

Running title: spillover effects of maternal chronic disease

Spillover effects of maternal chronic disease on children's quality of life and behaviors among low-income families

Authors: Vivian YW Guo ¹, Carlos KH Wong ¹ (ORCID: 0000-0002-6895-6071), Rosa SM Wong ^{1,2}, Esther YT Yu ¹, Patrick Ip ², (ORCID: 0000-0002-6797-6898), Cindy LK Lam ¹

¹ Department of Family Medicine and Primary Care, The University of Hong Kong

² Department of Paediatrics and Adolescent Medicine, The University of Hong Kong

Address for Correspondence:

Dr Carlos KH Wong

Department of Family Medicine and Primary Care, The University of Hong Kong

Rm 1-01, 1/F, Jockey Club Building for Interdisciplinary Research, 5 Sassoon Road, Pokfulam, Hong Kong

Tel.: (852) 28315055, Fax No.: (852) 28147475, Email: carlosheo@hku.hk

Running title: spillover effects of maternal chronic disease

Abstract

Background

Mothers with chronic diseases may have spillover effects on their children.

Objective

The aim of this study was to estimate the spillover effects of mothers with chronic disease on their children's health-related quality of life (HRQOL) and behavior.

Method

A cross-sectional study was conducted on 255 mother-child pairs (130 boys and 125 girls, mean age 8.4) from Chinese low-income families. We asked the mothers to self-report any doctor-diagnosed chronic diseases, and evaluate their children's HRQOL and behaviors with the Child Health Questionnaire-Parent Form-50 (CHQ-PF50) and the Strengths and Difficulties Questionnaire (SDQ), respectively. Multiple linear regression analysis was conducted to assess the independent spillover effect of maternal chronic disease on children's HRQOL and behaviors with adjustment for confounders. Differential impact of maternal physical and mental diseases was also investigated.

Results

Over one-third mothers (n=88, 34.5%) reported one or more doctor-diagnosed chronic disease. Multiple linear regression analysis showed that children of mothers with chronic diseases had significantly lower CHQ-PF50 scores in the parental impact-time, parental impact-emotional, and family activities subscales and psychosocial summary scores, as well as more hyperactive and inattentive problems measured by SDQ after adjustment for confounders. Maternal mental and physical disease showed differential impact on their children's HRQOL and behavior.

Conclusions

Chronic disease in mothers might exert adverse effect on their children's HRQOL and behaviors. The effects could differ by maternal physical or mental disease status. Special attention and support should be paid to children of mothers with chronic disease, as these children are at an increased risk of poor HRQOL and problematic behaviors.

Key Points for Decision Makers

Chronic disease in mothers might exert spillover effect on their young children, leading to impaired health-related quality of life and problematic behaviors.

Special attention and support should be paid to children of mothers with chronic disease in order to improve their health-related quality of life and prevent problematic behaviors.

Health economic analysis might also include the spillover effect of non-caregivers, such as young dependent children, in order to avoid biased estimation and spurious recommendations.

Acknowledgements

We are most grateful to Kerry Group Kuok Foundation (Hong Kong) Limited (KGKF) for their funding support. We thank the Neighborhood Advice-Action Council (NAAC) and Yat Tung (I/II) Estate Property Management in providing venue for our study. A special thanks to Versitech Ltd for granting us a complementary license to use the OPine Software for data collection in our study. The timely completion of the telephone surveys by the HKU Social Science Research Center is much appreciated. The hard work of our research staff in data collection and analysis must be acknowledged. We thank Dr. Colman Fung for his input to study design and continual support to the study implementation.

Author Contributions

VG and CW developed the research question and methodology; VG conducted the statistical analysis; VG initiated the writing; CW critically reviewed the manuscript. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Compliance with Ethical Standards

Funding: This study was funded by Kerry Group Kuok Foundation (Hong Kong) Limited.

Conflict of Interest: Vivian YW Guo, Carlos KH Wong, Rosa SM Wong, Esther YT Yu, Patrick Ip, Cindy LK Lam each declare that they have no conflicts of interest in relation to the material reported in this manuscript.

Informed consent: Adult participants provided written consent for themselves, and parents or guardians provided written consent for children under the age of 18 years to participate in the study. Informed consent was obtained from all individual participants included in the study.

Manuscript Text

1 Introduction

Illness may not only impair the patient's health but also affect the well-being and health of the informal caregivers because of the considerable contribution of time, money and effort to take care of the patients (1-3). The adverse effect that the patient's acute or chronic disease imposes on the well-being, health, and health-related quality of life (HRQOL) of the informal caregivers is called spillover effect, which has been widely observed (1-4). A previous meta-analysis found that 34% of the informal caregivers of patients with Alzheimer's disease reported depression and around 44% reported anxiety because of caregiving (2). Another study showed that the informal caregivers with mental or emotional strain in the course of care for spouses with physical or mental health problems had 63% higher mortality risk than non-caregiving controls (3). In addition, the burden of caregiving may also cause stress that can impair the HRQOL of informal caregivers (5, 6). Spillover effect is even more severe in parents caregiving their ill children (7). Having a child with chronic disease was associated with greater spillover effect, e.g. mental illness and poor HRQOL, than having an ill spouse with the same condition (6-8), suggesting a need for research to examine spillover effect in the intergenerational context.

Apart from the impact on informal caregivers, the spillover effect might also impose great burden to other people who are emotionally connected or physically present to the patient, leading to impaired health, increased stress, and reduced HRQOL, even when the person is not involved in providing care to the patient (4, 5, 7, 9). It is therefore probable that children living with chronically ill parents might also be negatively affected as a result of spillover effect. Previous research found that around 4-15% of children had a parent with chronic disease (10, 11). These children are found to have an increased risk of psychological and behavioral problems compared to children with healthy parents (11-14). Furthermore, the needs and problems of these children might not be easily detected, addressed, and intervened in a timely manner when family and health care professionals give much of their time and attention to the ill parents. Studies also found that children of parents with chronic disease such as cancer had more internalizing problems (e.g. symptoms of depression, anxiety and stress) and externalizing problems (e.g. aggressive and rule-breaking behavior) than the general child population as well as their counterparts with healthy parents (12-15).

