo (RR) e razão de chances (RC) para diferentes valores de prevalência (P) ou incidência (I) entre grupos de expostos e não expostos.

P ou I entre Expostos	P ou I entre Não Expostos	P ou I Geral	RR	RC
2/100	1/100	0,015	2	2,02
20/100	10/100	0,150	2	2,25
40/100	20/100	0,300	2	2,67
80/100	40/100	0,600	2	6

O exemplo mostra que a RC aumenta conforme o evento torna-se comum. Isso reforça que a interpretação da RC como RR ou RP pode ser inapropriada em estudos transversais ou coorte quando o desfecho é comum (Nijem *et al*, 2005).

Zhang & Yu (1998) ilustram a relação entre RC e RR para diferentes incidências em não expostos, como ilustra a Figura 1.

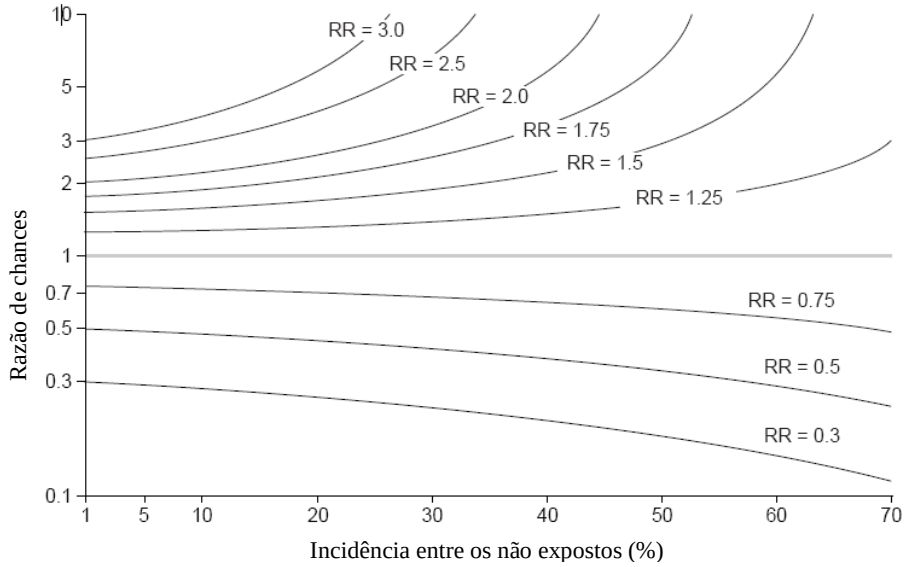

Figura 1- A relação entre RR e RC para a incidência do desfecho
Fonte: adaptado de Zhang & Yu (1998,p.1690).

Observa-se uma discrepância entre a RC e o RR à medida que a incidência entre os não expostos aumenta. Por exemplo, quando a incidência no grupo dos não expostos é 40% e o RR é 1,75, a RC será aproximadamente 3, superestimando o RR. Porém, se considerar uma incidência de 5% entre os não expostos e o mesmo RR, a RC é muito próxima de 1,75. Neste caso, a RC poderia ser utilizada para interpretar RR. Entre os métodos sugeridos pela literatura para medir a associação entre um conjunto de fatores e um desfecho binário em estudos do tipo coorte ou transversal, destacam-se os modelos de regressão de Poisson e log-binomial, o procedimento de Mantel-Haenszel e a conversão de RC em RR proposta por Zhang & Yu. Exceto para a conversão de Zhang & Yu, Independente da prevalência ou incidência do desfecho ser alta, estes métodos estimam diretamente RR ou RP e deveriam ser utilizados, para evitar vieses.

O procedimento de Mantel-Haenszel, os modelos de regressão logística, log-binomial e de Poisson estão disponíveis nos principais aplicativos computacionais utilizados na área epidemiológica, tais como: SPSS, SAS, Stata, R e S-Plus.

3.1 Métodos de estimação das medidas de associação

Tem sido discutido na literatura métodos que estimam diretamente a RP e o RR e seus intervalos de confiança. A seguir serão apresentadas técnicas que estimam estas medidas de associação. A aplicação destes procedimentos é indicada quando o delineamento do estudo é do tipo transversal ou coorte e a variável de desfecho é dicotômica, podendo ou não haver variáveis de confusão.

3.1.1 Procedimento de Mantel-Haenszel

A análise estratificada de Mantel-Haenszel estima uma medida de associação entre uma exposição e um desfecho considerando possíveis variáveis de confusão, onde todas as variáveis devem ser categóricas (Gimeno & Souza,1995). O procedimento permite resumir em uma única medida de associação, informações de diferentes tabelas de contingência. Estas tabelas são definidas a partir da variável de confusão, onde cada categoria desta variável forma um subgrupo que associa o fator de exposição com o desfecho do estudo. Se o comportamento entre os subgrupos é homogêneo, os dados das diferentes tabelas podem ser combinados usando o procedimento estatístico de Mantel-Haenszel.

Porém, esse método tem como limitação o teste de homogeneidade, aplicado para todas as medidas de associação (Everitt, 1977). Se a suposição de homogeneidade for aceita, pode-se então estimar a RP ou RR ponderada que considera todos os estratos.

Outra limitação deste método é a quantidade de categorias e de variáveis de confusão a ser considerada no estudo, pois quanto maior o número de estratificações, maior deve ser o tamanho da amostra para que todas as tabelas tenham uma quantidade aceitável e significativa de indivíduos (Gimeno & Souza,1995; Zhang & Yu, 1998). Salienta-se que este procedimento não pode ser realizado quando as variáveis preditoras são contínuas, e para esses casos, sugere-se os outros métodos apresentados a seguir.

3.1.2 Conversão de RC para RR

Zhang & Yu (1998) propuseram uma fórmula de conversão da estimativa de razão de chances, obtidas pela regressão logística, para estimar RR ou RP para desfechos dicotômicos comuns. A conversão de RC em RR é definida por:

$$RR = \frac{RC}{(1 - P_0) + (P_0 \times RC)},$$

onde RR representa a estimativa corrigida do risco relativo, RC é a razão de chances obtida pela regressão logística e P_0 é a incidência do desfecho no grupo de indivíduos não expostos. Para estudos de prevalências, a aplicação desta correção estima RP. A mesma fórmula pode ser aplicada para obter o limite inferior e superior do intervalo de confiança (Zhang & Yu, 1998).

Porém, quando há uma variável de confusão pode não ser correto usar esta conversão para estimar risco relativo ajustado a partir de uma estimativa de razão de chances ajustada, pois produz estimativas enviesadas. Isso ocorre porque não há uma relação entre a incidência do desfecho com a exposição para cada variável confundidora (McNutt, *et al,* 2003). Estudos de simulação, apresentados nas próximas seções, mostraram que a correção de Zhang & Yu produz estimativas superestimadas do RR e intervalo de confiança viesado, pelo fato de que sua fórmula considera somente a incidência dos não expostos (McNutt *et al*, 2003).

3.1.3 Regressão de Poisson e regressão de Poisson com variância robusta

A razão de prevalência ou o risco relativo podem ser estimados pelo modelo de regressão de Poisson (McNutt *et al*, 2003; Barros & Hirakata, 2003). Este modelo coincide com o modelo de regressão de Cox com tempo constante (modelo de Breslow-Cox) e as medidas de RR e RP podem ser estimadas diretamente pelos coeficientes de regressão do modelo (Barros & Hirakata, 2003; Zou, 2004).

Para definir o modelo, considere um desfecho binário Y e k preditores definidos por $\underset{\sim}{x} = [x_1, x_2, ..., x_k]$. O modelo utiliza a função de ligação log para evitar que $P(Y = 1 \mid \underset{\sim}{x})$ assuma valores negativos. Assim, o modelo especifica que

$$\log\left(P\left(Y=1 \mid \underset{\sim}{x}\right)\right)=\beta_0+\beta_1 x_1+...+\beta_k x_k,$$

onde $\beta_0,\beta_1,...,\beta_k$ são os coeficientes de regressão do modelo. O erro aleatório deste modelo possui distribuição de Poisson. Se não houver termos de interação no modelo, a estimativa do RR ou RP é obtida pela exponencial dos coeficientes de regressão e cada uma das medidas de associação estimadas é ajustada pelos demais preditores.

Porém, se o desfecho for comum (>10%), a regressão de Poisson produz um intervalo de confiança para o RR menos preciso do que o verdadeiro. Isso ocorre em conseqüência dos erros do modelo seguirem uma distribuição Poisson, que superestima os erros no modelo com resposta dicotômica, cuja distribuição apropriada é binomial.

Entretanto, a precisão do intervalo de confiança pode ser corrigida com o modelo de Poisson com variância robusta, que utiliza um estimador robusto (estimador de Sanduíche) para as variâncias dos coeficientes de regressão (Zou, 2004, Nijem *et al*, 2005). A regressão de Poisson com variância robusta ao ser aplicada à preditores categóricos produz estimativas semelhantes ao procedimento de Mantel-Haenszel (Zou, 2004).

3.1.4 Regressão log-binomial

O modelo log-binomial estima diretamente o risco relativo ou a razão de prevalência e o erro do modelo segue uma distribuição binomial (McNutt *et al*, 2003; Barros e Hirakata, 2003; Schiaffino *et al*, 2003).

O modelo é definido por:

$$\log\left(P\left(Y=1 \mid \underset{\sim}{x}\right)\right)=\beta_0+\beta_1 x_1+...+\beta_k x_k$$

onde $P\left(Y=1 \mid \underset{\sim}{x}\right)$ é a probabilidade de indivíduos com o evento condicionado as variáveis de exposição $\underset{\sim}{x}$. Se não existem interações, o risco relativo associado a j-ésima variável é obtido pela exponencial dos coeficientes de regressão β_j,

$j = 1, 2, ..., k$, e esta medida de associação é ajustada pelas outras variáveis de exposição do estudo.

Uma restrição do modelo é que $\beta_0 + \beta_1 + ... + \beta_k < 0$, para assim, assegurar que as estimativas das proporções estejam entre 0 e 1 (Skov *et al*,1998; Schiaffino *et al*, 2003). A estimativa do RR é não viciada, mas o intervalo de confiança pode ser enviesado, produzindo um intervalo mais estreito que o verdadeiro (McNutt *et al*, 2003). Além disso, problemas de convergência podem ocorrer quando o evento do desfecho for alto ou as covariáveis forem contínuas ou politômicas (Barros e Hirakata, 2003; Coutinho *et al*, 2008; Deddens & Petersen, 2003; Petersen & Deddens, 2008, Schiaffino *et al*, 2003).

3.2 Estudos comparativos via simulação

Algumas publicações realizaram uma comparação entre métodos que estimam as medidas de associação RP e RR quando o desfecho é binário, através de estudos de simulação. A finalidade dos achados apresentados pelos artigos foi comparar as estimativas pontuais e seus intervalos de confiança do risco relativo e razão de prevalências.

McNutt *et al* (2003) comparam métodos de estimação do RR quando o evento é comum, considerando modelos que podem ser utilizados em pacotes estatísticos usuais. Para demonstrar os métodos, foram criados exemplos hipotéticos para mostrar qual é a relação entre fator e desfecho quando o modelo é ajustado para confundidores (covariáveis). As técnicas que foram comparadas neste estudo foram: procedimento de Mantel-Haenszel estratificado, logit estratificado, regressão log-binomial, regressão de Poisson, correção de Zhang & Yu e regressão logística. A conversão apresentada por Zhang & Yu apresenta o pior resultado entre os métodos testados, apresentado uma estimativa pontual consideravelmente maior que a estimativa verdadeira. O modelo que obteve os melhores resultados foi o log-binomial, com estimativa pontual muito próxima do valor verdadeiro e intervalo de confiança preciso. A regressão de Poisson mostrou uma estimativa pontual muito próxima da análise de Mantel-Haenszel (MH), porém produziu um intervalo de confiança impreciso, apresentando valores menos precisos que o obtido pelo modelo log-binomial e as análises estratificadas (McNutt *et al*, 2003). As técnicas estratificadas apresentaram uma estimativa pontual relativamente próxima do RR obtido pelo MH e um intervalo de confiança confiável, quando comparado com a

regressão log-binomial. Em termos de intervalo de confiança, a regressão log-binomial obteve alguns resultados mais estreito em relação ao intervalo de confiança da análise estratificada, mas considerado satisfatório. Mesmo assim, os autores concluem que em algumas situações o modelo log-binomial não converge.

Zou (2004) comparou o procedimento de Mantel-Haenszel, o modelo de Poisson, o modelo de Poisson com variância robusta e o modelo log-binomial. Os resultados das simulações mostram que, independente da técnica utilizada, à medida que o tamanho da amostra aumenta, a porcentagem de viés relativo diminui. Tanto para regressão de Poisson quanto para regressão de Poisson com variância robusta (modificada), a porcentagem de viés relativo é o mesmo, porém, a amplitude do intervalo de confiança da primeira é maior que da segunda. Tanto a regressão de Poisson modificada quanto a regressão log-binomial, os resultados apresentados foram similares e satisfatórios. Porém, o autor sugere a regressão de Poisson modificada como a técnica mais apropriada para estimar RR pelo fato de produzir estimativas muito próximas das produzidas pela técnica de Mantel-Haenszel quando a covariável de interesse é categórica e por não ter dificuldade em convergir, como o modelo log-binomial.

Schiaffino *et al* (2003) comparam métodos utilizados para medir a razão de prevalência em estudos transversais através de exemplos empíricos. Os modelos comparados nesse artigo foram: regressão logística, regressão de Breslow-Cox, regressão log-binomial e a fórmula de conversão de RC para RR proposta por Zhang & Yu (1998). A conversão proposta por Zhang & Yu, deve ser aplicada também nos limites dos intervalos de confiança, porém Schiaffino sugere aplicar a fórmula utilizada para estimar a RC em estudos de caso-controle, proposta por Miettinen (1976). Os resultados mostraram que, quando a prevalência do desfecho é rara, o RC, RR e a RP possuem suas estimativas e intervalos de confiança praticamente idênticos. Porém quando o desfecho é comum, tanto as estimativas pontuais como os intervalos de confiança tornam-se diferentes. A regressão logística superestimou a verdadeira medida de associação, além de fornecer o intervalo de confiança mais amplo, em relação às técnicas abordadas. A regressão log-binomial apresentou uma estimativa pontual similar às estimativas dos modelos de Breslow-Cox e a fórmula de conversão proposta por Zocchetti, porém com o menor intervalo de confiança.

Recentemente, foi publicado o artigo de Coutinho *et al* (2008) que faz o comparativo das regressões de Cox, Poisson com variância robusta, log-binomial e a

logística, utilizado como referência os resultados obtidos pela análise estratificada de Mantel-Haenszel. Nesse estudo foram comparados métodos para três desfechos diferentes, considerados de baixa, média e alta prevalência. Para prevalência baixa, os resultados dos modelos de Cox, Poisson e log-binomial se aproximaram da estimativa pontual obtida pela técnica de Mantel-Haenszel, com intervalos de confiança mais estreitos, e a regressão logística obteve uma estimativa pontual 13% maior, com intervalo de confiança mais amplo que os outros modelos. Considerando a prevalência média, os modelos de Cox, Poisson e log-binomial apresentaram estimativas pontuais e intervalares similares aos valores de referência, enquanto que a regressão logística apresentou uma estimativa pontual quase que 100% maior e intervalo de confiança mais amplo, em relação aos outros modelos. Para prevalência do desfecho alta no modelo ajustado com uma variável contínua, as estimativas pontuais e intervalares dos modelos de Poisson e Cox foram semelhantes e a regressão log-binomial apresentou uma dificuldade de convergência. A regressão logística produziu uma estimativa pontual muito maior que as estimativas produzidas pelos outros modelos, com intervalos de confiança amplo. Porém, este estudo teve a limitação de que as variáveis que foram associadas não tinham uma forte relação, produzindo, assim, estimativas dos métodos comparados muito próximas.

