# The epidemiologic burden of hepatitis C virus infection in Latin America

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## ABSTRACT

Chronic infection with hepatitis C virus (HCV) is a major and growing public health concern worldwide, including in Latin America. With more efficacious therapies becoming available, decision-makers will require accurate estimates of disease prevalence to assess the potential impact of new treatments. However, few estimates of the epidemiologic burden, either overall or by country, are available for Latin America; and the potential impact of currently-available treatments on the epidemiologic burden of HCV in Latin America has not been assessed. To address this, we systematically reviewed twenty-five articles presenting population-based estimates of HCV prevalence from general population or blood donor samples, and supplemented those with publically-available data, to estimate the total number of persons infected with HCV in Latin America at 7.8 million (2010). Of these, over 4.6 million would be expected to have genotype 1 chronic HCV, based on published data on the risk of progression to chronic disease and the HCV genotype distribution of Latin America. Finally, we calculated that between 1.6 and 2.3 million persons with genotype 1 chronic HCV would potentially benefit from current treatments, based on published estimates of genotype-specific treatment responsiveness. In conclusion, these estimates demonstrate the substantial present epidemiologic burden of HCV, and quantify the impending societal and clinical burden from untreated HCV in Latin America.

**Key words.** HCV. Prevalence. Liver disease. Burden. Systematic review.

## INTRODUCTION

Up to 3% of the population –equaling approximately 170 million individuals– are estimated to be infected with chronic hepatitis C virus (HCV), globally.[1] It is a leading cause of chronic liver disease, cirrhosis and hepatocellular carcinoma,[2,3] and is the underlying cause of over 475,000 deaths annually, worldwide.[4] While mortality due to chronic HCV infection is an important facet for determining the impact on public health, one of the challenges in characterizing the epidemiology of HCV is that the infection is asymptomatic in up to 75% of individuals.[5] New medical therapies are being developed which may be more effective in achieving a sustained viral response among treated patients with HCV. With these therapies coming to market, decision-makers have a pressing need for accurate estimates of disease prevalence, as well as estimates of those non-responsive to currently-available treatments, to understand the full economic impact of treating persons with HCV and plan the most effective use of resources.

Over recent years, some estimates of the epidemiologic burden of chronic HCV infection in Latin America have been published at the local and national level.[6] However, no overall estimates of the epidemiologic burden for Latin America have been presented, and the burden in many of the countries in the area remains unexamined. This burden due to HCV would vary geographically, as it is based both on the availability of treatments, as well as the distribution of genotypes (a known predictor of treatment responsiveness).[7] The recently published

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LATINO study showed that white Latinos with genotype 1 HCV were less likely to achieve a sustained viral response with current therapy (34%), compared to non-Latinos with genotype 1 HCV (49%; p < 0.001).[8] This finding could have major public health implications, as most Latin Americans infected with HCV –from 65 to 75%–[9-12] are infected with genotype 1; how these factors may impact the overall epidemiologic burden is unknown. The objectives of this study were to synthesize data on HCV prevalence, estimate the current country-specific number of cases, and assess the potential impact of currently-available treatments on the epidemiologic burden of HCV in Latin America.

## MATERIAL AND METHODS

We systematically reviewed the published literature to synthesize country-specific estimates of the epidemiologic burden of HCV infection. These data were supplemented with data extracted through a review of published and publically available government reports, health agency websites, and national blood banks and



***Figure 1.*** *A model of the progression of HCV infection. G1: genotype 1; HCV: hepatitis C virus.*

surveillance networks. The number of cases potentially responsive to currently-available therapies was estimated by applying assumptions about genotype distribution and treatment responsiveness to the proportion of those infected with HCV who do not spontaneously resolve their HCV infection (Figure 1).

### Systematic literature review

The systematic search was conducted of the Medline, Embase, and the Cochrane databases using customized terms to identify epidemiologic burden (incidence, prevalence, epidemiology) and hepatitis infection (by disease keywords: hepatitis, HCV and genotype). The search was performed in June 2011 for original studies published after January 1995. Searches were implemented for each country (Argentina, Belize, Bolivia, Brazil, Chile, Colombia, Costa Rica, Ecuador, El Salvador, Guatemala, Guyana, Honduras, Mexico, Nicaragua, Panama, Paraguay, Peru, Suriname, Uruguay, or Venezuela) independently, as well as overall for Latin, Central and South America. The search strategy is provided in Appendix 1. Individual Caribbean countries were not included due to a paucity of data identified that were specific to those on preliminary searching.

Published, peer-reviewed studies of the epidemiologic burden of HCV from representative samples of the general population or blood donors, identified by the search strategy, were selected for inclusion and reviewed by two independent reviewers. Only estimates based on laboratory-confirmed HCV infection were included. We included blood donor estimates from any studies reporting on HCV prevalence among individuals submitting blood tests for voluntary donation, or for purposes of employment, health, or travel. This review was limited to English, Spanish, and Portuguese language articles; data were extracted from the latter by native speakers.

Data elements extracted from each study included: study descriptors, details of study design (sampling frame, sample size, study period), baseline population characteristics, data source, duration of follow up, and HCV rates.

### Supplemental data review

Additionally, to supplement information on countries where published general population estimates do not exist, a comprehensive review of publically-available data was conducted to synthesize counts and rates of positive HCV tests from national blood bank and surveillance networks. These included:
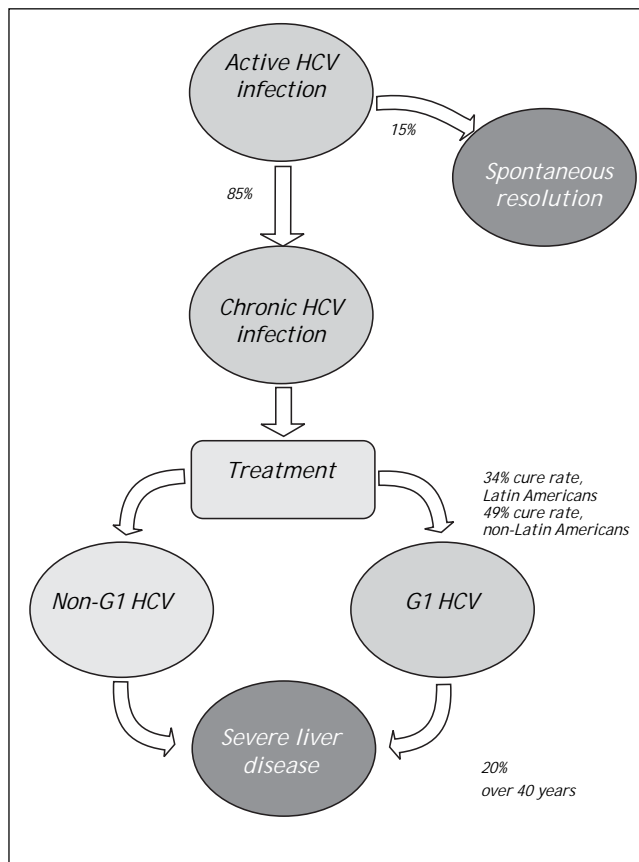
- The Pan American Health Organization;[13,14]
- **Argentina.** Instituto Nacional de Enfermedades Infecciosas/Centro Nacional de Red de Laboratorios,[15] Sistema Nacional de Vigilancia Epidemiológica;[16]
- **Brazil.** Agencia Nacional de Vigilancia Sanitoaria (National Agency for Health Surveillance);[17] Sistema de Informação de Agravos de Notificação;[18]
- **Mexico.** Instituto Mexicano del Seguro Social (Mexican Social Security Institute);[19] Encuesta Nacional de Salud y Nutrición 2007;[20] Encuesta Nacional de Salud 2000.[21]