Spillover effects have drawn much attention in recent years, especially in health economic evaluations. This could be because interventions for patients might also improve their informal caregivers' HRQOL. Without considering the spillover effect, the benefits of a health intervention might be underestimated, leading to biased estimation and spurious recommendations in effectiveness and cost-effectiveness analyses (16-18). A previous systematic review confirmed that the inclusion of spillover effects in economic evaluation would increase the relative effectiveness of an intervention compared to the model without considering the spillover effect (4). More evidence has demonstrated the importance of inclusion of informal care in health economic evaluation (19, 20). Research on intergenerational transmission of health also suggested the possibility of parent-child spillover effect through a variety of intrapersonal, interpersonal, and communicative factors. For example, in a longitudinal study of 588 households, income was found to predict adults' use of health information and in turn influence their own self-efficacy and diet behavior and finally a child's diet behavior (21). The findings further highlight the strong link between parent and child outcomes.

Mothers, often considered as a primary caregiver of a child, have a high potential to exert spillover effect on their children. In particular, when they have chronic disease, impaired parenting as a result of poor health might aggravate health problems in children. Given the established association of poor health and financial hardship (22), the impact of maternal chronic disease could be more significant and severe among children in low-income families. Most of the current evidence on spillover effect examined children's emotional and behavioral outcomes and focused on adolescence (12-15, 23, 24), but the spillover effect of maternal chronic disease for young children, especially on their HRQOL, has been rarely discussed. Therefore, we used a cross-sectional study design to explore the spillover effect of maternal chronic diseases on children's HRQOL and behavior among Chinese low-income families. The potential variation in the spillover effect of maternal physical and mental disease on child outcomes was also investigated. We hypothesized that young children of mothers with chronic disease would have poorer HRQOL and more behavioral problems than those children of mothers without chronic disease.

2 Methods

2.1 Study sample

The study families from a community family support programme, funded by a philanthropic foundation in Hong Kong, were invited to participate in a research that evaluated the effect of health empowerment on

health and HRQOL of adults and their dependent children. The detailed study protocol had been published previously (25-28). In order to examine the impact of low family income on young children and their parents, the inclusion criteria for participation in the study were: (1) at least one family member had a part-time or full-time job; (2) at least one dependent child was studying in grade 1-3 (aged from 6 to 11 years) at the time of recruitment and (3) with a monthly household income less than 75% of the median monthly household income in Hong Kong at the time of recruitment.

Initially, a total of 425 eligible low-income families joined the community family support programme and were invited to take part in our prospective health empowerment research study. Among these invited families, 379 families (89.2%) agreed to join the study. For adult participants, written consent forms were provided by themselves. For children under 18 years of age, their parents or guardians signed the written consent form on behalf of the children. As previous studies and our data suggested that a child's intelligence quotient (IQ) is associated with his/her ability to adjust to negative situations that would have an effect on their HRQOL and behavior (26, 29-32), we retrieved the data of child IQ and included it as a covariate in the current study analyses. Of the 379 families with consent form, children from 291 families had the IQ assessment. The parents from 286 families have further completed one or both of the Child Health Questionnaire-Parent Form-50 (CHQ-PF50) (33, 34) and the Strengths and Difficulties Questionnaire (parent proxy—report version) (SDQ) (35, 36) as indicators of children's HRQOL and behavior, respectively. Furthermore, we excluded 31 families of father-child pairs. Therefore, the current study included 255 mother-child pairs from Chinese low-income families. Flowchart of the subject recruitment, inclusion and exclusion is outlined in Figure 1.

The ethics of this study was approved by the Institutional Review Board (IRB) of the University of Hong Kong—the Hospital Authority Hong Kong West Cluster, Reference number: UW 12-517.

2.2 Measurement

Mother reported their age, marital status and history of doctor-diagnosed chronic disease through questionnaire. Maternal chronic disease included hypertension, diabetes, hyperlipidemia, coronary heart disease, stroke, epilepsy, hepatitis B, gastric peptic ulcer, anaemia, asthma, musculoskeletal disease, cancer and mental disease (i.e. doctor-diagnosed depression and other psychiatric problems). Physical disease was defined as chronic disease excluding those with mental disease. The status of maternal

intimate partner abuse (IPA) was captured by the Chinese Abuse Assessment Screen (AAS) questionnaire, which was valid in Chinese population (37, 38). AAS questionnaire consists of 5 yes/no questions covering emotional, physical, psychological and sexual abuse. A mother was considered as having a history of IPA if she reported a positive answer (i.e. yes) to any of the 5 questions.

CHQ-PF50 is a questionnaire consisting of 50 questions covering 12 subdomains, namely physical functioning (PF), role functioning—emotional and behavioral (REB), role functioning—Physical (RP), bodily pain (BP), general behavior (BE), mental health (MH), self-esteem (SE), general health perceptions (GH), parental impact—emotional (PE), parent impact—time (PT), family activities (FA) and family cohesion (FC) (33). The scores of the 12 subscales can be further calculated into a physical summary score and a psychosocial summary score (33). The score range of the 12 subscales and the two summary scores span from 0 to 100, with higher score indicating better HRQOL (33). The questionnaire has been validated in local Chinese children, which has been proven to be reliable and valid (34).