Quadro 1- Quadro resumos dos estudos de simulação

Estudo	Modelo menos adequado	Modelo sugerido	observação
McNutt	Conversão Zhang & Yu	Log-binomial	Log-binomial tem problema de convergência
Zou	Regressão logística (estimativa Pontual e intervalar enviesadas)	Reg. Poisson modificada	Log-binomial tem problema de convergência
Schiaffino	Conversão Zhang & Yu	Log-binomial	Log-binomial obteve IC estreito
Coutinho	Regressão logística (Pontual enviesada e IC amplo, mesmo para prev. Baixa)	Poisson e Log-binomial	Log-binomial tem problema de convergência

4. OBJETIVOS

O objetivo geral deste trabalho é selecionar artigos publicados em um conjunto importante de revistas da área epidemiológica através de uma busca na base de dados PubMed, e verificar a adequação do procedimento utilizado para estimar a medida de associação RR ou RP e sua respectiva interpretação.

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6. ARTIGO

ESTIMAÇÃO DE RISCO RELATIVO E RAZÃO DE PREVALÊNCIA COM DESFECHO BINÁRIO

ESTIMATION OF RELATIVE RISK AND PREVALENCE RATIO WITH BINARY OUTCOME

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A ser enviado aos Cadernos *de Saúde Pública.*

Resumo

A medida utilizada para verificar uma possível associação entre o desfecho binário e as variáveis de exposição depende do delineamento do estudo: em estudos em que o delineamento é uma coorte ou transversal, esta associação, chamada de risco relativo (RR) e razão de prevalência (RP), respectivamente, podem ser mensuradas por métodos específicos, tais como regressão de Poisson, regressão log-binomial, análise estratificada e conversão propostas por Zhang & Yu, e em estudos de caso-controle, a regressão logística é o modelo que estima esta associação, chamada razão e chances (RC). Comumente a RC é estimada em estudos de coorte e transversal, por sua facilidade em ser aplicada, embora os métodos específicos que estimam RR e RP estarem em evidência atualmente. Para verificar a constância desta aplicação na literatura médica, o presente estudo tem como objetivo apresentar uma revisão em 10 revistas da área médica, para verificar a constância da utilização dos métodos que estimam a RP ou RR e a interpretação da RC como RP e RR. Foram selecionados um total de 333 artigos do ano de 2007 e 381 artigos de 2008 que estimaram RP, RR e RC com desfecho binário. Entre os estudos de coorte e transversal, 76,2% aplicaram regressão logística e destes, 18,1% em 2007 e 14,7% em 2008 interpretaram a RC como RR ou RP. No caso desses estudos, seria aconselhável utilizar um modelo que estime diretamente essas medidas para evitar interpretação equivocadas. Uma vez que a regressão de Poisson com variância robusta e a regressão log-binomial são disponibilizadas em diversos pacotes estatísticos, não há mais motivos para não utilizá-los.

Palavras chave: Razão de Prevalência, Risco Relativo, Razão de Chances, Regressão de Poisson, Regressão Log-binomial

Abstract

The measure used to verify a possible association between the outcome binary and the exhibition variables, depends on the design of the study. In studies in which the design is a cohort or a cross-sectional this association, called respectively Relative Risk (RR) and Prevalence Ratio (PR), can be measure by specific methods such as Poisson Regression, log-binomial regression stratified analyses and conversions proposed by Zhang & Yu, and in studies of case-control the logistic regression is the model that estimate this association, called Odds Ratio (OR). The OR is commonly estimated in studies of cohort and cross-sectional because of its easy application, although the specific methods that estimate RR and PR are currently in evidence. To verify the constancy of this application in Medical literature this study has the objective to present a review in 10 journals of Medicine to verify the constancy of the application of methods that estimate the PR or RR and the interpretation of OR as PR and RR. It was selected a sum of 333 articles from 2007 and 381 articles from 2008 that estimated OR to be RR or PR with binary outcome. Between cohort and cross-sectional studies, 76.2% applied logistic regression and, among these, 18.1% in 2007 and 14.7% in 2008 interpreted OR as PR and RR. In these studies should be used a model that estimate directly in order to avoid misinterpretations. Once the Poisson regression with robust variance and the log-binominal regression are available in many statistics packages, there is no reason to not use them.

Keywords: Prevalence Ratio, Relative Risk, Odds Ratio**,** Poisson Regression, Log-binomial Regression

Introdução

É freqüente que estudos epidemiológicos tenham como objetivo estimar a associação entre uma variável de exposição e um desfecho binário. A Razão de Prevalência (RP) deve ser usada quando o delineamento é transversal, e o Risco Relativo (RR), quando delineamento é coorte[1,2,3]. Para ajustar a RP ou o RR para possíveis variáveis de confusão, pode-se utilizar análise estratificada ou modelos multivariáveis. A análise estratificada exige que a variável de exposição e as variáveis de confusão sejam categóricas[4], enquanto que, nos modelos multivariáveis, essas variáveis podem ser categóricas ou contínuas. Entretanto, a análise estratificada torna-se complexa à medida que aumenta o número de preditores, razão pela qual os modelos multivariáveis são normalmente utilizados.

Além da RP e RR, a Razão de Chances (RC) é uma medida de associação que pode ser estimada pelo modelo de regressão logística [5], independente do tipo de delineamento do estudo. Esse método é habitualmente utilizado para estimar RC em estudos transversais e coorte, porém, muitas vezes, a RC é interpretada como RP e RR [6,7,8,9,10]. Nesses casos, a estimativa de RC produzida pelo modelo logístico pode ser enviesada para RR ou RP [7]. Se o fator do estudo for de risco, a RC irá superestimar o RR ou RP e, se o fator for de proteção, a RC irá subestimar o RR ou RP. A RC produz uma estimativa afastada da RP e RR quando a variável de desfecho apresentar uma prevalência ou incidência comum (>10%) [9,11,12,13.] No entanto, em casos em que o desfecho do estudo não é comum, o resultado fornecido pela RC possivelmente será muito próximo dos resultados da RP e do RR, permitindo, talvez, que seja interpretado como RP ou RR [14].

Esta discussão surgiu em 1993, quando Lee e Chia (1993) publicaram um artigo sobre o assunto [15]. A partir disto, várias publicações abordaram este assunto, demonstrando através de exemplos e sugerindo métodos para obter o RR ou RP diretamente. Alguns destes métodos alternativos vêm sendo utilizados para estimar a medida de associação entre um desfecho dicotômico e um conjunto de preditores em estudos com delineamento coorte ou transversal, independente da prevalência ou incidência do desfecho [6,8,10], tais como os modelos de regressão de Poisson e log-binomial. A análise estratificada e a conversão de RC para RR propostas por Zhang & Yu (1998) também são usadas [16]. Algumas publicações comparam esses métodos através de simulações e exemplos empíricos, porém, nem todos os autores concordam

sobre qual é o método mais apropriado para estimar RP e RR. Embora atualmente os modelos de regressão de Poisson e log-binomial estejam facilmente disponíveis em software estatístico, tais como SPSS, R, SAS, entre outros, ainda há publicações que estimam a RC através da regressão logística, interpretando-a como RP ou RR.

O objetivo do presente estudo foi observar a frequência com que os métodos de estimação da RP e RR vêm sendo utilizados em publicações de revistas epidemiológicas e clínicas publicadas nos anos de 2007 e 2008, além de observar as publicações em que o modelo logístico está sendo utilizado, considerando o delineamento, a proporção do desfecho e a interpretação da medida de associação.

A análise estratificada de Mantel-Haenszel estima uma medida de associação entre uma exposição e um desfecho considerando possíveis variáveis de confusão, onde todas as variáveis devem ser categóricas [5]. O procedimento permite resumir em uma única medida de associação, informações de diferentes tabelas de contingência. Estas tabelas são definidas a partir da variável de confusão, onde cada categoria desta variável forma um subgrupo que associa o fator de exposição com o desfecho do estudo. Se o comportamento entre os subgrupos é homogêneo, os dados das diferentes tabelas podem ser combinados usando o procedimento estatístico de Mantel-Haenszel. O procedimento consiste em, inicialmente, obter a RP ou RR de cada subgrupo, e após, realizar um teste de homogeneidade para todas as medidas de associação [17]. Se a suposição de homogeneidade for aceita, pode-se então estimar a RP ou RR sumária, ponderada, que considera todos os estratos.

Zhang & Yu (1998) propuseram uma fórmula de conversão da estimativa de razão de chances, obtidas pela regressão logística, para estimar RR ou RP para desfechos dicotômicos comuns. A conversão de RC em RR considera, além da RC obtida pela regressão logística, a incidência do desfecho no grupo de indivíduos não expostos. Em estudos de prevalências, a aplicação dessa correção estima a RP. A mesma fórmula pode ser aplicada para obter o limite inferior e superior do intervalo de confiança 16. Porém, esta conversão não produz estimativas confiáveis. Além disso, em casos em que há uma variável de confusão, pode não ser correto usar esta conversão para estimar o Risco Relativo ajustado a partir de uma estimativa de Razão de Chances ajustada, uma vez que isso produziria estimativas enviesadas. Isso ocorre porque não há uma relação entre a incidência do desfecho e a exposição para cada variável confundidora [9].

A regressão de Poisson permite estimar diretamente as medidas de RR e RP

pelos coeficientes de regressão do modelo [18,19]. O erro aleatório deste modelo possui distribuição de Poisson. Se não houver termos de interação no modelo, a estimativa de RR ou RP é obtida pela exponencial dos coeficientes de regressão e cada uma das medidas de associação estimadas são ajustadas pelas outras variáveis de associação. Porém, se o desfecho for comum (>10%), a regressão de Poisson produz um intervalo de confiança para o RR menos preciso, como conseqüência dos erros do modelo seguirem uma distribuição Poisson, o que superestima a variância do erro aleatório no modelo com resposta dicotômica, cuja distribuição apropriada é a binomial. Entretanto, a precisão do intervalo de confiança pode ser corrigida com o modelo de Poisson com variância robusta, que utiliza um estimador robusto (estimador de Sanduíche) para as variâncias dos coeficientes de regressão [19,20]. A regressão de Poisson com variância robusta, ao ser aplicada à preditores categóricos, produz estimativas semelhantes ao procedimento de Mantel-Haenszel [19].

O modelo log-binomial estima diretamente o risco relativo ou a razão de prevalência e o erro do modelo segue uma distribuição binomial [9,10,18]. Uma restrição do modelo é que a soma dos coeficientes de regressão tem que ser inferior a zero, de modo a assegurar que as estimativas das proporções estejam entre 0 e 1 [10,21]. A estimativa do RR é não viciada, mas o intervalo de confiança pode ser enviesado, produzindo um intervalo mais estreito que o verdadeiro [9]. Adicionalmente, problemas de convergência podem ocorrer quando o desfecho do evento for alto ou as co-variáveis forem contínuas ou politômicas [6,10,18,22,23].

Recentemente, algumas publicações compararam, através de estudos de simulação, métodos que estimam as medidas de associação RP e RR quando o desfecho é binário. McNutt *et al.* (2003) relatam que a conversão proposta por Zhang & Yu obteve as piores estimativas dentre os métodos testados. O modelo que obteve os melhores resultados foi o log-binomial, com a estimativa pontual muito próxima do valor verdadeiro e o intervalo de confiança preciso. A regressão de Poisson mostrou uma estimativa pontual muito próxima da verdadeira, porém produziu um intervalo de confiança impreciso em relação ao modelo log-binomial e as análises estratificadas [9]. As técnicas estratificadas apresentaram uma estimativa pontual relativamente próxima ao RR verdadeiro e um intervalo de confiança confiável, quando comparado com a regressão log-binomial. Em termos de intervalo de confiança, a regressão log-binomial obteve alguns resultados mais estreitos em relação ao intervalo de confiança da análise estratificada, mas considerados satisfatórios. Uma limitação importante do

modelo log-binomial é o fato de que freqüentemente não há convergência no processo iterativo de estimação.

Zou (2004) comparou o procedimento de Mantel-Haenszel, o modelo de Poisson, o modelo de Poisson com variância robusta e o modelo log-binomial. Os resultados das simulações mostram que, independente da técnica utilizada, à medida que o tamanho da amostra aumenta, a porcentagem de viés relativo diminui. A regressão de Poisson modificada e a regressão log-binomial apresentaram resultados similares e satisfatórios. O autor sugere, no entanto, a regressão de Poisson modificada como técnica mais apropriada para estimar o RR. Isso se deve ao fato de que a regressão de Poisson modificada produz estimativas muito próximas das produzidas pela técnica de Mantel-Haenszel quando a covariável de interesse é categórica e, ao contrário do modelo log-binomial, não tem dificuldade em convergir.

Schiaffino et al*.* (2003) mostram através de seus resultados que, quando a prevalência do desfecho é rara, RC, RR e RP possuem estimativas e intervalos de confiança praticamente idênticos. No entanto, quando o desfecho é comum, tanto as estimativas como os intervalos de confiança tornam-se diferentes. A regressão logística superestimou a verdadeira medida de associação, além de fornecer o intervalo de confiança mais amplo, em relação às técnicas abordadas. A regressão log-binomial apresentou uma estimativa pontual similar às estimativas dos modelos de Breslow-Cox (regressão de Cox com tempo constante) e da fórmula de conversão de RC em RR, porém com o menor intervalo de confiança.

Coutinho *et al.* (2008) comparam empiricamente métodos para desfechos de baixa, média e alta prevalência. Para prevalência baixa, os resultados dos modelos de Cox, Poisson e log-binomial se aproximaram da estimativa pontual obtida pela técnica de Mantel-Haenszel, com intervalos de confiança mais estreitos, e a regressão logística obteve uma estimativa pontual 13% maior, com intervalo de confiança mais amplo que os outros modelos. Com relação à prevalência média, os modelos de Cox, Poisson e log-binomial apresentaram estimativas pontuais e intervalares similares aos valores de referência, enquanto a regressão logística apresentou, em relação aos outros modelos, uma estimativa pontual quase 100% maior e intervalo de confiança mais amplo. Quando a prevalência do desfecho foi alta e uma variável contínua foi incluída no modelo ajustado, as estimativas pontuais e intervalares dos modelos de Poisson e Cox foram semelhantes, enquanto a regressão log-binomial apresentou uma dificuldade de convergência. A regressão logística produziu uma estimativa pontual muito maior que

as estimativas produzidas pelos outros modelos, com intervalos de confiança amplos. Porém, este estudo teve a limitação de que as variáveis que foram associadas não tinham uma forte relação, produzindo, assim, estimativas dos métodos comparados muito próximas.

Métodos

A seleção de artigos foi realizada considerando um conjunto de revistas importantes da área epidemiológica, contemplando publicações realizadas em 2007 e em 2008. As revistas utilizadas estão indexadas na base de dados PubMed (Serviço de pesquisa da National Library of Medicine (NLM)). Criou-se uma sintaxe para a busca de artigos na PubMed considerando: operadores booleanos e limitadores, nomes de revistas, ano e descritores, para que a seleção filtrasse somente os artigos de interesse específico. A busca foi realizada no resumo e descritores dos artigos. Todos os resumos estão em língua inglesa, independente da nacionalidade da revista e do artigo.