### Data synthesis

HCV prevalence estimates (%) from general population and blood donor samples were tabulated according to country. Estimates from blood donor and general population samples were compared, for countries where both estimates exist. Prevalence estimates were extrapolated to countries without prevalence data, using the midpoint of the grouped general population prevalence estimate. The number of persons infected with HCV was assessed by applying prevalence estimates to 2010 population projections for each of the countries included in the review. The potential impact of currently-available treatments on the epidemiologic burden was estimated by assuming that: 70% of Latin Americans with HCV infection are genotype 1;[10,11] 85% progress to chronic HCV;[22] and 34% of those with chronic HCV attain sustained viral response with current pegylated-interferon plus ribavirin treatment. As a sensitivity analysis, the maximal rate of sustained viral response (49%) measured in the LATINO study was assumed.[8]
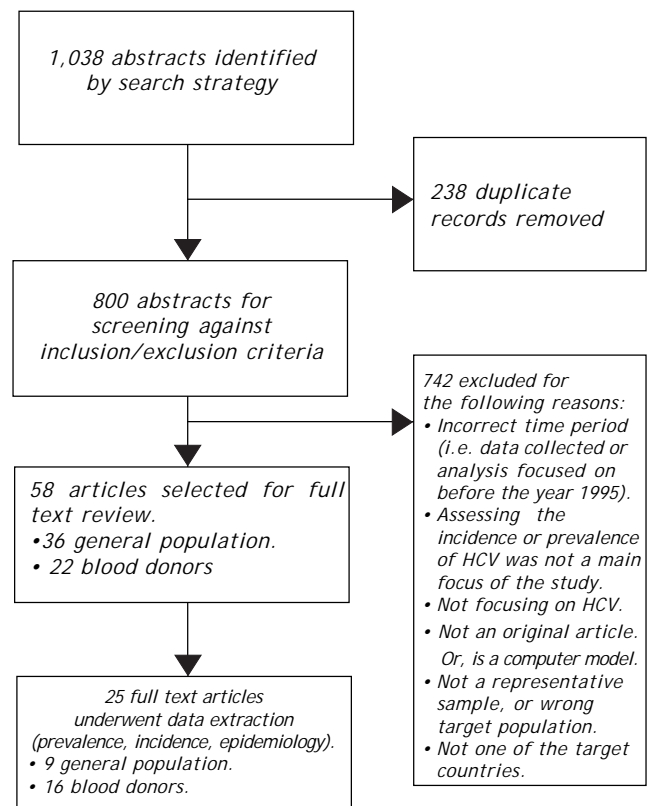
## RESULTS

### Synthesizing data on HCV prevalence

The literature search was implemented as outlined in Figure 2. The search strategy identified nine population-based studies of HCV prevalence in Latin America; the supplemental review identified three additional estimates (Appendix 2). General population estimates of HCV prevalence from Latin America ranged from 0.9%[23] to 5.8%.[24] The Sistema Nacional de Vigilancia Epidemiológica national surveillance system in Argentina estimated the national prevalence of HCV at between 1.3% and 1.7%,[25] slightly higher than the results of a 2003 study from

the province of Buenos Aires (0.9%).[23] The Brazilian Ministério de Saude estimated the age-specific prevalence of HCV nationally at 0.9 to 1.9%,[26,27] consistent with estimates from a large population-based study from Sao Paulo (1.4%).[28] Other Brazilian estimates from population-based studies ranged from 1.5% (in Salvador)[29] to 5.8% in Amazonian areas of high endemicity.[24] The only available Chilean study reported a 1.2%[30] prevalence estimate from a representative sample from Santiago. Mexican estimates ranged from 1.4%[31] to 2.0%,[32] and the former was based on the results of a large population-based national health survey (Encuesta Nacional de Salud 2000).[31] No other estimates of HCV prevalence among general population samples from Latin America were identified.

The search strategy also identified 16 studies reporting on HCV prevalence among representative samples of blood donors (Figure 3);[19,33-47] in addition to the surveillance estimates reported by the PAHO.[13,14] To assess the validity of using blood donor estimates in place of missing HCV general population prevalence estimates, we compared these



*Figure 2. Results of the literature search. HCV: hepatitis C virus.*

using data from the Latin American countries where both types of estimates were available (Table 1). Using the midpoint of the grouped estimates (0.5-0.7%), based on data from Mexico, Brazil, and Argentina, we found that relying on blood donor HCV prevalence estimates would underestimate the true prevalence of HCV infection by more than half.

## Estimating the country-specific number of cases

HCV prevalence estimates from general population samples were used to estimate the country-specific number of cases (Table 2). Based on the best available evidence, the Chilean- (1.2%)[30] and Mexican-(1.4%)[31] specific values were used to estimate the prevalence of HCV for those two countries, and the midpoint of the ranges of unpublished national estimates for HCV prevalence for Argentina (1.5%)[25]

and Brazil (1.5%).[26,27] Those 1.5% prevalence estimates were extrapolated for the remaining countries of Latin America.[48] Using those prevalence values, the total population infected with HCV in Latin America in 2010 was estimated at 7.8 million persons (Table 2). The largest epidemiologic burden due to HCV is in Brazil (2.7 million persons infected) and Mexico (1.6 million persons infected), followed by Colombia (690,000 persons infected).