SDQ contains 25 questions that measure five aspects of a child's behaviors including negative behaviors (emotional symptoms, conduct problems, hyperactivity/inattention, and peer relationship problems) and positive behaviors (prosocial behavior). Each domain has 5 items that can generate a score ranging from 0 to 10. The four subscales of negative behaviors can be summated to a total difficulties score. Higher score indicates more problematic behaviors. In contrast, for the prosocial behavior subscale, higher score indicates more positive and helping behavior. The reliability and validity of the Chinese version of SDQ has also been confirmed in local population (36).

The Wechsler Intelligence Scale for Children Fourth Edition – Hong Kong (Short Form) (WISC-IV-HK-SF), an individually administered intelligence screening test, was used to assess children's level of intelligence (39). Each child was individually interviewed by a clinical psychologist in clinical settings. The mean IQ score is 100 in a normative population with a standard deviation (SD) of 15.

Children's body mass index (BMI) was calculated as weight divided by the square of height. During physical examination, a trained research assistant measured the child participant's height using a stadiometer where participants are measured without shoes to the nearest 0.1cm and weight to the nearest 0.1kg using regularly calibrated scales where participants stand without shoes in light indoor clothing.

BMI z-score and percentiles was calculated by sex and age group according to the sex-specific BMI-for-age growth chart of the International Obesity Task Force (40). Underweight was defined as having a BMI less than the 5th percentile; while normal or healthy weight was defined as having a BMI at or above 5th percentile but less than 85th percentile of the sex-specific BMI for age growth chart. Overweight and obesity was defined a BMI percentile ranging between 85th and 95th percentile, and at or above 95th percentile of the sex-specific BMI for age growth chart, respectively.

2.3 Statistical analysis

The characteristics of children between those having mother with and without chronic disease were compared by independent student t tests for continuous variables and chi-square tests for categorical variables. Descriptive characteristics of continuous data were presented with mean value and its standard deviation, whereas the categorical characteristics were displayed with numbers and percentages.

The outcomes of this study were children's HRQOL measured by CHQ-PF50 and behavioral problems measured by SDQ, which were all continuous variables. Mother's chronic disease status was the exposure. Therefore, multiple linear regression models were established to examine the spillover effect of maternal chronic disease on their children's HRQOL and behavior, with adjustment for children's age, gender, IQ, BMI z-score, status of chronic disease, and their mothers' age, status of IPA and current marital status. To further investigate the independent spillover effect of maternal mental and physical disease on the outcomes, the presence of physical disease and mental disease were added into the model with the adjustment for the aforementioned set of variables. Goodness-of-fit of the regression models was measured by an R-squared statistic.

Data analyses were performed using with Stata/SE 13.0 (Stata-Corp, College Station, TX). Statistical significance was set at p value < 0.05.

3 Results

A total of 255 child-mother pairs were included, with 125 girls and 130 boys (Table 1). The mean ages of the children and their mothers were 8.4 (SD: 1.2) and 39.0 (5.5) years, respectively. Of the mothers, 16.4% had experienced IPA and 74.4% were currently married. The mean IQ of the children was 100.3

(13.8) and 12.2% of them had chronic disease. A total of 88 (34.5%) children had a mother with one or more chronic diseases, of which 12 mothers had mental disease only, 69 mothers had physical disease only and 7 mothers had both mental and physical diseases. Regarding the HRQOL, children of mothers without chronic disease were found to have significantly higher scores on the CHQ subscales of PT and FA, as well as less hyperactivity/inattention problems, compared to those of mothers with chronic diseases (Figure 2).

Table 1. Characteristics of mothers with and without chronic disease and their children

	Total (N=255)	Children of mothers without chronic diseases (n=167)	Children of mothers with chronic disease (n=88)	p-value
Maternal characteristics				
Age, mean ± SD	39.0 ± 5.5	38.6 ± 5.5	39.7 ± 5.5	0.112
IPA, n (%)	41 (16.4%)	22 (13.6%)	19 (21.6%)	0.102
Marital status, n (%)				0.120
Currently married	180 (74.4%)	124 (77.5%)	56 (68.3%)	
Divorced/Separated/Widowed	62 (25.6%)	36 (22.5%)	26 (31.7%)	
Physical disease, n (%)	76 (29.80%)		76 (86.36%)	
Hypertension	3 (1.18%)		3 (3.41%)	
Diabetes	2 (0.78%)		2 (2.27%)	
Hyperlipidemia	4 (1.57%)		4 (4.55%)	
Coronary heart disease	0 (0%)		0 (0%)	
Stroke	0 (0%)		0 (0%)	
Epilepsy	0 (0%)		0 (0%)	
Hepatitis B	24 (9.41%)	N/A	24 (27.27%)	
Thyroid disease	11 (4.31%)		11 (12.5%)	
Gastric peptic ulcer	8 (3.14%)		8 (9.09%)	
Anaemia	28 (10.98%)		28 (31.82%)	
Asthma	1 (0.39%)		1 (1.14%)	
Musculoskeletal disease	4 (1.57%)		4 (4.55%)	
Cancer	8 (3.14%)		8 (9.09%)	
Mental disease, n (%)	19 (7.45%)		19 (21.59%)	
Child characteristics				
Age, mean ± SD	8.4 ± 1.2	8.3 ± 1.0	8.6 ± 1.4	0.060
Gender, n (%)				0.624