A metodologia para busca utilizou-se somente de palavras em língua inglesa. Todos os artigos estão associados a descritores. Quando buscamos artigos somente pelo resumo e descritores (descrito na sintaxe por “Text Word”) limitamos a pesquisa, pois um assunto específico pode não estar escrito no resumo e descritores. O “MeSH terms” é uma ferramenta eficiente nessa busca, uma vez que possui a funcionalidade de selecionar artigos classificados por certas categorias, assuntos. Cada categoria identifica termos com grafia diferente, porém, de significado semelhante.

Quanto à seleção das revistas, buscou-se selecionar revistas importantes da área médica, com as mais diversas classificações em relação ao Fator de Impacto e ao Qualis, conforme descrito no Quadro 1.

Os critérios de seleção dos artigos foram:

1- palavras-chaves: prevalence, odds ratio, risk, logistic model, logistic regression.

2- revistas selecionadas: American Journal of Epidemiology, Journal of Clinical Epidemiology, International Journal of Epidemiology, British Medical Journal, Lancet, New England Journal of Medicine, Ciência & Saúde Coletiva, Revista de Saúde Pública, Cadernos de Saúde Pública, Brazilian Journal of Medical and Biological Research.

3- ano de publicação: 2007 e 2008.

4- exclusão: publicação que seja de editorial, cartas, comentários e revisões. Na sintaxe, houve a necessidade de excluir os artigos publicados em 2009, pois em algumas situações, estes artigos foram selecionados.

A sintaxe utilizada para a seleção das publicações foi:

("prevalence"[MeSH Terms] OR prevalence[Text Word]) OR ("odds ratio"[MeSH Terms] OR odds ratio[Text Word]) OR ("risk"[MeSH Terms] OR relative risk[Text Word]) OR (("logistic models"[TIAB] NOT Medline[SB]) OR "logistic models"[MeSH Terms] OR logistic regression[Text Word])AND ("Cad Saude Publica"[Journal] OR "Cien Saude Colet"[Journal] OR "Rev Saude Publica"[Journal] OR "Braz J Med Biol Res"[Journal] OR "Journal of clinical epidemiology"[Jour] OR "International journal of epidemiology"[Jour] OR "BMJ"[Jour] OR "Lancet"[Jour] OR "The New England journal of medicine"[Jour] OR "American journal of epidemiology"[Jour]) AND ("2007"[PDAT] : "2008"[PDAT])NOT (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp] OR Review[ptyp]) NOT ("2009"[PDAT])

Para encontrar o número total de artigos publicados no respectivo ano, foi realizada uma busca com sintaxe similar, considerando apenas os nomes das revistas como descritores, e excluindo editoriais, cartas, comentários e revisões.

Na revisão dos artigos selecionados na base de dados PubMed, foram registradas informações sobre o delineamento do estudo, a prevalência do desfecho binário, métodos de análise e medida de associação estimada. Foram selecionados, também, os estudos transversais e coorte que utilizaram a regressão logística para estimar RC, porém a interpretaram como RP ou RR.

Resultados

De um total de 3469 artigos publicados em 2007 e 3834 artigos publicados em 2008, foram selecionados através da busca estratégica 830 (23,9%) e 876 (22,8%), respectivamente; totalizando 1706 artigos (23,3%). Dentre os 830 artigos de 2007, 333 (40,1%) efetivamente utilizaram RR, RP ou RC para estimar a medida de associação; e em 2008, esse total foi de 381 artigos (43,4%) (Quadro 2). A diferença entre o número total de artigos selecionados pela busca e o número total de artigos que estimaram RR,

RP ou RC com desfecho binário ocorreu em função do critério de seleção abrangente que acabou por selecionar artigos que utilizaram análises não relevantes para o trabalho, como por exemplo, regressão linear, estudos com desfechos politômicos e meta-análise, entre outras. Além disso, mesmo que o critério de seleção excluísse editorial, cartas, comentários e revisões, alguns desses artigos foram eventualmente selecionados.

Aproximadamente 97% dos estudos de caso-controle utilizaram regressão logística para estimar a RC, conforme esperado. Considerando a busca estratégica dos estudos de coorte e transversal, 188 (79,3%) artigos em 2007 e 210 (73,6%) em 2008 utilizaram a regressão logística e, destes, 150 (79,7%) e 145 (69,0%) artigos, respectivamente, tinham a prevalência/incidência do desfecho maior que 10%. Em 2007, 20,8% (48) dos estudos de coorte e transversal utilizaram técnicas alternativas, como, por exemplo, regressão de Poisson e log-binomial, para estimar a RP ou o RR, e em 2008, este número foi similar, 25,9% (74).

O Quadro 3 apresenta os resultados do ano de 2007 separados por revista. Do total dos artigos com delineamento transversal ou coorte, 63,2% utilizaram regressão logística e possuíam o desfecho maior que 10%. Quanto aos artigos com delineamento transversal ou coorte, a revista que apresentou a maior proporção de artigos com desfecho maior que 10%, utilizando regressão logística nas análises, foi a *New England Journal of Medicine*, com 70,4% (19).

O Quadro 4 apresenta os resultados referentes ao ano de 2008, separados por periódico. Das 4 publicações da *Brazilian Journal of Medical and Biological Research* com delineamento transversal ou coorte e desfecho maior que 10%, 3 utilizaram regressão logística e somente uma utilizou regressão de Poisson. A revista *Cadernos de Saúde Pública* foi o periódico com maior proporção de métodos alternativos que estimam a RP e o RR, com 51% (27) dos artigos.

Os resultados referentes às interpretações realizadas para estudos de coorte e transversal que utilizaram regressão logística, são apresentados no Quadro 5. Em 2007, 12,6% (19) dos artigos com desfecho maior que 10% interpretaram RC como RP ou RR, e em 2008, o total foi de 10,3% (15). Já entre artigos com desfecho menor que 10%, esse número passou de 39,4% (15) em 2007 para 24,6% (16) em 2008. Independentemente do desfecho, em 2007, 18,1% das publicações interpretaram RC como RP ou RR; e em 2008, a proporção foi de 14,7%. De modo geral, as revistas apresentaram um comportamento semelhante.

Discussão

Já está estabelecido na literatura epidemiológica que os modelos de regressão de Poisson com variância robusta e a regressão log-binomial mostraram-se as alternativas mais recomendadas para estimar o RR e RP em estudos de coorte e transversal quando o desfecho é binário, embora esta última apresente certa dificuldade de convergência nos casos em que há uma covariável contínua. Além de produzirem estimativas pontuais exatas, seus intervalos de confiança apresentaram resultados precisos, como apresentaram e comprovaram os estudos empíricos abordados neste trabalho. Em ocasiões em que o desfecho é comum, os resultados produzidos pela regressão logística pode gerar estimativas pouco distantes daquelas obtidas através de outros métodos.

A partir da busca orientada estrategicamente, conforme o foco do presente estudo, 398 das 522 publicações (76,2%) encontradas com delineamento transversal e coorte, do período de 2007 a 2008, utilizaram o modelo de regressão logística para estimar a medida de associação entre as variáveis de exposição e o desfecho binário.

A revisão efetuada no presente estudo apresentou, de modo global, uma freqüência muito baixa para a utilização de técnicas alternativas à regressão logística para estimar e interpretar a RP ou RR. Dessa forma, tais resultados expõem a fragilidade e até mesmo certa desatenção quanto aos métodos aplicados nos trabalhos em questão, cujas conclusões incidem em estimativas viciadas, inviabilizando, portanto, a interpretação correta de tais estimativas.

Os resultados mostram uma pequena redução na proporção de artigos que interpretam a RC como RR ou RP, em estudos transversais ou coorte de 2007 e 2008: de 18,1% para 14,7%, respectivamente. Porém, estes resultados não devem ser interpretados como um melhor entendimento por parte dos autores de 2007 para 2008, pois o período avaliado é considerado relativamente pequeno.

Cabe destacar que, atualmente, a prática de utilizar os modelos mais adequados para os tipos de delineamento específicos é uma constante, não havendo mais quaisquer limitações para sua aplicação. Cada vez mais, os pacotes estatísticos vêm incorporando essas técnicas, tornando-as muito mais acessíveis. Por essa facilidade, pode-se dizer que não há mais justificativa para estimar e interpretar RR e RP através da RC. Assim, independentemente do desfecho ser ou não raro, a premissa básica é a

de que o modelo utilizado deve ser o mais adequado, tais como regressão log-binomial e Poisson, de modo a evitar vícios em estimativas pontuais, nas estimativas intervalares e suas interpretações.

Há ainda periódicos importantes que publicam trabalhos de estudos transversais ou coorte com desfecho dicotômico comum cujas análises foram realizadas por regressão logística. Isso não incorreria em problema algum se os autores interpretassem RC como RC; no entanto não há qualquer garantia de que os leitores interpretem tal medida de maneira correta.

Nesse sentido, é de suma importância que os editores das revistas reflitam sobre a necessidade de orientar os potenciais autores a analisar os dados com métodos que permitam estimar a medida de associação pertinente ao tipo de delineamento epidemiológico.

Cabe ressaltar que o presente estudo tem algumas limitações. As dez revistas selecionadas neste trabalho representam apenas uma parcela dos periódicos existentes da área médica. Portanto, os achados representam somente as revistas selecionadas, não devendo ser expandido para o universo de periódicos. Ainda, os artigos são analisados previamente antes de serem publicados. Isto indica que é possível que os resultados representem um comportamento dos pesquisadores de um ou dois anos anteriores. Possivelmente, os estudos recentes já estejam atualizados em relação ao assunto.

Por fim, recomenda-se que a comunidade científica e os editores das revistas estejam atentos ao divulgar estudos que estimem medidas de associação, a fim de evitar possíveis estimativas e interpretação imprecisas por parte dos leitores.

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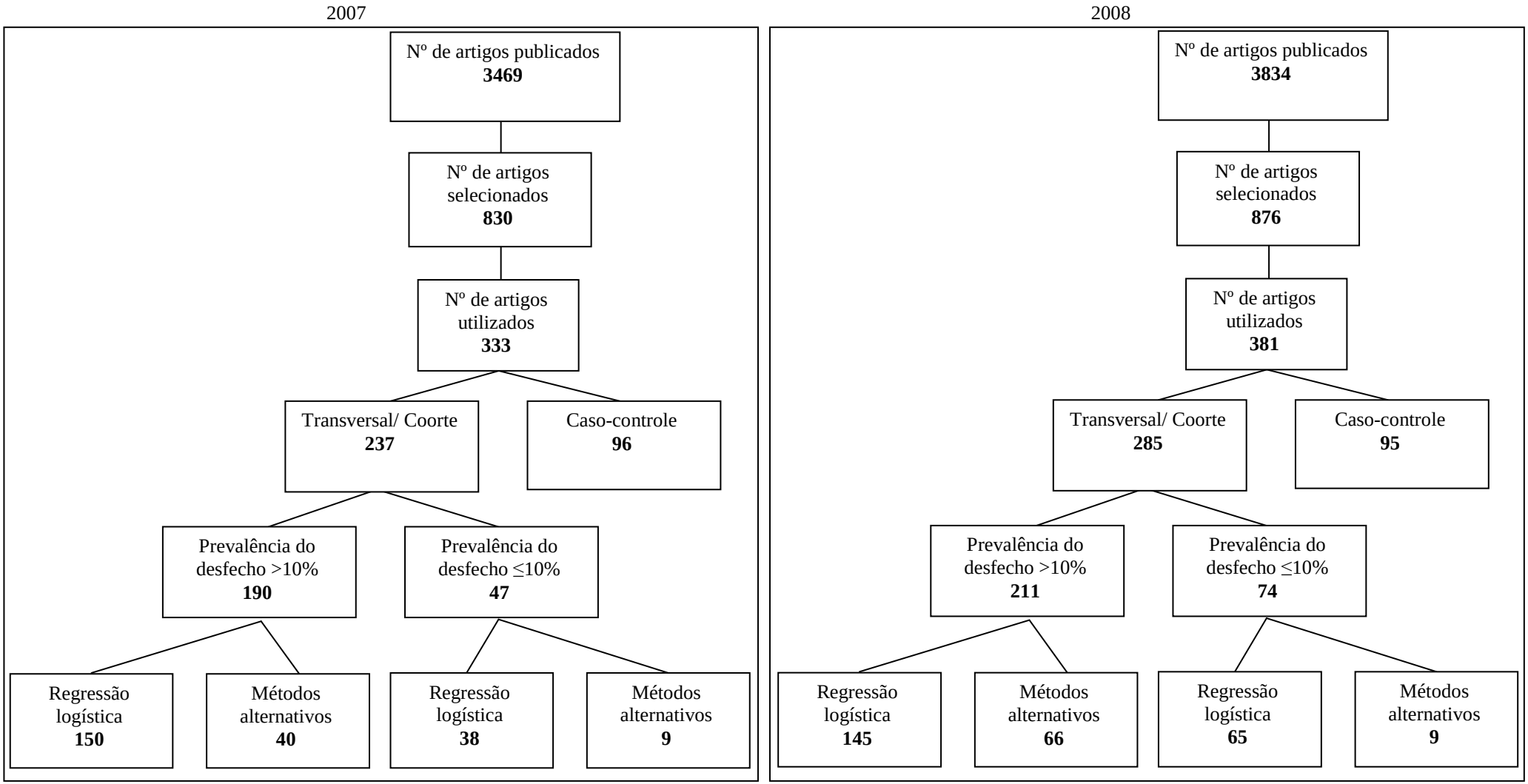
Quadro 1 – Classificação das revistas em relação ao Fator de Impacto (F.I.) e ao Qualis (Q)[*].

Revistas	Área de Avaliação	H (scopus)	F.I. (JCR)	Qualis
American Journal of Epidemiology	Ciências Biológicas I	13	5,285	A1
Brazilian Journal of Medical and Biological Research	Ciências Biológicas I	5	1,150	A2
British Medical Journal	Medicina II	17	9,723	A1
Cadernos de Saúde Pública	Ciências Biológicas I	0	-	B4
Ciência & Saúde Coletiva	Ciências Biológicas I	2	-	B1
International Journal of Epidemiology	Ciências Biológicas III	10	5,151	A1
Journal of Clinical Epidemiology	Medicina I	7	2,565	A1
Lancet	Ciências Biológicas I	41	28,638	A1
New England Journal of Medicine	Ciências Biológicas I	57	52,589	A1
Revista de Saúde Pública	Ciências Biológicas II	2	-	B4

Pesquisa realizada em 20 de setembro de 2008.
*Dados referentes ao ano de 2007.

Quadro 2 – Resultado da busca estratégica dos estudos com delineamentos coorte/transversal e caso-controle em relação à prevalência/incidência (P/I) de 10% para os anos de 2007 e 2008.



Quadro 3 – Resultados da busca estratégica de artigos por revistas no ano de 2007.