## The potential impact of currently-available treatments on the epidemiologic burden

The potential impact of currently-available treatments on the epidemiologic burden was estimated by implementing assumptions regarding the prevalence of HCV genotype 1 in Latin America,[10,11] rates of progression to chronic HCV,[22] and Latin American-
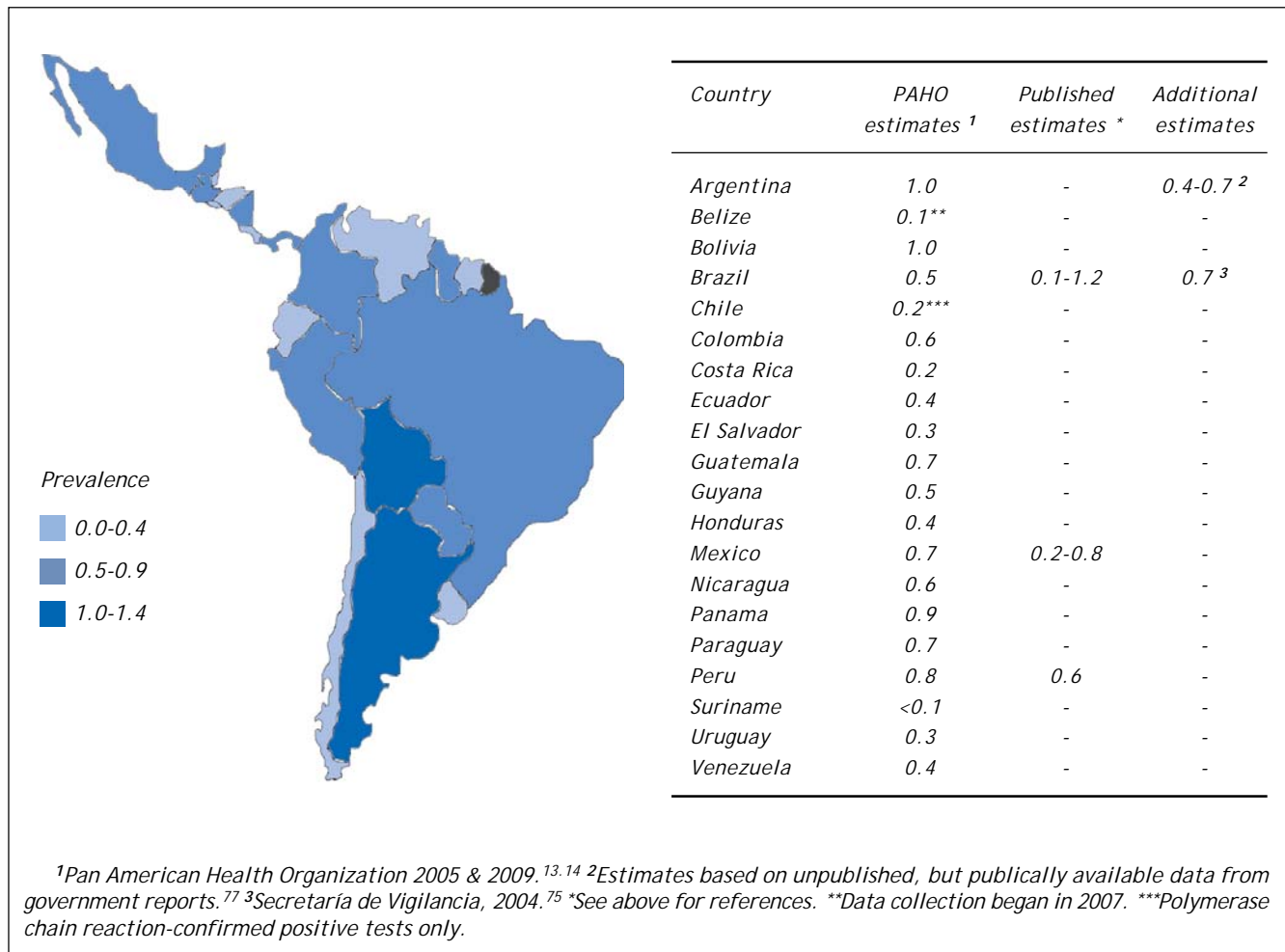
| Country | PAHO estimates [1] | Published estimates * | Additional estimates |
|---|---|---|---|
| Argentina | 1.0 | - | 0.4-0.7 [2] |
| Belize | 0.1** | - | - |
| Bolivia | 1.0 | - | - |
| Brazil | 0.5 | 0.1-1.2 | 0.7 [3] |
| Chile | 0.2*** | - | - |
| Colombia | 0.6 | - | - |
| Costa Rica | 0.2 | - | - |
| Ecuador | 0.4 | - | - |
| El Salvador | 0.3 | - | - |
| Guatemala | 0.7 | - | - |
| Guyana | 0.5 | - | - |
| Honduras | 0.4 | - | - |
| Mexico | 0.7 | 0.2-0.8 | - |
| Nicaragua | 0.6 | - | - |
| Panama | 0.9 | - | - |
| Paraguay | 0.7 | - | - |
| Peru | 0.8 | 0.6 | - |
| Suriname | <0.1 | - | - |
| Uruguay | 0.3 | - | - |
| Venezuela | 0.4 | - | - |

**Prevalence**
- 0.0-0.4
- 0.5-0.9
- 1.0-1.4

[1]*Pan American Health Organization 2005 & 2009.*[13,14] [2]*Estimates based on unpublished, but publically available data from government reports.*[77] [3]*Secretaría de Vigilancia, 2004.*[75] **See above for references. **Data collection began in 2007. ***Polymerase chain reaction-confirmed positive tests only.*

**Figure 3**. *Prevalence among adult blood donors.*

specific rates of treatment responsiveness for HCV genotype 1.[8] Available data on genotype of infection from representative samples from the countries of Latin America are summarized in Table 3. As expected, the majority of studies found genotype 1 to be the most prevalent, and a large nationally-represen-

tative study from Mexico estimated this frequency at 70%.[10] No estimates of the genotype distribution were identified for Belize, Bolivia, Costa Rica, Ecuador, Guatemala, Guyana, Honduras, Nicaragua, Panama, Paraguay, Suriname, or Uruguay. Assuming that 85% of those infected progressed to chronic

**Table 1.** Prevalence of HCV among adults in the general population, compared to estimates from blood testing networks.*

| Prevalence (%) | Argentina | Brazil | Mexico |
|---|---|---|---|
| General population | 1.3-1.7** [25] | 0.9-1.9** [27] | 1.4 [76]-1.5 [31] |
| Blood donors | 0.4**-1.0 [13] | 0.1 [43]-1.2 [36] | 0.2 [33]-0.8 [45] |

Chilean data not presented because blood donor estimates were not based on ELISA. *Estimates based on unpublished, but publically available data from government reports.[25] **Estimates based on unpublished, but publically available data from government reports.[77]