Running title: spillover effects of maternal chronic disease

Girl	125 (49.0%)	80 (47.9%)	45 (51.1%)	
Boy	130 (51.0%)	87 (52.1%)	43 (48.9%)	
Estimated IQ score, mean \pm SD	100.3 \pm 13.8	99.4 \pm 13.9	101.9 \pm 13.6	0.171
BMI z-score, mean \pm SD	0.35 (1.11)	0.36 (1.06)	0.33 (1.20)	0.850
BMI categories, n (%)				0.171
Normal weight	195 (77.4%)	132 (80.0%)	63 (72.4%)	
Abnormal weight (underweight/overweight/obesity)	57 (22.6%)	33 (20.0%)	24 (27.6%)	
Chronic disease, n (%)	28 (11.0%)	17 (10.2%)	11 (12.5%)	0.573
Epilepsy	1 (0.4%)	1 (0.6%)	0 (0%)	
Thyroid disease	1 (0.4%)	1 (0.6%)	0 (0%)	
Anemia	5 (2.0%)	1 (0.6%)	4 (4.6%)	
Asthma	13 (5.1%)	9 (5.4%)	4 (4.6%)	
Mental disease	2 (0.8%)	1 (0.6%)	1 (1.1%)	
Heart disease	2 (0.8%)	2 (1.2%)	0 (0%)	
Autism	2/167	1 (0.6%)	1 (1.0%)	
ADHD	2 (0.8%)	1 (0.6%)	1 (1.0%)	
Rheumatoid arthritis	1 (0.4%)	0 (0%)	1 (1.0%)	

Abbreviation: ADHD: attention deficit hyperactivity disorder; BMI: body mass index; IPA: intimate partner abuse; IQ: intelligence quotient, SD: standard deviation.

Note: Sample size for mother's IPA status: 250; marital status: 242; BMI: 252.

*: $p < 0.05$. Comparison was made by two-sample independent t test for continuous data and by χ^2 test for categorical data

The spillover effect of maternal chronic disease on their children's HRQOL and behaviors is shown in Table 2. After adjusting for confounders, children of mothers with chronic disease had higher scores on SDQ measured hyperactivity/inattention ($\beta = 0.83$, $p=0.010$) and lower scores on three CHQ subscales (PE: $\beta = -7.28$, $p=0.031$; PT: $\beta = -9.13$, $p=0.016$; FA: $\beta = -9.62$, $p=0.002$) and lower PSS ($\beta = -3.60$, $p=0.018$). In other words, having a mother with chronic disease resulted in an increase of 0.83 in the hyperactivity/inattention score measured by SDQ, and decreases of 7.28, 9.13, 9.62 and 3.60 in PE, PT, FA and PSS scores measured by CHQ-PF50, respectively.

Table 2. The spillover effect of maternal chronic disease on their children’s HRQOL and behavioral problems

	Child of mother with chronic disease			
	β	95%CI	p value	R-squared
Child HRQOL (measured by CHQ-PF-50)				
Physical functioning (PF)	0.27	-3.98, 4.53	0.899	0.050
Role functioning—emotional and behavioral (REB)	-6.32	-13.82, 1.19	0.099	0.106
Role functioning—physical (RP)	-1.50	-7.53, 4.54	0.625	0.041
Bodily pain (BP)	-3.00	-8.20, 2.20	0.257	0.037
General behavior (BE)	-4.71	-9.58, 0.17	0.059	0.106
Mental health (MH)	-3.18	-8.12, 1.76	0.206	0.087
Self-esteem (SE)	-1.29	-4.70, 2.12	0.458	0.109
General health perceptions (GH)	-3.64	-8.43, 1.15	0.136	0.083
Parental impact—emotional (PE)	-7.28	-13.88, -0.67	0.031*	0.102
Parental impact—time (PT)	-9.13	-16.54, -1.72	0.016*	0.070
Family activities (FA)	-9.62	-15.58, -3.66	0.002*	0.139
Family cohesion (FC)	6.31	-0.75, 13.36	0.079	0.111
Physical summary score (PHS)	-1.15	-3.52, 1.23	0.343	0.044
Psychosocial summary score (PSS)	-3.60	-6.58, -0.61	0.018*	0.136
Child behaviors (measured by SDQ)				
Emotional symptoms	0.14	-0.50, 0.79	0.663	0.053
Conduct problems	0.21	-0.29, 0.71	0.404	0.071
Hyperactivity/inattention	0.83	0.20, 1.46	0.010*	0.103
Peer relationship problems	0.07	-0.43, 0.57	0.769	0.100
Prosocial behaviors	-0.28	-0.82, 0.27	0.324	0.093
Total difficulties score	1.26	-0.31, 2.83	0.116	0.105

Abbreviation: CHQ-PF50: Child Health Questionnaire-Parent Form-50; CI: confidence interval; HRQOL: health-related quality of life, SDQ: strengths and difficulties questionnaire

*: $p < 0.05$. Multiple linear regression model with adjustment for children’s age, gender, IQ, status of chronic disease, BMI z-score, and their mothers’ age, status of IPA and current marital status

We further investigated the independent spillover effect of maternal mental versus physical disease on their children’s HRQOL and behavioral problems, which is shown in Table 3. After adjusting for confounders including maternal physical disease, children of mothers with mental disease had lower

scores on two CHQ subscales (REB: $\beta = -17.47$, $p=0.007$; PE: $\beta = -14.18$, $p=0.014$) and PSS ($\beta = -5.34$, $p=0.040$) and higher FC scores ($\beta = 14.07$, $p=0.021$) as well as higher SDQ total difficulties score ($\beta = 3.05$, $p=0.027$) than those of mothers without mental disease. After adjusting for confounders including maternal mental disease status, maternal physical disease was significantly associated with PT ($\beta = -9.88$, $p=0.013$) and FA ($\beta = -9.23$, $p=0.004$).