Revista	Nº total de artigos por revista	S/U/D*		Métodos					
			Prev / Inc	RL(%)	RP(%)	RPR(%)	LB(%)	ZY(%)	MH(%)
American Journal of Epidemiology	315	242/101/44	> 10	31(70,4)	3(6,8)		1(2,3)		
			≤ 10	8(18,2)	1(2,3)				
Brazilian Journal of Medical and Biological	182	31/10/5	> 10	3(60,0)		2(40,0)			
			≤ 10						
British Medical Journal	948	78/25/22	> 10	12(54,5)	3(13,6)				1(4,5)
			≤ 10	6(27,3)					
Cadernos de Saúde Pública	313	116/52/47	> 10	25(53,2)	10(21,3)	2(4,2)	1(2,1)		1(2,1)
			≤ 10	6(12,7)	2(4,2)				
Ciência & Saúde Coletiva	140	10/2/2	> 10	2(100,0)					
			≤ 10						
International Journal of Epidemiology	141	58/22/18	> 10	12(66,6)					1(5,5)
			≤ 10	5(27,7)					
Journal of Clinical Epidemiology	136	56/29/25	> 10	20(80,0)					
			≤ 10	4(16,0)	1(4,0)				
Lancet	584	87/22/19	> 10	12(63,1)	1(5,2)				
			≤ 10	5(26,3)			1(5,2)		
New England Journal of Medicine	541	99/38/27	> 10	19(70,4)	2(7,4)			1(3,7)	1(3,7)
			≤ 10	1(3,7)	2(7,4)		1(3,7)		
Revista de Saúde Pública	169	53/32/28	> 10	14(50,0)	8(28,6)	2(7,1)			
			≤ 10	3(10,7)		1(3,6)			
Total	3469	830/333/237	> 10	150(63,2)	27(11,4)	6(2,5)	2(0,8)	1(0,4)	4 (1,6)
			≤ 10	38(16,0)	6(2,5)		2(0,8)		

*S/U/D: número de artigos selecionados pela busca/ número de artigos utilizados/ número de artigos com delineamento transversal ou coorte.

Quadro 4 – Resultados da busca estratégica de artigos por revistas no ano de 2008.

Revista	Nº total de artigos por revista	S/U/D*		Métodos					
			Prev / Inc	RL(%)	RP(%)	RPR(%)	LB(%)	ZY(%)	MH(%)
American Journal of Epidemiology	304	229/118/58	> 10	32(55,2)	5(8,6)		3(5,1)		
			≤ 10	16(27,6)	1(1,7)		1(1,7)		
Brazilian Journal of Medical and Biological	166	17/4/4	> 10	3(75,0)	1(25,0)				
			≤ 10						
British Medical Journal	1190	115/36/33	> 10	16(48,5)	5(15,1)	1(3,0)	1(3,0)	1(3,0)	1(3,0)
			≤ 10	7(21,2)	1(3,0)				
Cadernos de Saúde Pública	330	129/57/53	> 10	18(33,9)	15(28,3)	9(17,0)	1(1,8)		
			≤ 10	8(15,1)	2(3,7)				
Ciência & Saúde Coletiva	169	20/3/3	> 10	2(66,6)					
			≤ 10	1(33,3)					
International Journal of Epidemiology	159	78/30/22	> 10	11(50,0)	1(4,5)	2(9,0)	1(4,5)		
			≤ 10	6(27,2)	1(4,5)				
Journal of Clinical Epidemiology	139	34/18/17	> 10	10(58,8)			1(5,9)		
			≤ 10	6(35,3)					
Lancet	686	95/30/27	> 10	14(51,8)	2(7,4)		1(3,7)		
			≤ 10	8(29,6)	1(3,7)				
New England Journal of Medicine	531	89/41/29	> 10	17(58,6)		1(3,4)	1(3,4)	1(3,4)	
			≤ 10	9(31,0)					
Revista de Saúde Pública	176	70/44/40	> 10	22(55,0)	11(27,5)	1(2,5)			
			≤ 10	4(10,0)	2(5,0)				
Total	3840	876/381/285	> 10	145(50,8)	40(14,0)	14(4,9)	9(3,1)	2(0,7)	1(0,4)
			≤ 10	65(22,8)	8(2,8)				

*S/U/D: número de artigos selecionados pela busca/ número de artigos utilizados/ número de artigos com delineamento transversal ou coorte.

Quadro 5- Resultados dos estudos que utilizaram regressão logística em estudos com delineamento de coorte ou transversal (N) e interpretaram RC como risco relativo ou razão de prevalência (n).

Revistas	Proporção do Desfecho %	Ano de 2007 n/N(%)	Ano de 2008 n/N(%)
American Journal of Epidemiology	> 10	1/31(3,2)	2/32(6,2)
	≤ 10	2/8(25,0)	3/16(18,7)
Brazilian Journal of Medical and Biological	> 10	1/3(33,3)	0/3(0,0)
	≤ 10	-	-
British Medical Journal	> 10	0/12(0,0)	2/16(12,5)
	≤ 10	4/6(66,6)	5/7(71,5)
Cadernos de Saúde Pública	> 10	4/25(16,0)	2/18(11,1)
	≤ 10	1/6(16,6)	0/8(0,0)
Ciência & Saúde Coletiva	> 10	0/2(0,0)	0/2(0,0)
	≤ 10	-	0/1(0,0)
International Journal of Epidemiology	> 10	3/12(25,0)	2/11(18,2)
	≤ 10	2/5(40,0)	1/6(16,6)
Journal of Clinical Epidemiology	> 10	2/20(10,0)	2/10(33,3)
	≤ 10	2/4(50,0)	2/6(33,3)
Lancet	> 10	2/12(16,6)	2/14(14,3)
	≤ 10	3/5(60,0)	2/8(25,0)
New England Journal of Medicine	> 10	3/19(15,8)	3/17(17,6)
	≤ 10	0/1(0,0)	1/9(11,1)
Revista de Saúde Pública	> 10	3/14(21,4)	0/22(0,0)
	≤ 10	1/3(33,3)	2/4(50,0)
Total	**> 10**	**19/150(12,6)**	**15/145(10,3)**
	≤ 10	**15/38(39,4)**	**16/65(24,6)**
Total geral		**34/188(18,1)**	**31/210(14,7)**

7. CONCLUSÕES E CONSIDERAÇÕES FINAIS

O modelo de regressão de Poisson com variância robusta mostra-se boa alternativa à regressão logística, visto que, estima diretamente a RP e o RR. A regressão log-binomial é um modelo que apresenta estimativas seguras, tanto por suas medidas pontuais como por seus intervalos de confiança, com a única consideração, de apresentar a dificuldade para convergir, uma vez da existência de uma covariável contínua.

Os resultados obtidos a partir da análise realizada sobre a seleção dos artigos indicam que a regressão logística tem sido aplicada, com freqüência, de maneira equivocada, situação essa, verificada nos diversos estudos em questão. Dessa forma, há de se ter uma especial atenção quanto aos métodos escolhidos e priorizados para estas pesquisas, sob o risco de uso indevido de determinado método e consequentemente, resultados submetidos a um viés que leva a estimação de medidas pouco adequadas, mais de acordo com interesses específicos dos estudos.

Ainda, verificou-se que revistas de renome ainda publicam artigos que interpretam de maneira equivocada as medidas de associação RR e RP, passando pela análise dos revisores dos periódicos.

Quanto às restrições, tanto matemáticas quando computacionais, para realizar uma regressão de Poisson ou log-binomial, por exemplo, pode-se afirmar que ficaram restritas ao passado, num período em que o uso desses modelos exigia do pesquisador o conhecimento específico dessas técnicas. A maioria dos pacotes estatísticos já tem incorporados métodos que estima diretamente a RP e RR. Orienta-se o uso destes métodos, mesmo nos casos em que a prevalência/ incidência do desfecho não seja considerada comum.

O presente estudo tem algumas limitações. As dez revistas selecionadas neste trabalho representam apenas uma parcela dos periódicos existentes da área médica. Portanto, os achados representam

somente as revistas selecionadas, não devendo ser expandido para o universo de periódicos. Ainda, os artigos são analisados previamente antes de serem publicados. Isto indica que é possível que os resultados representem um comportamento dos pesquisadores de um ou dois anos anteriores. Possivelmente, os estudos recentes já estejam atualizados em relação ao assunto.

Por fim, recomenda-se que a comunidade científica e os editores das revistas estejam atentos ao divulgar estudos que estimem medidas de associação, a fim de evitar possíveis estimativas e interpretação imprecisas por parte dos leitores.

8. ANEXOS

Anexo 1. Sintaxe da seleção de artigos

Anexo 2. Relação de artigos selecionados pela busca estratégica

Anexo 3. Relação de artigos utilizados

Anexo 4. Projeto de Pesquisa

ANEXO 1 – SINTAXE DA SELEÇÃO DE ARTIGOS

("prevalence"[MeSH Terms] OR prevalence[Text Word]) OR ("odds ratio"[MeSH Terms] OR odds ratio[Text Word]) OR ("risk"[MeSH Terms] OR relative risk[Text Word]) OR (("logistic models"[TIAB] NOT Medline[SB]) OR "logistic models"[MeSH Terms] OR logistic regression[Text Word])AND ("Cad Saude Publica"[Journal] OR "Cien Saude Colet"[Journal] OR "Rev Saude Publica"[Journal] OR "Braz J Med Biol Res"[Journal] OR "Journal of clinical epidemiology"[Jour] OR "International journal of epidemiology"[Jour] OR "BMJ"[Jour] OR "Lancet"[Jour] OR "The New England journal of medicine"[Jour] OR "American journal of epidemiology"[Jour]) AND ("2007"[PDAT] : "2008"[PDAT])NOT (Editorial[ptyp] OR Letter[ptyp] OR Comment[ptyp] OR Review[ptyp]) NOT (“2009”[PDAT])

ANEXO 2 – RELAÇÃO DE ARTIGOS SELECIONADOS PELA BUSCA ESTRATÉGICA

American Journal of Epidemiology – Ano: 2007

Nº	Vol/Pg	Autores	Título
1	166(11):1337-44	Cheung YB.	A modified least-squares regression approach to the estimation of risk difference.
2	166(11):1270-9	Park Y, Mitrou PN, Kipnis V, Hollenbeck A, Schatzkin A, Leitzmann MF.	Calcium, dairy foods, and risk of incident and fatal prostate cancer: the NIH-AARP Diet and Health Study.
3	166(12):1359-64	Romundstad PR, Davey Smith G, Nilsen TI, Vatten LJ.	Associations of prepregnancy cardiovascular risk factors with the offspring's birth weight.
4	166(11):1288-97	Kifley A, Liew G, Wang JJ, Kaushik S, Smith W, Wong TY, Mitchell P.	Long-term effects of smoking on retinal microvascular caliber.
5	166(12):1409-19	John EM, Schwartz GG, Koo J, Wang W, Ingles SA.	Sun exposure, vitamin D receptor gene polymorphisms, and breast cancer risk in a multiethnic population.
6	166(11):1259-69	Park SY, Murphy SP, Wilkens LR, Stram DO, Henderson BE, Kolonel LN.	Calcium, vitamin D, and dairy product intake and prostate cancer risk: the Multiethnic Cohort Study.
7	166(11):1312-9	Catov JM, Bodnar LM, Ness RB, Barron SJ, Roberts JM.	Inflammation and dyslipidemia related to risk of spontaneous preterm birth.
8	166(12):1374-80	Franco M, Orduñez P, Caballero B, Tapia Granados JA, Lazo M, Bernal JL, Guallar E, Cooper RS.	Impact of energy intake, physical activity, and population-wide weight loss on cardiovascular disease and diabetes mortality in Cuba, 1980-2005.
9	166(10):1174-85	Chan JM, Wang F, Holly EA.	Whole grains and risk of pancreatic cancer in a large population-based case-control study in the San Francisco Bay Area, California.
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7	335(7630):1134	Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D; Million Women Study Collaboration.	Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study.
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43	334(7607):1305	Montgomery AA, Emmett CL, Fahey T, Jones C, Ricketts I, Patel RR, Peters TJ, Murphy DJ; DiAMOND Study Group.	Two decision aids for mode of delivery among women with previous caesarean section: randomised controlled trial.
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3	60(12):1288-97	Saarni SI, Suvisaari J, Sintonen H, Koskinen S, Härkänen T, Lönnqvist J.	The health-related quality-of-life impact of chronic conditions varied with age in general population
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7	60(11):1149-55	Lietzau S, Raum E, von Baum H, Marre R, Brenner H.	Household contacts were key factor for children's colonization with resistant Escherichia coli in community setting
8	60(11):1140-8	Fu B, Tom BD, Delahooke T, Alexander GJ, Bird SM.	Event-biased referral can distort estimation of hepatitis C virus progression rate to cirrhosis, and of prognostic influences
9	60(11):1132-9	Filardo G, Hamilton C, Hamman B, Ng HK, Grayburn P.	Categorizing BMI may lead to biased results in studies investigating in-hospital mortality after isolated CABG
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5	370: 1811–13	Dandona L, Dandona R.	Drop of HIV estimate for India to less than half.
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65	369: 1149–50	Mukherjee R, Eastman N, Turk J, Hollins S.	Fetal alcohol syndrome: law and ethics.
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227	167(1):78-85	Thurston RC, Sowers MR, Chang Y, Sternfeld B, Gold EB, Johnston JM, Matthews KA.	Adiposity and reporting of vasomotor symptoms among midlife women
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3	41(10): 877-83	Ananias M, Yano T.	"Serogroups and virulence genotypes of
4	41(10):896-903	Moscoso-Solorzano GT, Mastroianni-Kirsztajn G, Ozaki KS, Araujo S, Franco MF, Pacheco-Silva A, Camara NO.	Are the current chronic allograft nephropathy grading systems sufficient to predict renal allograft survival?
5	41(8):728-33	Genta PR, Marcondes BF, Danzi NJ, Lorenzi-Filho G.	Ethnicity as a risk factor for obstructive sleep apnea: comparison of Japanese descendants and white males in São Paulo, Brazil.
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7	41(8):668-73	Gerchman F, Zanatta CM, Burttet LM, Picon PX, Lisboa HR, Silveiro SP, Gross JL, Canani LH.	Vascular complications of black patients with type 2 diabetes mellitus in Southern Brazil.
8	41(8):643-7	Vidigal PV, Reis FJ, Boson WL, De Marco LA, Brasileiro-Filho G.	p.F508del in a heterogeneous cystic fibrosis population from Minas Gerais, Brazil.
9	41(7):583-8	Godoy AE, Mandelli J, Oliveira FH, Calegari S, Moura LB, Serafini EP.	p16INK4 expression in precursor lesions of squamous cell cervical cancer related to the presence of HPV-DNA.
10	41(6):512-8	Cardoso RL, Nogueira AR, Salis LH, Urményi TP, Silva R, Moura-Neto RS, Pereira BB, Rondinelli E, Souza e Silva NA.	The association of ACE gene D/I polymorphism with cardiovascular risk factors in a population from Rio de Janeiro.
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12	41(3):215-22	Silva RS, Figueiredo AC, Mady C, Lorenzi-Filho G.	Breathing disorders in congestive heart failure: gender, etiology and mortality.