**Table 2.** Projected number of persons infected with HCV in Latin America, 2010.

| Country | Best prevalence estimate (%) | Total population | Projected HCV population | | |
|---|---|---|---|---|---|
| | | | Midpoint | Lower bound | Upper bound |
| Brazil | 0.9-1.9 [1] | 190,733,000 | 2,670,000 | 1,717,000 | 3,624,000 |
| Mexico | 1.4 [2] | 112,323,000 | 1,573,000 | - | - |
| Colombia | ~1.0-2.0 [4] | 45,877,000 | 688,000 | 459,000 | 918,000 |
| Argentina | 1.3-1.7 [3] | 40,091,000 | 601,000 | 521,000 | 682,000 |
| Peru | ~1.0-2.0 [4] | 29,462,000 | 442,000 | 295,000 | 589,000 |
| Venezuela | ~1.0-2.0 [4] | 29,137,000 | 437,000 | 291,000 | 583,000 |
| Chile | 1.2 [5] | 17,218,000 | 207,000 | - | - |
| Ecuador | ~1.0-2.0 [4] | 13,625,000 | 204,000 | 136,000 | 273,000 |
| Guatemala | ~1.0-2.0 [4] | 13,277,000 | 199,000 | 133,000 | 266,000 |
| Bolivia | ~1.0-2.0 [4] | 10,908,000 | 164,000 | 109,000 | 218,000 |
| Honduras | ~1.0-2.0 [4] | 7,811,000 | 117,000 | 78,000 | 156,000 |
| Paraguay | ~1.0-2.0 [4] | 6,349,000 | 95,000 | 63,000 | 127,000 |
| El Salvador | ~1.0-2.0 [4] | 6,134,000 | 92,000 | 61,000 | 123,000 |
| Nicaragua | ~1.0-2.0 [4] | 5,891,000 | 88,000 | 59,000 | 118,000 |
| Costa Rica | ~1.0-2.0 [4] | 4,254,000 | 64,000 | 43,000 | 85,000 |
| Uruguay | ~1.0-2.0 [4] | 3,494,000 | 52,000 | 35,000 | 70,000 |
| Panama | ~1.0-2.0 [4] | 3,323,000 | 50,000 | 33,000 | 66,000 |
| Guyana | ~1.0-2.0 [4] | 785,000 | 12,000 | 8,000 | 16,000 |
| Suriname | ~1.0-2.0 [4] | 525,000 | 8,000 | 5,000 | 11,000 |
| Belize | ~1.0-2.0 [4] | 333,000 | 5,000 | 3,000 | 7,000 |

Total projected cases: 7,768,000.

HCV: hepatitis C virus. [1]Health Surveillance Secretary, 2007.[27] [2]Valdespino, 2007.[31] [3]Estimates based on unpublished, but publically available data from government reports.[25] [4]Latin American Association for the Study of the Liver (ALEH), 2010.[48] [5]Gonzalez, 2005.[30]

**Table 3.** Frequency (%) of HCV genotypes.

| Country | 1 | 2 | 3 | 4 | Other |
|---|---|---|---|---|---|
| Argentina | 59.1 [78] | 21.7 [78] | 17.8 [78] | 1.3 [78] | 0.0 [78] |
| Brazil | 62.8 [79] - 89.1 [80] | 0.6 [80]-4.6[81] | 10.3 [80] -37.2 [79] | 0.0 [80] -0.2 [81] | 0.0 [80]-0.7 [82] |
| Colombia* | 88.5 [83] | 8.5 [83] | 2.8 [83] | - | 0.2 [83] |
| Mexico | 51.1 [84] - 70.3 [10] | 17.5 [84] - 21.8 [10] | 5.4 [84] - 7.2 [10] | 0.3 [10]-0.0 [84] | 0.4 [10] - 26.2 [84]** |
| Peru | 86.0 [85] | 2.0 [85] | 10.0 [85] | - | 2.0 [85] |
| Venezuela | 70.0 [86] | 26.0 [86] | - | - | 4.0 [86] |

*Estimates are from blood donors. **Also included undefined.

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HCV infection,[22] and that 70% of those have genotype 1 HCV,[10,11] results in an estimated 4.6 million individuals in Latin America projected to have chronic HCV genotype 1 infection (Table 4).

In the primary analysis, the rate of responsiveness measured among Latinos in the LATINO trial (34%) was assumed.[8] Under this assumption, while more than 1.6 million individuals with chronic HCV genotype 1 would be expected to be responsive to currently-available treatments, an estimated 3.1 million would remain without a viable therapeutic option. Even when the maximal 49% responsiveness rate was assumed in sensitivity analysis,[8] while 2.3 million individuals with chronic HCV genotype 1 infection in Latin America would be expected to be responsive to currently-available treatments, approximately 2.4 million would remain without a viable treatment option (Figure 4).

## DISCUSSION

Despite the World Health Organization citing a need to measure the epidemiologic burden of HCV in 2004,[49] we found few robust epidemiologic data from Latin America. Using all available published
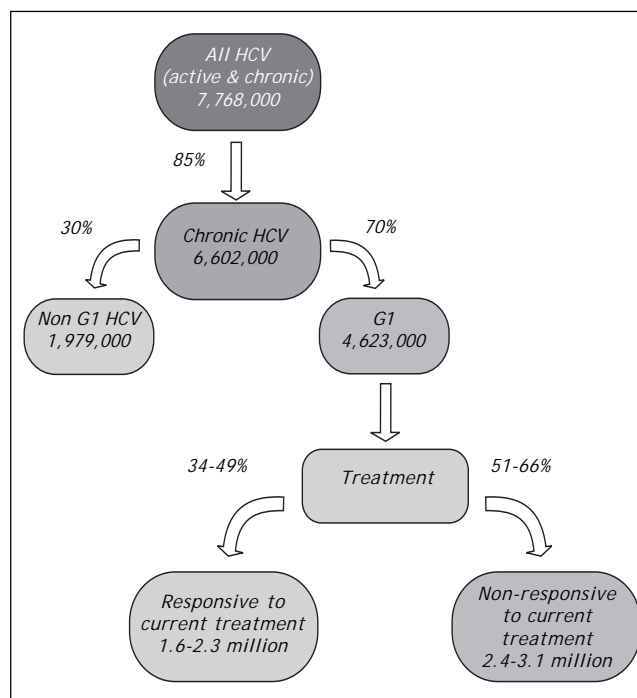


***Figure 4.*** *The potential impact of currently-available treatments on the epidemiologic burden of HCV in Latin America. G1: genotype 1. HCV: hepatitis C virus.*