Table 3. The spillover effect of maternal mental and physical disease status on their children’s HRQOL and behavioral problems, respectively

	Child of mother with mental disease			Child of mother with physical disease			R-squared
	β	95%CI	p value	β	95%CI	p value	
Child HRQOL (measured by CHQ-PF-50)							
Physical functioning (PF)	0.43	-6.87, 7.74	0.907	0.64	-3.85, 5.14	0.778	0.049
Role functioning—emotional and behavioral (REB)	-17.47	-30.19, -4.75	0.007*	-3.97	-11.81, 3.86	0.319	0.124
Role functioning—physical (RP)	-10.20	-20.47, 0.06	0.051	0.33	-5.99, 6.66	0.918	0.056
Bodily pain (BP)	-5.11	-14.01, 3.79	0.259	-2.89	-8.37, 2.59	0.300	0.043
General behavior (BE)	-5.78	-14.11, 2.55	0.173	-4.81	-9.94, 0.32	0.066	0.109
Mental health (MH)	-4.03	-12.49, 4.44	0.349	-2.03	-7.24, 3.19	0.444	0.083
Self-esteem (SE)	-4.12	-9.95, 1.71	0.165	-0.13	-3.72, 3.47	0.944	0.112
General health perceptions (GH)	-6.38	-14.61, 1.84	0.128	-2.62	-7.69, 2.45	0.309	0.081
Parental impact—emotional (PE)	-14.18	-25.46, -2.90	0.014*	-3.94	-10.89, 3.00	0.265	0.104
Parental impact—time (PT)	-7.15	-19.79, 5.50	0.266	-9.88	-17.67, -2.10	0.013*	0.076
Family activities (FA)	-7.26	-17.48, 2.95	0.162	-9.23	-15.52, -2.94	0.004*	0.139
Family cohesion (FC)	14.07	2.14, 25.99	0.021*	2.75	-4.60, 10.09	0.462	0.118
Physical summary score (PHS)	-3.15	-7.22, 0.92	0.129	-0.62	-3.12, 1.89	0.628	0.048
Psychosocial summary score (PSS)	-5.34	-10.43, -0.25	0.040*	-2.88	-6.02, 0.26	0.072	0.136
Child behaviors (measured by SDQ)							
Emotional symptoms	0.82	-0.29, 1.93	0.148	0.04	-0.64, 0.72	0.916	0.063
Conduct problems	0.76	-0.10, 1.62	0.081	0.09	-0.43, 0.62	0.730	0.080
Hyperactivity/inattention	0.71	-0.38, 1.81	0.200	0.65	-0.01, 1.32	0.055	0.095
Peer relationship problems	0.76	-0.10, 1.61	0.082	0.03	-0.49, 0.55	0.916	0.111
Prosocial behaviors	-0.81	-1.76, 0.13	0.092	-0.15	-0.73, 0.42	0.605	0.103
Total difficulties score	3.05	0.35, 5.76	0.027*	0.81	-0.84, 2.46	0.335	0.116

Abbreviation: CHQ-PF50: Child Health Questionnaire-Parent Form-50; CI: confidence interval; HRQOL: health-related quality of life, SDQ: strengths and difficulties questionnaire

*: $p<0.05$. Multiple linear regression model with adjustment for children’s age, gender, IQ, status of chronic disease, BMI z-score, and their mothers’ age, status of IPA, current marital status, presence of

physical disease (when the exposure was mental disease) and presence of mental disease (when the exposure was physical disease)

4 Discussions

This study examined the impact of maternal chronic disease on the HRQOL and behavior of children in Chinese low-income families. In line with previous evidence on intergenerational transmission of health (21), we found that maternal chronic disease was associated with worse HRQOL especially in the psychosocial domains and more behavioral problems among their dependent young children. Our study findings provide further support for the importance of examination of spillover effect in health-related research. It also adds to the current literature that the spillover effect phenomenon is widely observed in patient-caregiver relationship as well as in parent-child relationship. In addition, the impact and magnitude of the spillover effect on children's HRQOL and behaviors could differ by maternal physical and mental disease, suggesting a need for using different sets of approaches to intervene in the lives of children of mothers with physical and mental disease.

In this study, 34.5% of mothers had one or more chronic diseases. Although currently no population-level data is available showing the prevalence of children living with a chronically ill mother in Hong Kong, the figure observed in this study is much higher than the ones reported by representative samples drawn from the general populations of Germany or the United States (i.e. 4%-15%) (10, 11). It could be because our study included only low-income families, and Hong Kong is known to have a high Gini coefficient of 0.539 as reported in 2016, indicating great income inequality (41). Previous research suggested that income inequality at the population level most affects the health of the poor because of the accumulation of relativities in society including relative deprivation and relative social status (42). These relativities are posited to affect health through either material or psychosocial pathways including stress and less access to healthcare (43). Therefore, it is not surprising to find a high prevalence of chronic disease in this study of low-income mothers. Future studies should explore and identify factors that may help mitigate the negative effect of relative low income on health.

Specifically, we found that maternal chronic disease was associated with greater adverse impact on child, worse psychosocial health and more symptoms of hyperactivity and inattention in the child, and fewer family activities. The spillover effect of maternal chronic disease on children appeared to be stronger in the psychosocial health domains, possibly because having observed a mother being affected by disease

and treatment may render a child to experience greater psychological distress (15, 44, 45). Prolonged exposure to psychosocial stressors has been implicated in the development of brain abnormalities, which are associated with poor executive functions and psychiatric diseases including attention deficit and hyperactivity symptoms (46). Another plausible explanation is that chronic disease might impair a mother's parenting competence. It is well recognized that parenting is a demanding job requiring a large amount of time, patience and effort in order to foster positive child development. For most families, mothers are considered as a child's primary caregiver. Being affected by chronic disease may also disrupt mother-child interaction quality and increase the likelihood of negative parenting behaviors such as abuse and neglect (47), which can give rise to more emotional and behavioral problems in a child (48, 49). On the other hand, routine family activities and household chores might also be interrupted due to maternal absence from home for outpatient and inpatient visits/admissions. This may explain why we observed fewer family activities among children of mothers with chronic disease. The findings indicate that the spillover effect can influence people at multiple levels, but further research is needed to confirm whether the spillover effect is also significant in the higher income population.