13	41(3):202-8	Nunes JL, Silvany-Neto A, Pitta GB, Figueiredo LF, Oliveira I, Quadros R, Miranda-Junior F.	Prevalence of peripheral arterial occlusive disease in patients referred to a tertiary care hospital in Salvador, Bahia, Brazil, for coronary angiography.
14	41(4):324-32	Shuhama R, Del-Ben CM, Loureiro SR, Graeff FG.	Defensive responses to threat scenarios in Brazilians reproduce the pattern of Hawaiian Americans and non-human mammals.
15	41(2):89-94	Fuzikawa AK, Peixoto SV, Taufer M, Moriguchi EH, Lima-Costa MF.	Association of ApoE polymorphisms with prevalent hypertension in 1406 older adults: the Bambuí Health Aging Study (BHAS).
16	41(3):229-34	Leitão CB, Nabinger GB, Krahe AL, Bolson PB, Gerchman F, Friedman R, Gross JL, Canani LH.	The role of K121Q ENPP1 polymorphism in diabetes mellitus and its complications.
17	41(3):235-40	Alencar RS, Gomes MM, Sitnik R, Pinho JR, Malta FM, Mello IM, Mello ES, Bacchella T, Machado MC, Alves VA, Carrilho FJ.	Low occurrence of occult hepatitis B virus infection and high frequency of hepatitis C virus genotype 3 in hepatocellular carcinoma in Brazil.

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10	337:a2533.	Cohen-Cole E, Fletcher JM.	Detecting implausible social network effects in acne, height, and headaches: longitudinal analysis.
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29	337:a2030	Ashworth M, Medina J, Morgan M.	Effect of social deprivation on blood pressure monitoring and control in England: a survey of data from the quality and outcomes framework.
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35	337:a2081	Zarocostas J.	WHO agrees plan to speed up research on risk to human health from climate change.
36	337:a1170	Suresh K, Smalley D, Walker Z.	Memory problems in an older person.
37	337:a1682	Ganzini L, Goy ER, Dobscha SK.	Prevalence of depression and anxiety in patients requesting physicians' aid in dying: cross sectional survey.
38	337:a1618	Feehally J, Griffith KE, Lamb EJ, O'Donoghue DJ, Tomson CR.	Early detection of chronic kidney disease.
39	337:a1530	Crowe E, Halpin D, Stevens P; Guideline Development Group.	Early identification and management of chronic kidney disease: summary of NICE guidance.
40	337:a1680	Murphy HR, Rayman G, Lewis K, Kelly S, Johal B, Duffield K, Fowler D, Campbell PJ, Temple RC.	Effectiveness of continuous glucose monitoring in pregnant women with diabetes: randomised clinical trial.
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43	337:a1569	Lasserson DS, Chandratheva A, Giles MF, Mant D, Rothwell PM.	Influence of general practice opening hours on delay in seeking medical attention after transient ischaemic attack (TIA) and minor stroke: prospective population based study.
44	337:a1440	van Dam RM, Li T, Spiegelman D, Franco OH, Hu FB.	Combined impact of lifestyle factors on mortality: prospective cohort study in US women.
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46	337:a1603	Dobson R.	Known risk factors explain only one in three cancers, study finds.
47	337:a1379	Barennes H, Andriatahina T, Latthaphasavang V, Anderson M, Srour LM.	Misperceptions and misuse of Bear Brand coffee creamer as infant food: national cross sectional survey of consumers and paediatricians in Laos.
48	337:a1529	Tanne JH.	Most patients at risk of stroke fail to get adequate anticoagulation.
49	337:a1198	Price JF, Stewart MC, Deary IJ, Murray GD, Sandercock P, Butcher I, Fowkes FG; AAA Trialists.	Low dose aspirin and cognitive function in middle aged to elderly adults: randomised controlled trial.

50	337:a1371	Jackson R, Wells S, Rodgers A.	Will screening individuals at high risk of cardiovascular events deliver large benefits? Yes.
51	337:a1227	Douglas IJ, Smeeth L.	Exposure to antipsychotics and risk of stroke: self controlled case series study.
52	337:a1021	Hodnett ED, Stremler R, Willan AR, Weston JA, Lowe NK, Simpson KR, Fraser WD, Gafni A	Effect on birth outcomes of a formalised approach to care in hospital labour assessment units: international, randomised controlled trial.
53	337:a918	Gallego PH, Craig ME, Hing S, Donaghue KC.	Role of blood pressure in development of early retinopathy in adolescents with type 1 diabetes: prospective cohort study.
54	337:a802	Funatogawa I, Funatogawa T, Yano E.	Do overweight children necessarily make overweight adults? Repeated cross sectional annual nationwide survey of Japanese girls and women over nearly six decades.
55	337:a939	Collin S, Reeves BC, Hendy J, Fulop N, Hutchings A, Priedane E.	Implementation of computerised physician order entry (CPOE) and picture archiving and communication systems (PACS) in the NHS: quantitative before and after study.
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57	337:a695	McGorry PD.	Is early intervention in the major psychiatric disorders justified? Yes.
58	337:a811	Tim Rhodes, Milena Simic, Sladjana Baros, Lucy Platt and Bojan Zikic	Police violence and sexual risk among female and transvestite sex workers in Serbia: qualitative study.
59	337:a1057	Spurgeon D.	Evidence shows higher long term risks from gestational diabetes.
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61	337:a437	Tan T, Little P, Stokes T; Guideline Development Group.	Antibiotic prescribing for self limiting respiratory tract infections in primary care: summary of NICE guidance.
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66	337:a386	Liu B, Beral V, Balkwill A, Green J, Sweetland S, Reeves G, Million Women Study Collaborators.	Gallbladder disease and use of transdermal versus oral hormone replacement therapy in postmenopausal women: prospective cohort study.
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3	24(12):2926-36.	de Moura AT, Moraes CL, Reichenheim ME.	Detection of child abuse
4	24(12):2919-25.	Frei F, Juncansen C, Ribeiro-Paes JT.	Epidemiological survey of intestinal parasite infections
5	24(12):2909-18.	de Almeida S, Bettiol H, Barbieri MA, da Silva AA, Ribeiro VS.	Significant differences in cesarean section rates between a private and a public hospital in Brazil.
6	24(12):2901-8	Presgrave Rde F, Camacho LA, Villas Boas MH.	A profile of unintentional poisoning caused by household cleaning products, disinfectants and pesticides.
7	24(12):2881-90.	Pedrosa ML, Mattos IE, Koifman RJ.	Cervical intraepithelial lesions in adolescents
8	24(12):2871-80.	Rocha Rde A, de Goes PS.	Comparison of access to Oral Health Services between areas covered and not covered by the Family Health Program in Campina Grande, Paraíba State, Brazil
9	24(12):2861-70.	Vieira-Santos IC, de Souza WV, de Carvalho EF, de Medeiros MC, Nóbrega MG, Lima PM.	Prevalence of diabetic foot and associated factors in the family health units of the city of Recife, Pernambuco State, Brazil, in 2005
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11	24(12):2827-33.	de Oliveira AL, Paniago AM, Sanches MA, Dorval ME, Oshiro ET, Leal CR, de Paula FH, Pereira LG, da Cunha RV, Bóia MN.	Asymptomatic infection in family contacts of patients with human visceral leishmaniasis in Três Lagoas, Mato Grosso do Sul State, Brazil.
12	24(12):2767-74.	Capilheira MF, Santos IS, Azevedo MR Jr, Reichert FF.	Risk factors for chronic non-communicable diseases and the CARMEN Initiative
13	24(11):2623-32.	Amorim VM, Barros MB, César CL, Carandina L, Goldbaum M.	Factors associated with lack of mammograms and clinical breast examination by women
14	24(11):2593-602.	Nascimento EM, Costa Mda C, Mota EL, Paim JS.	Investigation of risk factors for infant mortality by linking health databases
15	24(11):2582-92.	Leimann BC, Koifman RJ.	Cryptococcal meningitis in Rio de Janeiro State, Brazil, 1994-2004.
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17	24(11):2521-31.	Paula Gde M, Silva LG, Moreira ME, Bonfim O.	Repercussions of premature rupture of fetal membranes on neonatal morbidity and mortality
18	24(11):2511-20.	Muller DK, Dias-da-Costa JS, Luz AM, Olinto MT.	Coverage of Pap smear tests in the city of São Leopoldo, Rio Grande do Sul State, Brazil
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23	24(10):2347-53	Silva RH, Castro RF, Cunha DC, Almeida CT, Bastos JR, Camargo LM.	Dental caries in a riverine community in Rondônia State, Amazon Region, Brazil, 2005-2006
24	24(10):2334-46.	Avanci JQ, Assis SG, Oliveira RV.	Depressive symptoms during adolescence
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27	24(10):2279-88.	de Castro IR, Cardoso LO, Engstrom EM, Levy RB, Monteiro CA.	Surveillance of risk factors for non-communicable diseases among adolescents
28	24 Suppl 2:S341-52.	Hasselmann MH, Werneck GL, Silva CV.	Symptoms of postpartum depression and early interruption of exclusive breastfeeding in the first two months of life.
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35	24(9):2115-22.	Matos MG, Hennington EA, Hoefel AL, Dias-da-Costa JS.	Lower back pain in health insurance policyholders
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43	24 Suppl 3:S461-7.	Barros FC, Victora CG.	Maternal-child health in Pelotas, Rio Grande do Sul State, Brazil
44	24 Suppl 3:S451-60.	Santos IS, Menezes AM, Mota DM, Albernaz EP, Barros AJ, Matijasevich A, Barros FC, Victora CG.	Infant mortality in three population-based cohorts in Southern Brazil
45	24 Suppl 3:S444-50.	Halpern R, Barros AJ, Matijasevich A, Santos IS, Victora CG, Barros FC.	Developmental status at age 12 months according to birth weight and family income
46	24 Suppl 3:S427-36.	Cesar JA, Matijasevich A, Santos IS, Barros AJ, Dias-da-Costa JS, Barros FC, Victora CG.	The use of maternal and child health services in three population-based cohorts in Southern Brazil, 1982-2004.
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68	24(7):1517-26.	Ferreira LR, Pinheiro TM, Siqueira AL, Carneiro AP.	Silicosis among semiprecious gem cutters in Joaquim Felício, Minas Gerais State, Brazil
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75	24(6):1271-8.	Conceição GM, Barbosa MT.	A methodology to estimate incidence from prevalence rates in household surveys
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28	42(4):590-7.	Ramiarina RA, Ramiarina BL, Almeida RM, Pereira WC.	Comorbidity adjustment index for the international classification of diseases, 10th revision.

29	42(5):786-95.	Engstrom EM, Castro IR, Portela M, Cardoso LO, Monteiro CA.	Effectiveness of daily and weekly iron supplementation in the prevention of anemia in infants.
30	42(5):877-85.	Audi CA, Segall-Corrêa AM, Santiago SM, Andrade Mda G, Pèrez-Escamila R.	Violence against pregnant women
31	42(5):838-43	Rozman MA, Alves IS, Porto MA, Gomes PO, Ribeiro NM, Nogueira LA, Caseiro MM, Silva VA, Massad E, Burattini MN.	HIV infection and related risk behaviors in a community of recyclable waste collectors of Santos, Brazil.
32	42 Suppl 1:127-37.	Schraiber LB, D'Oliveira AF, França Junior I; Grupo de Estudos em População, Sexualidade e Aids.	Intimate partner sexual violence among men and women in urban Brazil, 2005.
33	42 Suppl 1:98-108.	Bastos FI, Cunha CB, Hacker MA; Grupo de Estudos em População, Sexualidade e Aids.	Signs and symptoms associated with sexually transmitted infections in Brazil, 2005
34	42 Suppl 1:45-53.	Paiva V, Calazans G, Venturi G, Dias R; Grupo de Estudos em População, Sexualidade e Aids.	Age and condom use at first sexual intercourse of Brazilian adolescents
35	42 Suppl 1:34-44.	Berquó E, Barbosa RM, Lima LP; Grupo de Estudos em População, Sexualidade e Aids.	Trends in condom use
36	42(4):717-23.	Lima MC, Menezes PR, Carandina L, Cesar CL, Barros MB, Goldbaum M.	Common mental disorders and the use of psychoactive drugs
37	42(4):724-32.	Ribeiro AQ, Rozenfeld S, Klein CH, César CC, Acurcio Fde A.	Survey on medicine use by elderly retirees in Belo Horizonte, Southeastern Brazil
38	42(4):656-63.	Galli B, Chiaravalloti Neto F.	Temporal-spatial risk model to identify areas at high-risk for occurrence of dengue fever
39	42(3):517-23.	Casagrande RR, Pastorino AC, Souza RG, Leone C, Solé D, Jacob CM.	Asthma prevalence and risk factors in schoolchildren of the city of São Paulo, Brazil
40	42(3):471-9.	Marques LA, Eluf-Neto J, Figueiredo RA, Góis-Filho JF, Kowalski LP, Carvalho MB, Abrahão M, Wünsch-Filho V.	Oral health, hygiene practices and oral cancer.
41	42(3):450-6.	Gil-Monte PR, Marucco MA.	Burnout prevalence in pediatricians of general hospitals
42	42(3):402-10.	Caputo VG, Bordin IA.	Teenage pregnancy and frequent use of alcohol and drugs in the home environment
43	42(3):389-95.	Silveira MF, Barros AJ, Santos IS, Matijasevich A, Victora CG.	Socioeconomic differentials in performing urinalysis during prenatal care
44	42(4):607-14.	França MC, Giugliani ER, Oliveira LD, Weigert EM, Santo LC, Köhler CV, Bonilha AL.	Bottle feeding during the first month of life
45	42(4):598-606.	Amaral JJ, Victora CG, Leite AJ, Cunha AJ.	Implementation of the Integrated Management of Childhood Illnesses strategy in Northeastern Brazil
46	42(3):524-8. Epub 2008 Apr 25.	Paula CS, Vedovato MS, Bordin IA, Barros MG, D'Antino ME, Mercadante MT.	Mental health and violence among sixth grade students from a city in the state of São Paulo
47	42(3):457-63.	Sávio KE, Costa TH, Schmitz Bde A, Silva EF.	Sex, income and level of education associated with physical activity level among workers
48	42(3):443-9.	Huatuco EM, Durigon EL, Lebrun FL, Passos SD, Gazeta RE, Azevedo Neto RS, Massad E.	Seroprevalence of human parvovirus B19 in a suburban population in São Paulo, Brazil.
49	42(3):437-42.	Beloqui JA.	Relative risk for AIDS between homo/bisexual and heterosexual men
50	42(3):480-6.	Gushi LL, Rihs LB, Soares Mda C, Forni TI, Vieira V, Wada RS, Sousa Mda L.	Dental caries and treatment needs in adolescents from the state of São Paulo, 1998 and 2002
51	42(2):287-93.	Zangirolani LT, Cordeiro R, Medeiros MA, Stephan C.	Spatial distribution of risks for work-related injuries in a city of Southeastern Brazil
52	42(2):279-86.	Garcia LP, Blank VL.	Management of occupational exposures to potentially infectious materials in dentistry
53	42(2):224-33.	Noal RB, Menezes AM, Canani SF, Siqueira FV.	Habitual snoring and obstructive sleep apnea in adults
54	42(2):208-16.	Camões M, Lopes C.	Factors associated with physical activity in the Portuguese population
55	42(2):191-9.	Antunes JL, Peres MA, Frias AC, Crosato EM, Biazevic MG.	Gingival health of adolescents and the utilization of dental services, state of São Paulo, Brazil
56	42(2):234-41.	Bandeira FM, Santos MN, Bezerra MA, Gomes YM, Araujo AS, Braga MC, Souza WV, Abath FG.	Family screening for HBB*S gene and detection of new cases of sickle cell trait in Northeastern Brazil