**Table 4**. The impact of currently-available treatments on the epidemiologic burden.

| Country | Midpoint, prevalence estimate | Chronic HCV cases (85%) | Genotype 1 Chronic HCV cases (70%) | HCV cases responsive to treatment (34%) | Cases remaining (66%) | HCV cases responsive to treatment (49%) | Cases remaining (51%) |
|---|---|---|---|---|---|---|---|
| Brazil | 2,670,000 | 2,270,000 | 1,589,000 | 540,000 | 1,049,000 | 778,000 | 810,000 |
| Mexico | 1,573,000 | 1,337,000 | 936,000 | 318,000 | 618,000 | 459,000 | 477,000 |
| Colombia | 688,000 | 585,000 | 409,000 | 139,000 | 270,000 | 201,000 | 209,000 |
| Argentina | 601,000 | 511,000 | 358,000 | 122,000 | 236,000 | 175,000 | 182,000 |
| Peru | 442,000 | 376,000 | 263,000 | 89,000 | 174,000 | 129,000 | 134,000 |
| Venezuela | 437,000 | 371,000 | 260,000 | 88,000 | 172,000 | 127,000 | 133,000 |
| Chile | 207,000 | 176,000 | 123,000 | 42,000 | 81,000 | 60,000 | 63,000 |
| Ecuador | 204,000 | 173,000 | 121,000 | 41,000 | 80,000 | 59,000 | 62,000 |
| Guatemala | 199,000 | 169,000 | 118,000 | 40,000 | 78,000 | 58,000 | 60,000 |
| Bolivia | 164,000 | 139,000 | 98,000 | 33,000 | 64,000 | 48,000 | 50,000 |
| Honduras | 117,000 | 99,000 | 70,000 | 24,000 | 46,000 | 34,000 | 36,000 |
| El Salvador | 92,000 | 78,000 | 55,000 | 19,000 | 36,000 | 27,000 | 28,000 |
| Paraguay | 95,000 | 81,000 | 57,000 | 19,000 | 37,000 | 28,000 | 29,000 |
| Nicaragua | 88,000 | 75,000 | 52,000 | 18,000 | 35,000 | 26,000 | 27,000 |
| Costa Rica | 64,000 | 54,000 | 38,000 | 13,000 | 25,000 | 19,000 | 19,000 |
| Uruguay | 52,000 | 44,000 | 31,000 | 11,000 | 20,000 | 15,000 | 16,000 |
| Panama | 50,000 | 43,000 | 30,000 | 10,000 | 20,000 | 15,000 | 15,000 |
| Guyana | 12,000 | 10,000 | 7,000 | 2,000 | 5,000 | 3,000 | 4,000 |
| Suriname | 8,000 | 7,000 | 5,000 | 2,000 | 3,000 | 2,000 | 2,000 |
| Belize | 5,000 | 4,000 | 3,000 | 1,000 | 2,000 | 1,000 | 2,000 |
| | 7,768,000 | 6,602,000 | 4,623,000 | 1,571,000 | 3,051,000 | 2,264,000 | 2,358,000 |

HCV: hepatitis C virus.

estimates as well as unpublished data identified by an iterative comprehensive review, we projected the prevalence of chronic HCV infection in Latin America at over 6.6 million individuals. In absolute terms, the challenge is most acute in Brazil and Mexico, with over four million individuals infected with HCV in those two countries alone. Based on the distribution of genotype in the region, we estimated that while between 1.6 and 2.3 million individuals living with chronic HCV infection could potentially be responsive to currently-available treatments, an additional 2.4 to 3.1 million individuals infected would be non responsive. The estimates of the epidemiologic burden calculated here are broadly consistent with those from other investigators,[50,51] as well as a recent review of the prevalence of HCV from selected countries in Latin America and the Caribbean.[6] We extended upon the latter study's findings by synthesizing epidemiologic data for the entire region, estimating country-specific parameters, and assessing the potential impact of currently-available treatments on the present epidemiologic burden.

To help quantify the consequences of present HCV infections in Latin America, we synthesized data on the distribution of genotype of HCV infections in Latin America, as this is a known predictor of treatment responseiveness.[7] As expected, genotype 1 was the predominant form of HCV infection in Latin America; most studies estimated the proportion of cases with genotype 1 HCV at between 65 and 75%.[10,11] We then applied genotype 1-specific effectiveness rates associated with pegylated interferon with ribavirin, to quantify the potential impact of currently-available (and reimbursed) treatments[48,52] on the epidemiologic burden of HCV in Latin America. The overall rates of sustained viral response after pegylated interferon and ribavirin range between approximately 35% and 50% for HCV genotype 1,[8,53,54] however responsiveness may be lower for Latin Americans. While the LATINO study reported responsiveness rates of 49% among non-Latino whites and 34% among Latino whites with HCV genotype 1,[8] other studies conducted among predominantly Latino populations have reported rates as low as 24%.[55,56] Using the responsiveness rates from the LATINO study, we estimated that between 1.6 and 2.3 million individuals with HCV in Latin America could potentially benefit from currently-available treatments, although an additional 2.4 to 3.1 million individuals infected would remain without a viable treatment.

Understanding the epidemiologic, and attendant economic, burden of HCV is challenging, as infection is largely asymptomatic until late in the disease course for most individuals afflicted,[5] and only a subset of patients progress to severe liver disease.[22] The present economic burden of HCV is predominantly driven by treating identified cases to prevent severe liver disease, however, the future economic burden will include treating severe liver disease among those who have progressed. In Canada and the United States, an exponential increase in the incidence of severe liver disease over the next two decades has been predicted; and the same for the attendant economic burden of HCV.[57,58] While no robust economic data are available for Latin America, the situation is likely even more grave, given the high rates of comorbid metabolic disease which would make achieving a sustained viral response among those with HCV difficult.[59]

Despite there being few data to assess the future burden of present HCV infections,[9,58] there are some clues by which this may be imputed. While injection drug use is now the primary risk factor for acquiring HCV,[60] transfusion prior to the widespread testing of the blood supply in the mid-1990s remains the primary known risk factor for most Latin Americans already infected.[61,62] Indeed, studies from Brazil and Argentina have suggested transfusions to be causative in about one third of those patients,[6,23,63] and one half to three quarters of those infected in Mexico and Chile.[30,64,65] Such individuals would have become infected with HCV up to 20 years ago, and would therefore be at higher risk of progression to severe liver disease. When we consider that at least 2.4 million Latin Americans are infected with genotype 1 HCV and would not be responsive to available treatments, and assuming that at least one third of these were infected by transfusion, would mean that there are approximately 800,000 infected individuals at risk of developing severe liver disease over the next few years. Exact estimates of the risk of progression to severe liver disease due to HCV infection are variable,[55,64,66] and challenging to derive given that the exact time of infection is often unknown. However, as treatment for severe liver disease is costly –from $4,300 to $30,000 (USD, 2009) per year depending on severity –these individuals will contribute a substantial burden to the health care systems in the near future.[67]

This review and synthesis is useful for identifying where more information is needed. The lack of country-specific population-based prevalence data on HCV infection in Latin America limits precise estimates of the true HCV burden.[49] Although HCV prevalence estimates from blood donors were readily

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available, these have limited utility as they underestimate the true prevalence of HCV. This is not unexpected, as blood donors tend to be healthier than other subgroups of the population[68] and prescreening practices would eliminate potential donors at higher risk of HCV infection.[69] Nonetheless, these data can serve as a basis for comparing subsequent measures obtained from similar populations and tested under the same conditions; and therefore are useful for determining epidemiologic trends to infection.