More importantly, the spillover effect was found to differ between children of mothers with mental disease and those of mothers with physical disease. Mental disease in mothers was associated with greater impact of child problems on mental distress and worry as well as worse emotional and behavioral functioning, poorer psychosocial health, and more behavioral problems among children. On the other hand, physical disease in mothers was associated with greater impact of child problems on the personal time of mothers and fewer family activities. It appears that compared to maternal mental disease, maternal physical disease impaired a child's HRQOL and behaviors to a lesser extent. This could be because although maternal physical disease might reduce the quantity of parenting due to symptom burden and energy loss, it might not reduce the quality of parenting. Literature has posited that the quality matters more than quantity and can attenuate the negative impact of less time in care (50). By contrast, mental disease is associated with poor skills in behavioral inhibition and emotion regulation (51). These poor skills in mothers are known to have negative impacts on parenting quality in turn increasing the risk of adjustment problems among children (52). Although our study results support a stronger link of child psychosocial health with maternal mental disease than physical disease, the findings pertain to low income family environment where other stressors might influence the relationships. Moreover, given that our study did not measure the quality and quantity of parenting, more research will be needed to substantiate the claim that parenting plays a role in the spillover effect of maternal mental disease on child health and development.

Interestingly, previous studies found that parental chronic disease was associated with lower levels of family cohesion (23, 53, 54), but we observed higher levels of family cohesion among children of mothers with mental disease. Family activities were fewer among children of mothers with physical disease but not those of mothers with mental disease. It is unclear why family cohesion was better among children of mothers with mental disease but not among those of mothers with physical disease. A possible explanation is that since family activities reflect the quantity of family interactions, whereas family cohesion reflects the quality of family interaction, perception of family cohesion might be more susceptible to mental health influences. It has been posited that family cohesion is highly related to mental health (55). Family support might become more valuable when a person experience significant emotional distress (56), Hence, mothers with mental disease might rate higher on family closeness and support than mothers with physical disease even when they are placed in the same family environment. For more objective measures such as family activities, their ratings might be comparable. On the other hand, for people with physical disease, physical limitations might reduce family activities but might not much affect how they perceive the quality of family interactions. As this is only a speculation, further research on family processes within the context of maternal or paternal chronic disease and their impacts on children is warranted.

The strength of this study included using Although our sample size was not large, it was adequate to detect associations between variables of interest. According to Austin and Steverberg(57), two subjects per variable is an adequate sample size estimation for linear regression model estimated using ordinary least squares. This regression analysis had adequate sample size with that rule of thumb. Moreover, we targeted mother-child pairs from low-income families whose individual members are usually reluctant to be reached, and hence a sufficient sample size is the strength of this study. In addition, we measured children's HRQOL and behaviors with valid questionnaires to measure children's HRQOL and behaviors, which would increase the scientific values of the results. Furthermore, apart from adjusting for the common confounders of mothers and children in the regression analyses, we also adjusted for the potential confounding effect of children's IQ, which were well-established but rarely measured factors related to children's HRQOL and behavior (26, 29-32). There are several limitations deserve discussion. First, only 19 mothers with mental disease were included in current study, in part underestimating the spillover effects of maternal mental disease on children's HRQOL and behavioral problems. Secondly, the cross-sectional nature of this study precludes us from drawing a causal relationship between maternal chronic disease and children's poor HRQOL and problematic behaviors. Third, young children may not

understand the questions on health-related perceptions and behaviors. Therefore, we have to used parent-proxy report to measure children's HRQOL and behaviors. Although the results are not based upon a child's self-perception, this is a common limitation faced by child health researchers. To examine the presence of reporting bias in the results, we further compared the parent-reported HRQOL between children with and without chronic disease. Although the correlations were not significant due to insufficient power, children with chronic disease tended to have poorer parent-reported HRQOL, suggesting limited reporting bias. Last, although we understand that different types of maternal chronic disease may have differential influences on children's HRQOL and behaviors, we were unable to examine the independent effect of individual disease because of limited mother-child pairs in each subtype of chronic disease.

5 Conclusion

In conclusion, the present study found that chronic disease in mothers was common among Chinese low-income families, and maternal chronic disease exerted significant spillover effects on children's HRQOL and behaviors. Notably, maternal mental disease appeared to have stronger influences on child psychosocial health when compared to maternal physical disease. Different types of interventions and support should be made for children of mothers with physical and mental disease, respectively. Our study also adds to the current literature that the phenomenon of spillover effect is not only restricted to patient-caregiver relationship but it might also be found in the relationship between mother and their young children even if they do not need to assume any caregiving roles.

Data Availability Statement

The software code used are available from the corresponding author at carlosho@hku.hk. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Reference