57	42(2):324-34.	Bastos JL, Peres MA, Peres KG, Dumith SC, Gigante DP.	Socioeconomic differences between self- and interviewer-classification of color/race
58	42(2):302-7.	Benedetti TR, Borges LJ, Petroski EL, Gonçalves LH.	Physical activity and mental health status among elderly people
59	42(1):143-5.	Ledesma RD, Peltzer RI.	Helmet use among motorcyclists
60	42(1):123-30.	Rama CH, Roteli-Martins CM, Derchain SF, Longatto-Filho A, Gontijo RC, Sarian LO, Syrjänen K, Aldrighi JM.	Prevalence of genital HPV infection among women screened for cervical cancer
61	42(1):108-16.	Walsh IA, Oishi J, Coury HJ.	Clinical and functional aspects of work-related musculoskeletal disorders among active workers.
62	42(1):100-7.	Lima-Costa MF.	Factors associated with influenza vaccination among elderly in a metropolitan area in Southeastern Brazil
63	42(1):89-99.	Loyola Filho AI, Uchoa E, Firmo JO, Lima-Costa MF.	Influence of income on the association between cognitive impairment and polypharmacy
64	42(1):82-8.	Duro LN, Assunção MC, Costa JS, Santos IS.	Performance of lipid profile request between public and private sectors
65	42(1):73-81.	Theme Filha MM, Szwarcwald CL, Souza Junior PR.	Measurements of reported morbidity and interrelationships with health dimensions
66	42(1):41-8.	Peluso Ede T, Blay SL.	Public perception of depression in the city of São Paulo
67	42(1):34-40.	Zinn-Souza LC, Nagai R, Teixeira LR, Latorre MR, Roberts R, Cooper SP, Fischer FM.	Factors associated with depression symptoms in high school students in São Paulo, Brazil.
68	42(1):26-33.	Haack RL, Horta BL, Cesar JA.	Sunburn in young people
69	42(1):19-25.	Cornejo LS, Brunotto M, Hilas E.	Salivary factors associated to the prevalence and increase of dental caries in rural schoolchildren
70	42(1):1-9.	Barros AJ, Matijasevich A, Santos IS, Albernaz EP, Victora CG.	Neonatal mortality

ANEXO 3 – RELAÇÃO DE ARTIGOS UTILIZADOS

American Journal of Epidemiology – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
5	Caso-controle	Regressão logística		
9	Caso-controle	Regressão logística		
12	Coorte	Regressão logística	>10%	RC
14	Transversal e Coorte	Regressão logística	>10%	RC
15	Caso-controle	Regressão logística		
18	Caso-controle	Regressão logística		
19	Caso-controle	Regressão logística		
21	Coorte	Regressão logística	>10%	RC
22	Caso-controle	Regressão logística		
26	Caso-controle	Regressão logística		
27	Coorte	Regressão logística	>10%	RC
28	Coorte	Regressão logística	>10%	RC
30	Transversal	Regressão logística	>10%	RC
31	Transversal	Regressão logística	>10%	RC
32	Caso-controle	Regressão logística		
36	Coorte	Regressão logística	>10%	RC
37	Coorte	Regressão logística	>10%	RC
38	Caso-controle	Regressão logística		
39	Caso-controle	Regressão logística		
44	Caso-controle	Regressão logística		
45	Caso-controle	Regressão logística		
50	Caso-controle	Regressão logística		
53	Caso-controle	Regressão logística		
54	Caso-controle	Regressão logística		
58	Caso-controle	Regressão logística		
59	Coorte	Regressão de Poisson	>10%	
60	Coorte	Regressão logística	>10%	RC
62	Coorte	Regressão logística	>10%	RC
63	Transversal	Regressão logística	>10%	RC
66	Caso-controle	Regressão logística		
69	Caso-controle	Regressão logística		
77	Caso-controle	Regressão logística		
78	Caso-controle	Regressão logística		
79	Caso-controle	Regressão logística		
80	Coorte	Regressão logística	<10%	RC
82	Coorte	Regressão logística	<10%	RC
87	?	Regressão logística	>10%	RC
88	Caso-controle	Regressão logística		
90	Coorte	Regressão logística	<10%	RC
91	Caso-controle	Regressão logística		
96	Caso-controle	Regressão logística		
99	Caso-controle	Regressão logística		
103	Coorte	Regressão logística	<10%	RC
104	Caso-controle	Regressão logística		
107	Caso-controle	Regressão logística		
108	Coorte	Regressão logística	>10%	RC
110	Coorte	Regressão logística	>10%	RC
112	Caso-controle	Regressão logística		
113	Caso-controle	Regressão logística		
120	Caso-controle	Regressão logística		
121	Coorte	Regressão de Poisson	>10%	
128	Coorte	Regressão logística	<10%	RR
131	Coorte	Regressão logística	>10%	RC
134	Coorte	Regressão logística	>10%	RC
139	Caso-controle	Regressão logística		
140	Caso-controle	Regressão logística		
141	Caso-controle	-		
145	Caso-controle	Regressão logística		

146	Coorte	Regressão logística	>10%	RC
147	Caso-controle	Regressão logística		
151	Caso-controle	Regressão logística		
155	Coorte e Transversal	Regressão logística	>10%	RC
158	Coorte	Regressão logística	>10%	RC
162	Coorte	Regressão logística	>10%	RC
163	Caso-controle	Regressão logística		
164	Caso-controle	Regressão logística		
165	Coorte	Regressão logística	<10%	RR
166	Coorte	Regressão logística	<10%	RC
177	Transversal	Regressão logística	>10%	RC
181	Coorte	Regressão logística	<10%	RC
183	Caso-controle	Regressão logística		
184	Caso-controle	Regressão logística		
186	Caso-controle	Regressão logística		
187	Coorte	Regressão de Poisson	<10%	
188	Caso-controle	Regressão logística		
189	Transversal	Regressão logística	>10%	RC
190	Caso-controle	Regressão logística		
192	Caso-controle	Regressão logística		
193	Caso-controle	Regressão logística		
197	Caso-controle	Regressão logística		
198	Caso-controle	Regressão logística		
199	Caso-controle	Regressão logística		
200	Transversal	Regressão logística	>10%	RC
204	Coorte	Regressão logística	>10%	RC
206	Coorte	Regressão logística	>10%	RC
211	Caso-controle	Regressão logística		
212	Caso-controle	Regressão logística		
214	Coorte	Regressão logística	>10%	RR
215	Caso-controle	Regressão logística		
216	Coorte e Transversal	Regressão logística	>10%	RC
219	Transversal	Regressão logística	>10%	RC
221	Caso-controle	Regressão logística		
222	Caso-controle	Regressão logística		
223	Transversal	Regressão de Poisson	>10%	
224	Transversal	Regressão logística	>10%	RC
228	Caso-controle	Regressão logística		
233	Coorte	Regressão binomial	>10%	
234	Caso-controle	Regressão logística		
236	Transversal	Regressão logística	>10%	RC
240	Caso-controle	Regressão logística		
241	Caso-controle	Regressão logística		

Brazilian Journal of medical and Biological – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
2	Coorte	Regressão logística	>10%	RC
7	Coorte	Reg. de Poisson var. robusta	>10%	
8	Coorte	Reg. de Poisson var. robusta	>10%	
10	Coorte	Regressão logística	>10%	RR
13	Coorte	Regressão logística	>10%	RC
15	Caso-controle	-		
19	Caso-controle	-		
24	Caso-controle	Regressão logística		
27	Caso-controle	Regressão logística		
28	Caso-controle	-		
29	Caso controle	-		

British Medical Journal – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
8	Coorte	Regressão logística	<10%	RR
10	Caso-controle	Regressão logística		
11	Caso-controle	Regressão logística		
12	Coorte	Regressão logística	<10%	RR
13	Transversal	Regressão logística	>10%	RC

14	Coorte	Mantel-Haenszel	>10%	
16	Coorte	Regressão logística	<10%	RR
18	Transversal	Regressão logística	>10%	RC
19	Transversal	Regressão de Poisson	>10%	
27	Transversal	Regressão logística	<10%	RC
29	Coorte	Regressão logística	>10%	RC
36	Coorte	Regressão de Poisson	>10%	
38	Coorte	Regressão logística	>10%	RC
43	Coorte	Regressão logística	>10%	RC
46	Coorte	Regressão logística	<10%	RR
48	Coorte	Regressão logística	>10%	RC
49	Coorte	Regressão logística	>10%	RC
50	Transversal	Regressão logística	>10%	RC
55	Coorte	Regressão logística	>10%	RC
60	Coorte	Regressão logística	>10%	RC
61	Coorte	Regressão logística	<10%	RC
68	Coorte	Regressão logística	>10%	RC
69	Caso-controle	-		
74	Coorte	Regressão logística	>10%	RC
77	Coorte	Regressão de Poisson	>10%	

Cadernos de Saúde Pública – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
5	Coorte	Regressão logística	>10%	RC
6	Transversal	Regressão logística	>10%	RR
7	Caso-controle	Regressão logística		
9	Caso-controle	Regressão logística		
11	Transversal	Regressão logística	>10%	RC
12	Transversal	Regressão logística	>10%	RC
13	Transversal	Regressão logística	<10%	RC
17	Transversal	Regressão logística	<10%	RC
19	Transversal	Regressão de Poisson	>10%	
21	Transversal	Regressão logística	>10%	RR
23	Transversal	Regressão de Poisson	>10%	
27	Transversal	Regressão de Poisson	>10%	
30	Transversal	Regressão logística	>10%	RC
32	Transversal	Log binomial	>10%	
33	Transversal	Regressão logística	>10%	RC
35	Transversal	Regressão logística	<10%	RC
40	Transversal	Regressão logística	>10%	RC
41	Transversal	Mantel-Haenszel	>10%	
44	Coorte	Regressão logística	>10%	RC
45	Transversal	Regressão logística	>10%	RC
47	Transversal	Regressão de Poisson	>10%	
48	Transversal	Regressão logística	>10%	RC
49	Transversal	Regressão de Poisson	>10%	
50	Transversal	Reg. de Poisson var. robusta	>10%	
55	Transversal	Regressão logística	>10%	RC
56	Transversal	Regressão logística	>10%	RC
57	Caso-controle	Regressão logística		
58	Transversal	Regressão logística	<10%	RR
59	Transversal	Regressão de Poisson	>10%	
60	Transversal	Regressão logística	>10%	RC
61	Coorte	Regressão logística	>10%	RC
64	Transversal	Regressão logística	>10%	RC
65	Caso-controle	Regressão logística		
67	Transversal	Regressão logística	<10%	RC
69	Transversal	Regressão de Poisson	>10%	
70	Transversal	Regressão de Poisson	>10%	
73	Transversal	Reg. de Poisson var. robusta	>10%	
77	Transversal	Regressão de Poisson	>10%	
79	Transversal	Regressão logística	>10%	RR
82	Transversal	Regressão logística	>10%	RC
84	Transversal	Regressão de Poisson	<10%	
90	Transversal	Regressão logística	>10%	RC
92	Transversal	Regressão logística	>10%	RC
93	Caso-controle	Regressão logística		

100	Transversal	Regressão logística	<10%	RC
104	Coorte	Regressão logística	>10%	RC
105	Transversal	Regressão de Poisson	>10%	
106	Transversal	Regressão logística	>10%	RR
107	Transversal	Regressão logística	>10%	RC
109	Transversal	Regressão de Poisson	<10%	
110	Transversal	Regressão logística	>10%	RC
115	Transversal	Regressão logística	>10%	RC

Ciência e Saúde Coletiva – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
1	Transversal	Regressão logística	>10%	RC
8	Transversal	Regressão logística	>10%	RC

International Journal of Epidemiology – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
1	Coorte	Regressão logística	<10%	RC
3	Caso-controle	Regressão logística		
4	Transversal	Regressão logística	<10%	RC
6	Transversal	Regressão logística	>10%	RC
7	Tranversal	Regressão logística	>10%	RC
9	Caso-controle	Regressão logística		
15	Coorte	Regressão logística	>10%	RC
19	Coorte	Regressão logística	>10%	RC
23	Transversal	Regressão logística	>10%	RC
24	Transversal	Regressão logística	<10%	RR
26	Coorte	Regressão logística	>10%	RC
27	Coorte	Regressão logística	>10%	RR
34	Coorte	Mantel- Haenszel	>10%	
35	Transversal	Regressão logística	>10%	RC
36	Coorte	Regressão logística	>10%	RR
39	Coorte	Regressão logística	<10%	RC
43	Coorte	Regressão logística	>10%	RC
45	Coorte	Regressão logística	>10%	RR
47	Transversal	Regressão logística	<10%	RR
48	Caso controle	Regressão logística		
49	Caso controle	Regressão logística		
52	Transversal	Regressão logística	>10%	RC

Journal of Clinical Epidemiology – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
4	Transversal	Regressão logística	>10%	RC
6	Coorte	Regressão logística	>10%	RC
7	Trasnversal	Regressão logística	>10%	RC
9	Coorte	Regressão logística	<10%	RC
10	Caso-controle	Regressão logística		
11	Transversal	Regressão logística	>10%	RC
12	Transversal	Regressão logística	>10%	RC
13	Transversal	Regressão logística	>10%	RC
14	Caso controle	Regressão logística		
15	Coorte	Regressão logística	>10%	RC
18	Caso-controle	Regressão logística		
22	Transversal	Regressão logística	>10%	RC
23	Coorte	Regressão logística	>10%	RC
24	Coorte	Regressão de Poisson	<10%	
25	Coorte	Regressão logística	>10%	RC
28	Transversal	Regressão logística	>10%	
29	Coorte	Regressão logística	>10%	RR
30	Coorte	Regressão logística	>10%	RC
31	Transversal	Regressão logística	<10%	RC
32	Transversal	Regressão logística	>10%	RC
36	Transversal	Regressão logística	>10%	RC

40	Coorte	Regressão logística	>10%	RR
41	Coorte	Regressão logística	>10%	RC
48	Coorte	Regressão logística	>10%	RC
49	Caso-controle	-		
50	Transversal	Regressão logística	>10%	RC
52	Coorte	Regressão logística	<10%	RR
54	Coorte	Regressão logística	>10%	RC
55	Coorte	Regressão logística	<10%	RR

Lancet – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
3	Coorte	Regressão logística	>10%	RC
17	Coorte	Regressão logística	<10%	RR
20	Coorte	Regressão logística	>10%	RC
23	Coorte	Regressão logística	>10%	RR
25	Coorte	Regressão logística	>10%	RC
28	Transversal	Regressão logística	<10%	RR
29	Transversal	Regressão logística	>10%	RC
31	Coorte	Regressão logística	>10%	RC
34	Coorte	Regressão log-binomial	<10%	
42	Caso-controle	Regressão logística		
47	Coorte	Regressão logística	<10%	RR
53	Coorte	Regressão de Poisson	>10%	
55	Coorte	Regressão logística	>10%	RC
56	Caso-controle	Regressão logística		
61	Coorte	Regressão logística	>10%	RC
64	Coorte	Regressão logística	>10%	RC
68	Coorte	Regressão logística	<10%	RC
72	Coorte	Regressão logística	<10%	RC
76	Coorte	Regressão logística	>10%	RR
78	Coorte	Regressão logística	>10%	RC
79	Coorte	Regressão logística	>10%	RC
82	Caso-controle	Regressão logística	Caso-controle	