In this review, Mexico was the only Latin American country with published population-based estimates at the national level.[31,70] In the absence of published national estimates, regional general population prevalence estimates were incorporated, but these estimates were variable;[28,29,71-73] due both to the varying distribution of risk factors for HCV infection, but also due to differences in the design of the studies that reported them. We approximated the epidemiologic burden based on the midpoint of available estimates for countries where specific estimates were not available, and a similar strategy may be used to inform estimates for the Caribbean nations that were not included in the present review. While likely broadly reflective, these projections may under or overestimate the country-specific burden, depending on the risk factor composition of each country. Finally, genetic variation in interleukin-28b is also a known predictor of treatment responsiveness,[74] and would also be expected to impact the epidemiologic burden of HCV in Latin America. The impact of interleukin-28b was not incorporated here, however, as beyond preliminary investigations among Latin Americans with European ancestry, little is known about the distribution of variants in Latin American populations.[75]

The absence of general-population based estimates for many Latin American countries, as well as the discrepancies between blood donor and general-population estimates highlight the need for additional, methodologically-rigorous studies of the epidemiologic and clinical burden to inform decision-makers in Latin America. Nonetheless, the projections indicate that the current, and impending, epidemiologic, clinical, and likely economic burden of HCV infection in Latin America is substantial. We estimated that 7.8 million individuals in Latin America would be infected with HCV, 4.6 million with the genotype 1 form. Of these, between 1.6 and 2.3 million individuals could benefit from currently-available treatments, although the remaining 2.4 to 3.1 million individuals with HCV genotype 1 in Latin America would not presently have a viable treatment option. These estimates may be useful in quantifying the growing societal and clinical burden due to HCV infection, and to identify subgroups of the population that are potential targets for new treatments that include direct-acting antivirals and improved interferons.

## ABBREVIATIONS

- **HCV:** Hepatitis C virus.

## FINANCIAL SUPPORT

## REFERENCES

1. World Health Organization. Hepatitis C: Fact Sheet No. 164. World Health Organization 2011; Available from: http://www.who.int/mediacentre/factsheets/fs164/en/index.html
2. Lauer GM, Walker BD. Hepatitis C virus infection. *N Engl J Med* 2001; 345: 41-52.
3. US Department of Health and Human Services. Centers for Disease Control and Prevention. Recommendations for Prevention and Control for Hepatitis C Virus (HCV) Infection and HCV Related Chronic Disease. 1998. Report No.: 47.
4. Torresi J, Johnson D, Wedemeyer H. Progress in the development of preventive and therapeutic vaccines for hepatitis C virus. *J Hepatol* 2011.
5. American Association for the Study of Liver Disease (AASLD). HBV & HCV: America's Hidden Epidemics. 2010 Jan 9.
6. Kershenobich D, Razavi HA, Sanchez-Avila JF, Bessone F, Coelho HS, Dagher L, Goncales FL, et al. Trends and projections of hepatitis C virus epidemiology in Latin America. *Liver Int* 2011; 31(Suppl. 2): 18-29.
7. Te HS, Jensen DM. Epidemiology of hepatitis B and C viruses: a global overview. *Clin Liver Dis* 2010; 14: 1-21, vii.
8. Rodriguez-Torres M, Jeffers LJ, Sheikh MY, Rossaro L, Ankoma-Sey V, Hamzeh FM, Martin P. Peginterferon alfa-2a and ribavirin in Latino and non-Latino whites with hepatitis C. *N Engl J* 2009; 360: 257-67.
9. Dehesa-Violante M, Nunez-Nateras R. Epidemiology of Hepatitis Virus B and C. *Archives of Medical Research* 2007; 38: 606-11.
10. Jiménez-Méndez R, Uribe-Salas F, López-Guillen P, Cisneros-Garza L, Castaneda-Hernandez G. Distribution of HCV genotypes and HCV RNA viral load in different regions of Mexico. *Ann Hepatol* 2010; 9: 33-9.
11. Sanchez-Avila JF, Gonzalez E, Vazquez V, Suarez S, Uribe M. Geographical distribution of HCV genotypes in Mexico. *Ann Hepatol* 2007; 6: 156-60.
12. Kwo PY. Response-guided Therapy for HCV. *Gastroenterology and Hepatology* 2011; 7: 43-5.
13. Pan American Health Organization. Supply of blood for transfusion in the Caribbean and Latin American countries in 2006 and 2007: Progress since 2005 of the Regional Plan of Action for Transfusion Safety. 2009.

14. Pan American Health Organization (PAHO) Technology and Health Services Delivery Area. Essential Medicines VaHT. Supply of blood for transfusion in the Caribbean and Latin American countries in 2005: Base line data for the Regional Plan of Action for Transfusion Safety 2006-2010. Washington, DC: PAHO; 2005.

15. Ministerio de Salud. Ministry of Health, Argentina. Ministerio de Salud 2011. Available from: http://www.msal.gov.ar/htm/site/Default.asp

16. Dirección de Estadística e Información de Salud. Sistema Nacional de Vigilancia Epidemiológica, SINAVE. Dirección de Estadística e Información de Salud 2011. Available from: http://www.msal.gov.ar/htm/site/estadisticas.asp

17. Agencia Nacional de Vigilancia Sanitaria. National Agency for Health Surveillance (ANVISA). Agencia Nacional de Vigilancia Sanitaria 2011. Available from: http://websphere.anvisa.gov.br/wps/portal/anvisa/home/!ut/p/c5/04_SB8K8xLLM9MSSzPy8xBz9CP0os3hnd0cPE3MfAwMDMydnA093Uz8z00B_AwN_Q_1wkA48Kowg8gY4gKOBvp9Hfm6qfkF2dpqjo6liAJYj_8M!/dl3/d3/L2dBISEvZ0FBIS9nQSEh/

18. Information System of Notifiable Diseases. Sistema de Informação de Agravos de Notificação (SINAN). Information System of Notifiable Diseases 2011. Available from: http://dtr2004.saude.gov.br/sinanweb/index.php

19. Vivas-Arceo C, Benavides SA, De Jesus TJ, Panduro A, Rivas-Estilla AM. Hepatitis C virus: Prevalence and routes of infection among blood donors of West Mexico. *Hepatology Research* 2003; 25: 115-23.