1. van den Berg B, Fiebig DG, Hall J. Well-being losses due to care-giving. *J Health Econ.* 2014;35:123-31.
2. Bin Sallim A, Sayampanathan AA, Cuttilan A, Ho RCM. Prevalence of Mental Health Disorders Among Caregivers of Patients With Alzheimer Disease. *J Am Med Dir Assoc.* 2015;16(12):1034-41.
3. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA.* 1999;282(23):2215-9.
4. Wittenberg E, Prosser LA. Disutility of Illness for Caregivers and Families: A Systematic Review of the Literature. *Pharmacoeconomics.* 2013;31(6):489-500.
5. Bobinac A, van Exel NJA, Rutten FFH, Brouwer WBF. Health Effects in Significant Others: Separating Family and Care-Giving Effects. *Medical Decision Making.* 2011;31(2):292-8.
6. Salvador A, Crespo C, Martins AR, Santos S, Canavarro MC. Parents' Perceptions About Their Child's Illness in Pediatric Cancer: Links with Caregiving Burden and Quality of Life. *J Child Fam Stud.* 2015;24(4):1129-40.
7. Lavelle TA, Wittenberg E, Lamarand K, Prosser LA. Variation in the spillover effects of illness on parents, spouses, and children of the chronically ill. *Appl Health Econ Health Policy.* 2014;12(2):117-24.
8. Yamazaki S, Sokejima S, Mizoue T, Eboshida A, Fukuhara S. Health-related quality of life of mothers of children with leukemia in Japan. *Qual Life Res.* 2005;14(4):1079-85.
9. Brouwer WB. Too important to ignore: informal caregivers and other significant others. *Pharmacoeconomics.* 2006;24(1):39-41.
10. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. 2001;50:120-5.
11. Barkmann C, Romer G, Watson M, Schulte-Markwort M. Parental physical illness as a risk for psychosocial maladjustment in children and adolescents: Epidemiological findings from a national survey in Germany. *Psychosomatics.* 2007;48(6):476-81.
12. Sieh DS, Meijer AM, Oort FJ, Visser-Meily JM, Van der Leij DA. Problem behavior in children of chronically ill parents: a meta-analysis. *Clin Child Fam Psychol Rev.* 2010;13(4):384-97.
13. Huizinga GA, Visser A, van der Graaf WT, Hoekstra HJ, Klip EC, Pras E, et al. Stress response symptoms in adolescent and young adult children of parents diagnosed with cancer. *Eur J Cancer.* 2005;41(2):288-95.
14. Visser A, Huizinga GA, Hoekstra HJ, van der Graaf WT, Klip EC, Pras E, et al. Emotional and behavioural functioning of children of a parent diagnosed with cancer: a cross-informant perspective. *Psychooncology.* 2005;14(9):746-58.
15. Pederson S, Revenson TA. Parental illness, family functioning, and adolescent well-being: a family ecology framework to guide research. *J Fam Psychol.* 2005;19(3):404-19.
16. Krol M, Papenburg J, van Exel J. Does Including Informal Care in Economic Evaluations Matter? A Systematic Review of Inclusion and Impact of Informal Care in Cost-Effectiveness Studies. *Pharmacoeconomics.* 2015;33(2):123-35.
17. Hoefman RJ, van Exel J, Brouwer W. How to Include Informal Care in Economic Evaluations. *Pharmacoeconomics.* 2013;31(12):1105-19.
18. Dixon S, Walker M, Salek S. Incorporating carer effects into economic evaluation. *Pharmacoeconomics.* 2006;24(1):43-53.
19. Brouwer WB, van Exel NJ, Koopmanschap MA, Rutten FF. The valuation of informal care in economic appraisal. A consideration of individual choice and societal costs of time. *Int J Technol Assess Health Care.* 1999;15(1):147-60.
20. Oliva-Moreno J, Trapero-Bertran M, Pena-Longobardo LM, del Pozo-Rubio R. The Valuation of Informal Care in Cost-of-Illness Studies: A Systematic Review. *Pharmacoeconomics.* 2017;35(3):331-45.

21. Rimal RN. Intergenerational transmission of health: the role of intrapersonal, interpersonal, and communicative factors. *Health Education & Behavior*. 2003;30(1):10-28.
22. Jeon Y-H, Essue B, Jan S, Wells R, Whitworth JA. Economic hardship associated with managing chronic illness: a qualitative inquiry. *BMC Health Services Research*. 2009;9(1):182.
23. De Judicibus MA, McCabe MP. The impact of parental multiple sclerosis on the adjustment of children and adolescents. *Adolescence*. 2004;39(155):551-69.
24. Sieh DS, Dikkers AL, Visser-Meily JM, Meijer AM. Stress in Adolescents with a Chronically Ill Parent: Inspiration from Rolland's Family Systems-Illness Model. *J Dev Phys Disabil*. 2012;24(6):591-606.
25. Fung CS, Yu EY, Guo VY, Wong CK, Kung K, Ho SY, et al. Development of a Health Empowerment Programme to improve the health of working poor families: protocol for a prospective cohort study in Hong Kong. *BMJ Open*. 2016;6(2):e010015.
26. Lam CLK, Guo VY, Wong CKH, Yu EYT, Fung CSC. Poverty and health-related quality of life of people living in Hong Kong: comparison of individuals from low-income families and the general population. *J Public Health (Oxf)*. 2017;39(2):258-65.
27. Wong RSM, Guo VY, Ip P, Wong CKH, Yu EYT, Fung CSC, et al. Mothers' health-related quality of life: Its relationship with children's health-related quality of life and behavior in low-income families. *Family Medicine and Community Health*. 2016;4(4):4-12.
28. Guo VY, Yu EYT, Wong RSM, Ip P, Tiwari AFY, Wong CKH, et al. Maternal mental quality of life mediates the associations between intimate partner abuse against mothers and their children's behaviours and quality of life in low-income Chinese families. *Quality of Life Research*. 2017;26(12):3297-306.
29. Goodman R, Simonoff E, Stevenson J. The impact of child IQ, parent IQ and sibling IQ on child behavioural deviance scores. *Journal of Child Psychology and Psychiatry*. 1995;36(3):409-25.
30. Chen A, Schwarz D, Radcliffe J, Rogan WJ. Maternal IQ, child IQ, behavior, and achievement in urban 5-7 year olds. *Pediatr Res*. 2006;59(3):471-7.
31. Kuhlthau KA, Pulsifer MB, Yeap BY, Rivera Morales D, Delahaye J, Hill KS, et al. Prospective study of health-related quality of life for children with brain tumors treated with proton radiotherapy. *J Clin Oncol*. 2012;30(17):2079-86.
32. Seid M, Huang B, Niehaus S, Brunner HI, Lovell DJ. Determinants of health-related quality of life in children newly diagnosed with juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)*. 2014;66(2):263-9.
33. Landgraf JM, Abetz L, Ware JE. *The CHQ User's Manual*. Boston, MA: Health Act; . 1999.
34. Ng JY, Landgraf JM, Chiu CS, Cheng NL, Cheung YF. Preliminary evidence on the measurement properties of the Chinese version of the Child Health Questionnaire, parent form (CHQ-pF50) and child form (CHQ-CF87). *Qual Life Res*. 2005;14(7):1775-81.
35. Goodman R. The Strengths and Difficulties Questionnaire: a research note. *J Child Psychol Psychiatry*. 1997;38(5):581-6.
36. Lai KY, Luk ES, Leung PW, Wong AS, Law L, Ho K. Validation of the Chinese version of the strengths and difficulties questionnaire in Hong Kong. *Social Psychiatry and Psychiatric Epidemiology*. 2010;45(12):1179-86.
37. Parker B, McFarlane J. Identifying and helping battered pregnant women. *MCN: The American Journal of Maternal/Child Nursing*. 1991;16(3):161-4.
38. Tiwari A, Fong DY, Chan KL, Leung WC, Parker B, Ho PC. Identifying intimate partner violence: Comparing the Chinese Abuse Assessment Screen with the Chinese Revised Conflict Tactics Scales. *BJOG*. 2007;114(9):1065-71.
39. Wechsler D. *Wechsler intelligence scale for children*. 4th edn, revised. New York: Psychological Corporation. 2003.

40. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatric Obesity*. 2012;7(4):284-94.
41. Wong RSM, Yu EYT, Guo VY, Wan EY-F, Chin W-Y, Wong CKH, et al. A prospective cohort study to investigate parental stress and child health in low-income Chinese families: protocol paper. *BMJ Open*. 2018;8(2).
42. Wagstaff A, Doorslaer Ev. Income Inequality and Health: What Does the Literature Tell Us? *Annual Review of Public Health*. 2000;21(1):543-67.
43. Blázquez M, Cottini E, Herrarte A. The socioeconomic gradient in health: how important is material deprivation? *The Journal of Economic Inequality*. 2014;12(2):239-64.
44. Forehand R, Biggar H, Kotchick BA. Cumulative risk across family stressors: short- and long-term effects for adolescents. *J Abnorm Child Psychol*. 1998;26(2):119-28.
45. Krohne H. Stress and coping theories. *The international encyclopedia of the social and behavioral sciences*. 2001;22:15163-70.
46. Babenko O, Kovalchuk I, Metz GAS. Stress-induced perinatal and transgenerational epigenetic programming of brain development and mental health. *Neuroscience & Biobehavioral Reviews*. 2015;48:70-91.
47. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G. Maternal depression and parenting behavior: a meta-analytic review. *Clin Psychol Rev*. 2000;20(5):561-92.
48. Najman JM, Williams GM, Nikles J, Spence S, Bor W, O'CALLAGHAN M, et al. Mothers' mental illness and child behavior problems: cause-effect association or observation bias? *Journal of the American Academy of Child & Adolescent Psychiatry*. 2000;39(5):592-602.
49. Kahn RS, Brandt D, Whitaker RC. Combined effect of mothers' and fathers' mental health symptoms on children's behavioral and emotional well-being. *Archives of Pediatrics & Adolescent Medicine*. 2004;158(8):721-9.
50. Love JM, Harrison L, Sagi-Schwartz A, IJzendoorn MHV, Ross C, Ungerer JA, et al. Child Care Quality Matters: How Conclusions May Vary With Context. *Child Development*. 2003;74(4):1021-33.
51. Gross JJ, Muñoz RF. Emotion Regulation and Mental Health. *Clinical Psychology: Science and Practice*. 1995;2(2):151-64.
52. Chang L, Schwartz D, Dodge KA, McBride-Chang C. Harsh Parenting in Relation to Child Emotion Regulation and Aggression. *Journal of family psychology : JFP : journal of the Division of Family Psychology of the American Psychological Association (Division 43)*. 2003;17(4):598-606.
53. Peters LC, Esses LM. Family Environment as Perceived by Children with a Chronically Ill Parent. *J Chron Dis*. 1985;38(4):301-8.
54. Pakenham KI, Cox S. Test of a Model of the Effects of Parental Illness on Youth and Family Functioning. *Health Psychol*. 2012;31(5):580-90.
55. Barrett AE, Turner RJ. Family structure and mental health: The mediating effects of socioeconomic status, family process, and social stress. *Journal of health and social behavior*. 2005;46(2):156-69.
56. Serovich JM, Kimberly J, Mosack K, Lewis T. The role of family and friend social support in reducing emotional distress among HIV-positive women. *Aids Care*. 2001;13(3):335-41.
57. Austin PC, Steyerberg EW. The number of subjects per variable required in linear regression analyses. *Journal of Clinical Epidemiology*. 2015;68(6):627-36.

Figure Legend

Figure 1. Flowchart of the study recruitment, inclusion and exclusion

Figure 2. Comparison of children’s HRQOL and behaviors between those of mothers with and without chronic disease.

Abbreviation: PF: physical functioning, REB: role functioning—emotional and behavioral, RP: role functioning—Physical, BP: bodily pain, BE: general behavior, MH: mental health, SE: self-esteem. GH: general health perceptions, PE: parental impact—emotional, PT: parent impact—time, FA: family activities, FC: family cohesion, PHS: physical summary score, PSS: psychosocial summary score; CHQ-PF50: Child Health Questionnaire-Parent Form-50; SDQ: strengths and difficulties questionnaire. *
p<0.05