New England of Medicine – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
1	Coorte	Regressão logística	<10%	RC
2	Coorte	Regressão logística	>10%	RC
3	Coorte	Regressão logística	>10%	RC
7	Coorte	Regressão logística	>10%	RC
10	Coorte	Regressão logística	>10%	RC
14	Coorte	Regressão logística	>10%	RC
16	Coorte	Regressão logística	>10%	RC
19	Caso-controle	Regressão logística		
21	Coorte	log binomial regression	<10%	
26	Caso-controle	Regressão logística		
27	Coorte	Regressão logística	>10%	RC
28	Coorte	Regressão logística	>10%	RC
32	Coorte	Regressão logística	>10%	RR
37	Coorte	Zhang & Yu	>10%	
41	Coorte	Regressão logística	>10%	RR
46	Caso-controle	Regressão logística		
47	Caso-controle	Mantel–Haenszel		
48	Coorte	Regressão logística	>10%	RC
50	Coorte	Regressão logística	>10%	RC
53	Caso-controle	Regressão logística		
54	Caso-controle	Regressão logística		
55	Coorte	Regressão logística	>10%	RC
61	Transversal	Regressão logística	>10%	RC
62	Coorte	Regressão logística	>10%	RC
66	Caso-controle	Regressão logística		
68	Coorte	Regressão de Poisson	<10%	
69	Coorte	Regressão logística	>10%	RR
70	Transversal	Regressão logística	>10%	RC
71	Coorte	Regressão de Poisson	<10%	

72	Caso-controle	-		
74	Caso-controle	Regressão logística	<10%	
77	Transversal	Regressão logística	>10%	RC
80	Coorte	Regressão logística	>10%	RC
83	Coorte	Regressão de Poisson	>10%	
91	Coorte	Mantel–Haenszel	>10%	
93	Caso-controle	Regressão logística		
94	Coorte	Regressão de Poisson	<10%	
98	Caso-controle	Regressão logística		

Revista de Saúde Pública – Ano: 2007

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
5	Transversal	Regressão logística	>10%	RC
6	Coorte	Regressão logística	>10%	RC
8	Coorte	Reg. de Poisson var. robusta	>10%	
10	Transversal	Regressão de Poisson	>10%	
11	Transversal	Regressão logística	>10%	RC
13	Transversal	Regressão logística	>10%	RC
14	Transversal	Regressão logística	>10%	RC
15	Coorte	Regressão de Poisson	>10%	
16	Transversal	Regressão de Poisson	>10%	
17	Transversal	Regressão logística	>10%	RC
18	Transversal	Regressão logística	>10%	RC
20	Transversal	Regressão logística	>10%	RR
23	Coorte	Regressão logística	<10%	RR
24	Transversal	Regressão logística	>10%	RR
25	Transversal	Regressão logística	>10%	RC
28	Transversal	Reg. de Poisson var. robusta	>10%	
29	Transversal	Regressão logística	>10%	RC
30	Transversal	Regressão logística	<10%	RC
33	Caso controle	Regressão logística		
34	Transversal	Regressão de Poisson	>10%	
35	Transversal	Regressão de Poisson	>10%	
36	Transversal	Regressão de Poisson	>10%	
37	Transversal	Regressão de Poisson	>10%	
39	Transversal	Regressão logística	>10%	RC
40	Transversal	Regressão logística	<10%	RC
42	Caso controle	Regressão logística		
43	Transversal	Regressão logística	>10%	RC
47	Transversal	Regressão de Poisson	>10%	
49	Caso controle	Regressão logística		
51	Caso controle	Regressão logística		
52	Coorte	Reg. de Poisson var. robusta	<10%	
53	Transversal	Regressão logística	>10%	RR

American Journal of Epidemiology – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
3	Coorte	Regressão logística	>10%	RC
6	Caso-controle	Regressão logística		
8	Caso-controle	Regressão logística		
9	Caso-controle	Regressão logística		
10	Caso-controle	Regressão logística		
12	Transversal	Regressão logística	>10%	RC
13	Caso-controle	Regressão logística		
16	Transversal	Regressão logística	>10%	RC
18	Transversal	Regressão logística	>10%	RC
23	Caso-controle	Regressão logística		
24	Caso-controle	Regressão logística		
26	Caso-controle	Regressão logística		
28	Coorte	Regressão logística	>10%	RC
32	Coorte	Regressão de Poisson	<10%	
34	Caso-controle	Regressão logística		
35	Coorte	Regressão logística	>10%	RC
38	Caso-controle	Regressão logística		

40	Caso-controle	-		
44	Caso-controle	Regressão logística		
45	Caso-controle	Regressão logística		
47	Coorte	Regressão logística	<10%	RC
48	Caso-controle	Regressão logística		
49	Caso-controle	Regressão logística		
51	Coorte	Regressão logística	>10%	RC
55	Caso-controle	Regressão logística		
59	Coorte	Regressão logística	>10%	RC
60	Caso-controle	Regressão logística		
66	Coorte	Regressão logística	<10%	RR
67	Caso-controle	Regressão logística		
70	Transversal	Regressão logística	>10%	RC
71	Coorte	Regressão logística	<10%	RR
72	Caso-controle	Regressão logística		
74	Caso-controle	Regressão logística		
76	Caso-controle	Regressão logística		
80	Coorte	Regressão logística	>10%	RC
83	Caso-controle	Regressão logística		
85	Caso-controle	-		
86	Coorte	Regressão de Poisson	>10%	
89	Caso-controle	Regressão logística		
90	Caso-controle	Regressão logística		
93	Coorte	Regressão logística	>10%	RR
95	Coorte	Regressão logística	>10%	RC
96	Coorte	Regressão logística	<10%	RC
97	Coorte	Regressão logística	>10%	RR
100	Coorte	Regressão log- binomial	>10%	
101	Caso-controle			
102	Transversal	Regressão de Poisson	>10%	
106	Coorte	Regressão logística	<10%	RC
110	Caso-controle			
111	Caso-controle			
113	Caso-controle	Regressão logística		
114	Caso-controle	Regressão logística		
115	Caso-controle	Regressão logística		
116	Caso-controle	Regressão logística		
120	Coorte	Regressão log-binomial	>10%	
121	Coorte	Regressão logística	<10%	RC
123	Transversal	Regressão logística	>10%	RC
124	Transversal	Regressão logística	>10%	RC
126	Caso-controle			
128	Coorte	Regressão logística	>10%	RC
131	Caso-controle			
133	Caso-controle			
134	Coorte	Regressão logística	<10%	RC
135	Caso-controle			
136	Transversal	Regressão logística	>10%	RC
141	Caso-controle			
143	Coorte	Regressão logística	>10%	RC
145	Caso-controle			
146	Caso-controle			
147	Transversal	Regressão logística	>10%	RC
157	Coorte	Regressão logística	>10%	RC
160	Coorte	Regressão binomial	>10%	
165	Caso-controle	Regressão logística		
166	Transversal	Regressão logística	>10%	RC
168	Caso-controle	Regressão logística		
170	Coorte	Regressão logística	>10%	RC
171	Transversal	Regressão logística	<10%	RR
173	Transversal	Regressão logística	<10%	RC
174	Caso-controle	Regressão logística		
175	Transversal	Regressão logística	>10%	RC
176	Coorte	Regressão logística	<10%	RC
178	Transversal	Regressão logística	>10%	RC
179	Caso-controle	Regressão logística		
180	Coorte	Regressão de Poisson	>10%	
181	Caso-controle	Regressão logística		
182	Caso-controle	Regressão logística		

183	Caso-controle	Regressão logística		
184	Transversal	Regressão Logística	>10%	RC
185	Caso-controle	Regressão logística		
186	Caso-controle	Regressão logística		
187	Transversal	Regressão logística	<10%	RC
189	Caso-controle	Regressão logística		
192	Coorte	Regressão log-binomial	<10%	
193	Caso-controle	Regressão logística		
194	Transversal	Regressão logística	>10%	RC
195	Coorte	Regressão logística	<10%	RC
196	Caso-controle			
197	Transversal	Regressão logística	<10%	RC
199	Coorte	Regressão de Poisson	>10%	
200	Coorte	Regressão logística	<10%	RC
202	Transversal	Regressão logística	>10%	RC
203	Caso-controle			
205	Transversal	Regressão logística	> 10%	RC
206	Coorte	Regressão logística	<10%	RC
207	Caso-controle	Regressão logística		
209	Caso-controle	Regressão logística		
213	Coorte	Regressão logística	>10%	RC
214	Caso-controle	Regressão logística		
215	Caso-controle	Regressão logística		
216	Coorte	Regressão de Poisson	>10%	
217	Caso-controle			
218	Caso-controle			
220	Coorte	Regressão logística	<10%	RC
221	Coorte	Regressão logística	>10%	RC
224	Coorte	Regressão logística	>10%	RC
226	Caso-controle	Regressão logística		
227	Transversal	Regressão logística	>10%	RC
228	Caso-controle			

Brazilian Journal of medical and Biological – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
6	Transversal	Regressão logística	>10%	RC
7	Transversal	Regressão logística	>10%	RC
13	Coorte	Regressão logística	>10%	RC
15	Transversal	Regressão de Poisson	>10%	

British Medical Journal – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
3	Coorte	Regressão logística	>10%	RC
4	Caso-controle	Regressão logística		
8	Coorte	Regressão de Poisson	>10%	
10	Coorte	Regressão Logística	>10%	RC
22	Coorte	Regressão logística	>10%	RC
23	Coorte	reg log binomial	>10%	
24	Coorte	Regressão de Poisson	<10%	
27	Coorte	Regressão logística	>10%	RC e RR
32	Transversal	Regressão logística	>10%	RC
34	Coorte	Regressão logística	<10%	RC
41	Coorte	Regressão logística	>10%	RC
42	Coorte	Zhang e Yu	>10%	
51	Coorte	Regressão de Poisson	>10%	
52	Coorte	Regressão logística	>10%	RC
55	Transversal	Regressão logística	<10%	RC
56	Coorte	Regressão logística	>10%	RC
69	Transversal	Regressão logística	<10%	RR
73	Caso-controle	Regressão logística		
74	Coorte	Regressão logística	>10%	RC
77	Coorte	Regr de Poisson var. robusta	>10%	
80	Coorte	Regressão logística	<10%	RR
81	Coorte	Mantel Haenszel	>10%	RC

84	Coorte	Regressão logística	<10%	RC
85	Coorte	Reg. Logística e Poisson	>10%	RC
88	Coorte	Regressão logística	<10%	RR e RC
92	Caso-controle	Regressão logística		
93	Coorte	Regressão logística	>10%	RR
95	Coorte	Regressão de Poisson	>10%	
98	Coorte	Regressão logística	>10%	RC
99	Coorte	Regressão logística	>10%	RC
100	Coorte	Regressão logística	>10%	RC
101	Coorte	Regressão logística	<10%	RR
106	Coorte	Regressão logística	>10%	RC
109	Coorte	Regressão logística	>10%	RC
113	Coorte	Reg. Logística e Poisson	>10%	RC
114	Coorte	Regressão logística	<10%	RR

Cadernos de Saúde Pública – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
5	Transversal	Reg. de Poisson var. robusta	>10%	
8	Transversal	Regressão logística	>10%	RC
10	Transversal	Regressão de Poisson	>10%	
13	Transversal	Reg. de Poisson var. robusta	>10%	
14	Caso-controle	Regressão logística		
16	Transversal	Regressão de Poisson	>10%	
17	Transversal	Regressão logística	>10%	RC
18	Transversal	Regressão de Poisson	>10%	
21	Transversal	Reg. de Poisson var. robusta	>10%	
22	Transversal	Regressão de Poisson	>10%	
24	Transversal	Regressão logística	<10%	RC
25	Transversal	Regressão logística	>10%	RR
27	Transversal	Regressão logística	-	
28	Coorte	Reg. de Poisson var. robusta	>10%	
35	Transversal	Regressão de Poisson	>10%	
45	Coorte	Regressão de Poisson	>10%	
54	Transversal	Regressão logística	>10%	RC
55	Transversal	Regressão de Poisson	>10%	
58	Transversal	Regressão de Poisson	>10%	
59	Transversal	Regressão de Poisson	<10%	
60	Transversal	Regressão logística	>10%	RC
62	Transversal	Regressão de Poisson	<10%	
63	Transversal	Reg. de Poisson var. robusta	>10%	
64	Transversal	Reg. de Poisson var. robusta	>10%	
65	Transversal	Regressão logística	>10%	RC
67	Transversal	Regressão logística	<10%	RC
69	Transversal	Regressão logística	>10%	RC
71	Transversal	Regressão logística	<10%	RC
73	Transversal	Regressão logística	>10%	RC
76	Transversal	Regressão logística	>10%	
79	Transversal	Regressão logística	>10%	RR
81	Transversal	Regressão Log binomial	>10%	
83	Transversal	Regressão de Poisson	>10%	
85	Coorte	Reg. de Poisson var. robusta	>10%	
88	Transversal	Regressão de Poisson	>10%	
90	Transversal	Regressão logística	<10%	RC
92	Transversal	Regressão logística	>10%	RC
93	Transversal	Regressão logística	<10%	RC
94	Transversal	Regressão de Poisson	>10%	
97	Transversal	Regressão logística	>10%	RC
99	Transversal	Reg. de Poisson var. robusta	>10%	
101	Caso-controle	Regressão logística		
102	Transversal	Regressão logística	>10%	RC
104	Caso-controle	Regressão logística		
106	Transversal	Regressão logística	<10%	RC
107	Transversal	Regressão logística	>10%	RC
108	Transversal	Regressão de Poisson	>10%	
110	Transversal	Regressão logística	>10%	RC
113	Transversal	Regressão logística	>10%	RC
115	Transversal	Regressão logística	<10%	RC

117	Transversal	Regressão logística	<10%	RC
119	Transversal	Regressão de Poisson	>10%	
121	Transversal	Regressão de Poisson	>10%	
123	Caso-controle	Regressão logística		
124	Transversal	Regressão logística	>10%	RC
126	Transversal	Reg. de Poisson var. robusta	>10%	
127	Transversal	Regressão logística	>10%	RC
129	Transversal	Regressão de Poisson	>10%	

Ciência e Saúde Coletiva – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
8	Coorte	Regressão logística	<10%	RC
9	Transversal	Regressão logística	>10%	RC
18	Transversal	Regressão logística	>10%	RC

International Journal of Epidemiology – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
1	Coorte	Regressão logística	<10%	RR
9	Caso-controle	Regressão logística		
11	Transversal	Regressão de Poisson	<10%	
12	Transversal	Regressão logística	<10%	RC
13	Caso-controle	Regressão logística		
14	Transversal	Regressão logística	>10%	RC
18	Caso-controle	Regressão logística		
19	Caso-controle	Regressão logística		
20	Transversal	Regressão logística	>10%	RC
23	Transversal	Regressão logística	<10%	RC
26	Coorte	Regressão logística	<10%	RC
27	Transversal	Regressão logística	<10%	RC
28	Coorte	Regressão logística	>10%	RC
31	Coorte	Regressão Log binomial	>10%	
32	Caso-controle	Regressão logística		
33	Coorte	Regressão logística	<10%	RC
36	Caso-controle	Regressão logística		
37	Transversal	Regressão logística	>10%	RC
39	Transversal	Regressão de Poisson	>10%	
41	Coorte	Reg. de Poisson var. robusta	>10%	
46	Transversal	Regressão logística	>10%	RC
48	Transversal	Reg. de Poisson var. robusta	>10%	
50	Transversal	Regressão logística	>10%	RR
55	Transversal	Regressão logística	>10%	RC
59	Coorte	Regressão logística	>10%	RR
62	Caso-controle	Regressão logística		
67	Caso-controle	Regressão logística		
69	Coorte	Regressão logística	>10%	RC
71	Transversal	Regressão logística	>10%	RC
77	Transversal	Regressão logística	>10%	RC