20. Instituto Nacional de Salud Pública de México. Encuesta Nacional de Salud y Nutrición-ENSANUT 2006. Instituto Nacional de Salud Pública de México 2010. Available from: URL: http://www.insp.mx/ensanut/

21. Encuesta Nacional de Salud (ENSA) Instituto Nacional de Salud Pública (INSP). ENSA 2000, national results, data on file. 2000.

22. Hoofnagle JH. Course and outcome of hepatitis C. Hepatology 2002 November; 36(5 Suppl. 1): S21-S29.

23. Insua JT, O'Flaherty M, Frontera Vacca MJ, Camino A, Maria Pia R, Silva M. HCV infection prevalence in Argentine and impact of unsage health care parenteral practices (HC-UPP): a seroprevalence survey. Society of General Internal Medicine 28th Annual General Meeting. 2003.

24. El KM, Cordeiro Q, Da Luz DABP, Duarte LS, Gama MEA, Corbett CEP. Endemic hepatitis B and C virus infection in a Brazilian Eastern Amazon region. *Arquivos de Gastroenterologia* 2010; 47: 35-41.

25. Ministerio de Salud. Implementación de unidades centinela: Hepatitis virales. 2002.

26. Ximenes RA, Pereira LM, Martelli CM, Merchan-Hamann E, Stein AT, Figueiredo GM, Braga MC, et al. Methodology of a nationwide cross-sectional survey of prevalence and epidemiological patterns of hepatitis A, B and C infection in Brazil. *Cad Saude Publica* 2010; 26: 1693-704.

27. Ministerio da Saude. Secretaría de Vigilancia em Saude. Departmento de DST A. Brazil. Health Ministry. Health Surveillance Secretary. Department of STDs, AaVH, Brazil. 2010.

28. Focaccia R, Conceicao O, Sette H, Sabino E, Bassit L, Nitrini D, et al. Estimated prevalence of viral hepatitis in the general population of the municipality of São Paulo, measured by a serologic survey of a stratified, randomized and residence-based population. *Brazilian J Infectious Diseases* 1998; 2: 269-84.

29. Zarife MA, Silva LK, Silva MB, Lopes GB, Barreto ML, Teixeira MG, Dourado I, Reis MG. Prevalence of hepatitis C virus infection in north-eastern Brazil: a population-based study. *Trans R Soc Trop Med Hyg* 2006; 100: 663-8.

30. Gonzalez R, Soza A, Hernandez V, Perez RM, Alvarez M, Morales A, Arellano M, et al. Incidence and prevalence of hepatitis C virus infection in Chile. *Ann Hepatol* 2005; 4: 127-30.

31. Valdespino JL, Conde-Gonzalez CJ, Olaiz-Fernandez G, Palma O, Kershenobich D, Sepulvida J. Seroprevalencia de la hepatitis C en adultos de México: un problema de salud pública emergente. *Sal Pub Mex* 2007; 49: S395-S403.

32. Méndez-Sánchez N, Ponciano-Rodríguez G, Chávez-Tapia NC, Motola-Kuba D, Meda-Valdes P, Sanchez-Lara K, Ramos MH, Uribe M. Prevalence of hepatitis C infection in a population of asymptomatic people in a checkup unit in Mexico city. *Digestive Diseases & Sciences* 2005; 50: 733-7.

33. Benitez-Arvizu, Cortez-Gómez R, Novelo-Garza B, Malagon-Martínez A, Guerra-Márquez A, Alvarado-Maldonado M, et al. Prevalencia del virus de hepatitis C: en el banco de sangre del Centro Médico Nacional La Raza. *Rev Med IMSS* 2005; 44: 227-33.

34. García FB, Pereira GA, Martins PR, Moraes-Souza H. Epidemiological profile of hepatitis C in blood donors at the Uberaba Regional Blood Center. *Revista Da Sociedade Brasileira de Medicina Tropical* 2009; 42: 1-4.

35. Andrade AF, Oliveira-Silva M, Silva SG, Motta IJ, Bonvicino CR. Seroprevalence of hepatitis B and C virus markers among blood donors in Rio de Janeiro, Brazil, 1998-2005. Memorias do Instituto Oswaldo Cruz 2006 September; 101: 673-6.

36. Valente VB, Covas DT, Passos AD. Hepatitis B and C serologic markers in blood donors of the Ribeirao Preto Blood Center. [Portuguese]. *Revista Da Sociedade Brasileira de Medicina Tropical* 2005; 38: 488-92.

37. Salles NA, Sabino EC, Barreto CC, Barreto AM, Otani MM, Chamone DF. The discarding of blood units and the prevalence of infectious diseases in donors at the Pro-Blood Foundation/Blood Center of Sao Paulo, Sao Paulo, Brazil. [Portuguese]. *Pan American Journal of Public Health* 2003; 13: 111-6.

38. Rosini N, Mousse D, Spada C, Treitinger A. Seroprevalence of HbsAg, Anti-HBc and anti-HCV in Southern Brazil, 1999-2001. *Brazilian J Infectious Diseases* 2003; 7: 262-7.

39. Oliveira-Filho AB, Pimenta AS, Rojas MF, Chagas MC, Crescente JA, Crespo DM, Lemos JA. Prevalence and genotyping of hepatitis C virus in blood donors in the state of Para, Northern Brazil. *Mem Inst Oswaldo Cruz* 2010; 105: 103-6.

40. Torres K, Tateno A, Lima T, Malheiro A, Morais M, Levi J, et al. Characterization of hepatitis C virus infection in Amazon blood donors, Brazil. *Vox Sanguinis* 2010; 99(Supp. 1): 297.

41. de Almeida Neto C, Sabino E, Liu J, Mendrone-Junior A, Salles N, Barros E, et al. Current prevalence and incidence of serologic markers for hepatitis C and prevalence of HBsAg among blood donors in Brazil. *Transfusion* 2010; 50(Suppl.): 202A.

42. Nascimento MC, Mayaud P, Sabino EC, Torres KL, Franceschi S. Prevalence of hepatitis B and C serological markers among first-time blood donors in Brazil: A multi-center serosurvey. *J Medical Virology* 2008; 80: 53-7.

43. Levi J, Wendel S, Takaoka D, Foglietto M. Results of routine screening of Brazilian blood donors with the Roche Cobas S 201/TAQSCREEN MPX System. *Vox Sanguinis* 2010; 99(Suppl. 1): 88.

44. Rivera-Lopez MR, Zavala-Mendez C, Renas-Esqueda A. Prevalence for seropositivity for HIV, hepatitis B and hepatitis C in blood donors. [Spanish]. *Gaceta Médica de México* 2004;140: 657-60.