Journal of Clinical Epidemiology – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
2	Transversal	Regressão logística	>10%	RC
5	Transversal	Regressão logística	<10%	RC
6	Coorte	Regressão logística	>10%	RC
7	Transversal	Regressão logística	>10%	RC
9	Transversal	Regressão logística	<10%	RC
10	Transversal	Regressão logística	<10%	RC
12	Coorte	Regressão logística	<10%	RC
15	Coorte	Regressão logística	>10%	RC
17	Transversal	Regressão log binomial	>10%	
18	Transversal	Regressão logística	>10%	RR
20	Coorte	Regressão logística	<10%	RR
21	Caso-controle	Regressão logística		
23	Transversal	Regressão logística	>10%	RC
24	Coorte	Regressão logística	<10%	RR

28	Coorte	Regressão logística	>10%	RC
29	Transversal	Regressão logística	>10%	RC
31	Coorte	Regressão logística	>10%	RC
32	Coorte	Regressão logística	>10%	RR

Lancet – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
10	Coorte	Regressão logística	>10%	RC
17	Caso-controle	Regressão logística		
23	Coorte ou Transversal	Regressão logística	>10%	RR
24	Coorte	Regressão logística	>10%	RC
25	Coorte	Regressão logística	>10%	RC
26	Coorte	Regressão logística	>10%	RC
28	Coorte	Regressão logística	>10%	RC
33	Coorte	Mantel-Haenzel	>10%	
34	Transversal	Regressão logística	>10%	RC
35	Coorte	Regressão logística	<10%	RR
38	Caso-controle	Regressão logística		
39	Coorte	Regressão logística	<10%	RC
41	Transversal	Regressão de Poisson	>10%	
44	Coorte	reg log binomial	>10%	
45	Caso-controle	Regressão logística		
47	Coorte	Regressão logística	>10%	RC
48	Coorte	Regressão logística	>10%	RC
63	Transversal	Regressão de Poisson	>10%	
64	Coorte	Regressão logística	>10%	RC
67	Coorte	Regressão logística	<10%	RC
71	Transversal	Regressão logística	>10%	RC
72	Coorte	Regressão de Poisson	<10%	
75	Coorte	Regressão logística	>10%	RC
80	Coorte	Regressão logística	>10%	RC
82	Coorte	Regressão logística	>10%	RR
87	Coorte	Regressão logística	<10%	RC
89	Coorte	Regressão logística	<10%	RC
92	Coorte	Regressão logística	<10%	RR
93	Coorte	Regressão logística	<10%	RC
94	Coorte	Regressão logística	<10%	RC

New England of Medicine – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
4	Coorte	Regressão logística	>10%	RC
5	Coorte	Regressão logística	<10%	RC
6	Coorte	Regressão logística	<10%	RC
7	Transversal	Regressão logística	>10%	RC
8	Coorte	Reg. de Poisson var. robusta	>10%	
9	Caso-controle	Regressão logística		
10	Caso-controle	Regressão logística		
11	Transversal	Regressão logística	>10%	RC
12	Transversal	Regressão logística	>10%	RC
13	Coorte	Regressão logística	>10%	RC
14	Coorte	Regressão logística	>10%	RC
22	Coorte	Log-binomial	>10%	
28	Caso-controle	Regressão logística		
29	Coorte	Regressão logística	>10%	RC
30	Caso-controle	Regressão logística		
34	Coorte	Regressão logística	<10%	RC
35	Transversal	Regressão logística	>10%	RC
42	Coorte	Regressão logística	>10%	RC
44	Coorte	Regressão logística	>10%	RR
46	Coorte	Regressão logística	>10%	RC
47	Coorte	Regressão logística	<10%	RC
49	Transversal	Regressão logística	<10%	RC
51	Caso-controle	Regressão logística		
53	Transversal	Regressão logística	<10%	RC
55	Coorte	Regressão logística	>10%	RC

60	Transversal	Regressão logística	<10%	RC
61	Coorte	Correção de Zhang e Yu	>10%	
64	Coorte	Regressão logística	>10%	RC
66	Caso-controle	Regressão logística		
70	Caso-controle	Regressão logística		
71	Transversal	Regressão logística	>10%	RC
72	Coorte	Regressão logística	<10%	RR
73	Caso-controle	Regressão logística		
74	Caso-controle	Regressão logística		
76	Caso-controle	Regressão logística		
77	Coorte	Regressão logística	>10%	RR
78	Transversal	Regressão logística	>10%	RR
80	Transversal	Regressão logística	<10%	RC
83	Caso-controle	Regressão logística		
84	Caso-controle	Regressão logística		
89	Coorte	Regressão logística	>10%	RC

Revista de Saúde Pública – Ano: 2008

Nº	Delineamento	Técnica	Prev/Inc	Interpretação
1	Coorte	Regressão de Poisson	<10%	
2	Coorte	Regressão de Poisson	>10%	
3	Coorte	Regressão de Poisson	>10%	
4	Coorte	Regressão de Poisson	>10%	
5	Coorte	Regressão de Poisson	<10%	
6	Coorte	Regressão de Poisson	>10%	
8	Coorte	Regressão de Poisson	>10%	
10	Transversal	Regressão de Poisson	>10%	
13	Transversal	Regressão de Poisson	>10%	
14	Transversal	Regressão de Poisson	>10%	
15	Transversal	Regressão logística	>10%	RC
17	Transversal	Regressão logística	>10%	RC
18	Transversal	Regressão logística	>10%	RC
23	Transversal	Regressão logística	>10%	RC
24	Transversal	Regressão logística	>10%	RC
28	Transversal	Regressão logística	<10%	RR
29	Coorte	Regressão de Poisson	>10%	
30	Transversal	Regressão logística	>10%	RC
31	Transversal	Regressão logística	<10%	RR
33	Transversal	Regressão logística	>10%	RC
35	Transversal	Regressão logística	>10%	RC
36	Transversal	Regressão logística	>10%	RC
39	Caso-controle	Regressão logística		
40	Caso-controle	Regressão logística		
42	Caso-controle	Regressão logística		
43	Transversal	Regressão logística	<10%	RC
44	Transversal	Regressão logística	>10%	RC
46	Transversal	Regressão logística	>10%	RC
47	Transversal	Regressão logística	>10%	RC
51	Caso-controle	Regressão logística		
53	Transversal	Regressão de Poisson	>10%	
54	Transversal	Regressão logística	>10%	RC
55	Transversal	Regressão logística	>10%	RC
58	Transversal	Regressão logística	>10%	RC
59	Transversal	Regressão logística	>10%	RC
60	Transversal	Regressão logística	>10%	RC
61	Transversal	Regressão logística	>10%	RC
62	Transversal	Regressão de Poisson	>10%	
65	Transversal	Regressão logística	>10%	RC
66	Transversal	Regressão logística	>10%	RC
67	Transversal	Regressão logística	<10%	RC
68	Transversal	Reg. de Poisson var. robusta	>10%	
69	Coorte	Regressão logística	>10%	RC
70	Coorte	Regressão logística	>10%	RC

ANEXO 4 - PROJETO DE PESQUISA

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL

FACULDADE DE MEDICINA

PROGRAMA DE PÓS-GRADUAÇÃO EM EPIDEMIOLOGIA

PROJETO DE PESQUISA

UTILIZAÇÃO DOS MODELOS DE REGRESSÃO PARA ESTIMAÇÃO DE RISCO RELATIVO E RAZÃO DE PREVALÊNCIA COM DESFECHO BINÁRIO

Aluno: Cecília de Leão Martins Papaléo

Orientador: Prof. Dr. Álvaro Vigo

Porto Alegre, setembro 2007

1. INTRODUÇÃO

Muitas pesquisas epidemiológicas têm como objetivo central identificar uma possível associação entre variáveis para compreender e concluir sobre a presença ou desenvolvimento de doenças, tratamentos e afins. Porém as medidas de associação adequadas variam de acordo com o delineamento do estudo. Quando temos um desfecho binário, em estudos com o delineamento caso-controle, a medida de associação entre as variáveis é obtida pelo odds ratio (OR). Já estudos com delineamento transversal a associação entre um desfecho dicotômico e os preditores é classicamente descrita pela razão de prevalência (RP). Similarmente, em estudos de coorte, a medida de interesse é, geralmente, o risco relativo (RR). Para eventos raros o RR ou a RP podem ser estimados pelo OR através do modelo de regressão logística (Barros e Hirakata, 2003; McNutt *et al*,2003; Schiaffino *et al*, 2003; Zhang & Yu, 1998). Para eventos comuns (usualmente > 10%), não se recomenda a estimação desses parâmetros da mesma forma, pois o modelo logístico tende a superestimar ou subestimar razão de prevalências e risco relativo Barros e Hirakata, 2003; Schiaffino *et al*, 2003; Greenland, 2004). Contudo, e apesar das facilidades computacionais atuais, muitos trabalhos continuam sendo analisados (e publicados) utilizando a razão de chances como medida de associação, mesmo quando o desfecho é comum.

Para estimar RR ou RP no caso do evento ser comum alguns modelos são sugeridos que permitem associar diretamente, e sem viés, as medidas entre os preditores e o desfecho dicotômico.

1.1 Métodos de estimação de medidas de associação

Muitos métodos de estimação de medidas de associação têm sido discutidos na literatura para a análise de desfechos binários em estudos transversais ou de coorte. Há métodos estatísticos que estimam diretamente a RP ou RR e seus intervalos de confiança, tais como: conversão de OR em RR proposta por Zhang & Yu, regressão de Poisson, regressão de Poisson modificada, modelo log-binomial e procedimento de Mantel-Haenszel. Mais importante do que a estimativa pontual, é importante também considerar a precisão dos estimadores do RR ou RP, produzindo intervalos de confianças com maior amplitude, dependendo do modelo usado(Greenland, 2004; Zocchetti *et al*, 1997; Zou, 2004).

O modelo que Zhang & Yu (1998) propuseram para estimar RR ou RP para desfecho dicotômico é uma fórmula que converte o OR obtido pela regressão logística em RR ou RP. Um problema que ocorre ao fazer essa conversão, é que esse modelo produz estimativas inconsistentes, comprovado em estudos de simulação McNutt *et al*, 2003).

Na situação em que o desfecho é comum a razão de prevalência ou o risco relativo podem ser estimados pelo modelo de regressão de Poisson

(Barros e Hirakata, 2003; Zou, 2004). As medidas de RR e RP podem ser estimadas diretamente pelos coeficientes de regressão do modelo. O modelo de regressão considera uma função de ligação log para modelar o risco de certo indivíduo apresentar o desfecho. Para definir o modelo, considere um desfecho binário Y e um fator um fator de exposição dicotômico x genericamente representado pelos valores 1 (expostos) e 0 (não expostos). Para cada indivíduo da amostra, $P\left(Y=1 \mid \underset{\sim}{x}\right)$ representa a probabilidade do desfecho assumir o valor 1, condicional a exposição $x_i = 0$ ou 1. Assim, o modelo especifica que

$$\log\left(P\left(Y=1 \mid \underset{\sim}{x}\right)\right) = \beta_0 + \beta_1 x_1 + ... + \beta_k x_k ,$$

tal que o logaritmo natural do coeficiente de regressão do modelo é igual ao risco relativo (Zou, 2004).

Porém, a regressão de Poisson produz um intervalo de confiança para a estimativa pontual do RR grande, quando comparado com o modelo log-binomial, por exemplo. Isso se deve ao fato dos erros seguirem uma distribuição Poisson, que acabam por superestimar os erros do modelo log-binomial, onde os erros seguem uma distribuição binomial, quando o desfecho é comum.

Para obter maior precisão nas estimativas de RP ou RR o modelo de regressão de Poisson modificada utiliza um estimador robusto (estimador de Sanduíche) para as variâncias no qual a probabilidade da função log de verossimilhança da distribuição de Poisson é derivada e as variâncias estimadas do RR estimado sofrem uma adaptação para dados que possuam distribuição binomial (Zou, 2004).

Outra alternativa para estimar o RR quando o evento é comum é o modelo log-binomial, que utiliza o mesmo modelo da regressão logística, que relaciona a variável de desfecho com as covariáveis, porém, a função de ligação é diferente: logit para regressão logística e log para regressão log-binomial (Barros e Hirakata, 2003; McNutt *et al*,2003; Schiaffino *et al*, 2003).

O modelo é definido por:

$$\log\left(P\left(Y=1 \mid \underset{\sim}{x}\right)\right)=\beta_0+\beta_1 x_1+...+\beta_k x_k$$

onde $P\left(Y=1 \mid \underset{\sim}{x}\right)$ é a proporção de indivíduos com o evento e $\underset{\sim}{x}$ são as covariáveis. O risco relativo é obtido pela e^{β_i}, ou seja, pela exponencial do valor beta da expressão.

A distribuição da proporção e dos erros segue uma distribuição Binomial (Barros e Hirakata, 2003; Schiaffino *et al*, 2003).

O modelo é definido somente se $\beta_0+\beta_1+...+\beta_k<0$, para assegurar que a estimação da proporção esteja entre 0 e 1 (Skov *et al*, 1998). A estimativa do RR não é viciada, mas o intervalo de confiança pode ser enviesado, produzindo intervalos de confiança mais estreitos. Além disso, problemas de convergência podem ser encontrados quando o evento do desfecho for alto ou as covariáveis forem contínuas ou politômicas (Barros e Hirakata, 2003).

2. OBJETIVOS

2.1 Objetivo Geral:

O objetivo geral desse trabalho é verificar a aplicação de modelos estatísticos, que estimam risco relativo ou razão de prevalência com desfecho binário considerado comum, utilizados em publicações de revistas da área epidemiológica.

2.2 Objetivo Específico:

Realizar uma revisão de literatura sobre a metodologia de modelos adequados para eventos comuns (precedimento de Mantel-haenszel, correção de Zhang & Yu, regressão de Poisson, Poisson modificada e log-binomial e suas possíveis discrepâncias (magnitude, viés, precisão).

3. MÉTODOS

Será realizada uma revisão de publicações em revistas da área epidemiológica e clínica geral dos artigos publicados no ano de 2007 e 2008.

A busca dos artigos será realizada através da base de dados bibliográficos PUBMED (Serviço de pesquisa da National Library of Medicine (NLM)), onde haverá critérios de seleção dos artigos. Será criada de uma sintaxe com operadores boleanos e limitadores, por exemplo, nomes de revistas, ano e palavras-chaves, para selecionar os artigos do interesse específico. A busca será feita pelo resumo dos artigos e não pelo texto completo. Todos os resumos estão escritos em inglês, independente da nacionalidade da revista e do artigo.

O registro das informações dos artigos será disposto em uma tabela (anexo 1) onde conterão informações relevantes quanto à revista, número total de artigos selecionados no ano de 2007, métodos de estimação da medida de associação e números de artigos que aplicaram regressão logística quando a prevalência ou incidência do desfecho for maior que 10%. A descrição geral de cada artigo que usou algum método para estimar alguma medida de associação será disposta em uma tabela (anexo 2) onde detalhes dos estudos serão descritos.

4. CRONOGRAMA

	2008				2009		
	1°Trim.	**2º Trim.**	**3º Trim.**	**4º Trim.**	**1°Trim.**	**2°Trim.**	**3°Trim.**
Revisão da literatura							
Defesa do projeto							
Redação da dissertação							
Revisão dos artigos							
Defesa preliminar							
Sessão pública							

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