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45. Sosa-Jurado F, Santos-López G, Guzmán-Flores B, Ruiz-Conde JI, Meléndez-Mena D, Vargas-Maldonado MT, Martinez-Laguna Y, et al. Hepatitis C virus infection in blood donors from the state of Puebla, Mexico. *Virol J* 2010; 7: 18.

46. Vazquez-Flores JA, Valiente-Banuet L, Lopez RA, Sanchez-Guerrero SA. Safety of the blood supply in Mexico from 1999 to 2003. [Spanish]. *Rev Invest Clin* 2006; 58: 101-8.

47. Farfan G, Cabezas C. Prevalence of viral hepatitis type C in blood donors in Peru. [Spanish]. *Rev Gastroenterol Peru* 2003; 23: 171-6.

48. Latin American Association for the Study of the Liver Practice Guidelines. Diagnosis, management, and treatment of hepatitis C. *Ann Hepatol* 2010; 9(Suppl.): 8-26.

49. The Global Burden of Hepatitis. Global Burden of Disease (GBD) for Hepatitis C. *J Clin Pharmacol* 2004; 44: 20-9.

50. Mendez-Sanchez N, Gutierrez-Grobe Y, Kobashi-Margain RA. Epidemiology of HCV infection in Latin America. *Ann Hepatol* 2010; 9(S1): S27-S29.

51. Dávalos Moscol M. Epidemiology of hepatitis C virus in Peru and Latin America [Spanish]. *Rev Gastroenterol Peru* 2009; 29: 347-54.

52. Jimenez-Mendez R, Castaneda-Hernandez G. Characteristics of hepatitis C treatment with pegylated interferons and ribavirin. *Ann Hepatol* 2010; 9(Suppl.): 61-4.

53. Manns MP, McHutchison JG, Gordon SC, Rustgi VK, Shiffman M, Reindollar R, Goodman ZD, et al. Peginterferon alfa-2b plus ribavirin compared with interferon alfa-2b plus ribavirin for initial treatment of chronic hepatitis C: a randomised trial. *The Lancet* 2001; 358(9286): 958-65.

54. Fried MW, Shiffman ML, Reddy KR, Smith C, Marinos G, Goncales FL Jr., Haussinger D, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* 2002; 347: 975-82.

55. Hepburn MJ, Hepburn LM, Cantu NS, Lapeer MG, Lawitz EJ. Differences in treatment outcome for hepatitis C among ethnic groups. *Am J Med* 2004; 117: 163-8.

56. Munoz H, Arroyo J, Torres EA, De Jesus-Monge WE, Chinea B, Gonzalez H, Aponte N, et al. Response to combination therapy of interferon alfa-2b plus ribavirin in Hispanics with chronic hepatitis C. *PR Health Sci J* 2004; 23(2 Suppl.): 61-7.

57. El SS, Coyle D, Giulivi A, Afzal M. Economic burden of hepatitis C in Canada and the potential impact of prevention: Results from a disease model. *European J Health Economics* 2005; 6: 159-65.

58. Wong JB, McQuillan GM, McHutchison JG, Poynard T. Estimating future hepatitis C morbidity, mortality, and costs in the United States. *Am J Public Health* 2000; 90: 1562-9.

59. Hanouneh IA, Feldstein AE, Lopez R, Yerian L, Pillai A, Zein CO, Zein NN. Clinical significance of metabolic syndrome in the setting of chronic hepatitis C virus infection. *Clin Gastroenterol Hepatol* 2008; 6: 584-9.

60. Lelutiu-Weinberger C, Pouget ER, Des Jarlais DD, Cooper HL, Scheinmann R, Stern R, et al. A meta-analysis of the hepatitis C virus distribution in diverse racial/ethnic drug injector groups. *Social Science & Medicine* 2009; 68: 579-90.

61. Schmunis GA, Cruz JR. Safety of the blood supply in Latin America. *Clin Microbiol Rev* 2005;18: 12-29.

62. Schmunis GA, Zicker F, Pinheiro F, Brandling-Bennett D. Risk for transfusion-transmitted infectious diseases in Central and South America. *Emerg Infect Dis* 1998; 4: 5-11.

63. Cavalheiro NP, Barone AA, Tengan FM. HCV serotypes in Brazilian patients. *Int J Infect Dis* 2002; 6: 228-32.

64. Soza A, Arrese M, Gonzalez R, Alvarez M, Perez RM, Cortes P, Patillo A, et al. Clinical and epidemiological features of 147 Chilean patients with chronic hepatitis C. *Ann Hepatol* 2004; 3: 146-51.

65. Rivas-Estilla AM, Cordero-Perez P, Trujillo-Murillo KDC, Ramos-Jimenez J, Chen-Lopez C, Garza-Rodriguez MDL, Ramirez-Gutierrez A, Munoz-Espinosa L. Genotyping of hepatitis C virus (HCV) in infected patients from Northeast Mexico. *Ann Hepatol* 2008; 7: 144-7.

66. Fattovich G, Giustina G, Degos F, Tremolada F, Diodati G, Almasio P, Nevens F, et al. Morbidity and mortality in compensated cirrhosis type C: a retrospective follow-up study of 384 patients. *Gastroenterology* 1997; 112: 463-72.

67. Quiroz ME, Flores YN, Aracena B, Granados-Garcia V, Salmeron J, Perez R, Cabrera G, et al. Estimating the cost of treating patients with liver cirrhosis at the Mexican Social Security Institute. *Sal Pub Mex* 2010; 52: 493-501.

68. Merk K, Mattsson B, Mattsson A, Holm G, Gullbring B, Bjorkholm M. The incidence of cancer among blood donors. *Int J Epidemiol* 1990; 19: 505-9.

69. Ashour D, Moftah F, Gobran H, Ekram D. Decreasing the risk of transfusion transmitted infections (TTIS) in the Egyptian Blood Transfusion Services. Vox Sanguinis Conference: 19th Regional Congress of the ISBT-Eastern Mediterreanean and Europe Cairo Egypt Conference Start: 20090321 Conference End: 20090325 Conference: 19th Regional Congress of the ISBT-Eastern Mediterreanean and Europe Cairo Eg 2009; (var. pagings): 103-4.

70. Burguete-Garcia AI, Conde-Gonzalez C, Jimenez-Mendez R, Juarez-Diaz Y, Meda-Monzon E, Torres-Poveda K, et al. Hepatitis C seroprevalence and correlation between viral load and viral genotype among primary care clients in Mexico. *Sal Pub Mex* 2011; 53(Suppl. 1): S7-S12.

71. El KM, Cordeiro Q, Luz DA, Duarte LS, Gama ME, Corbett CE. Endemic hepatitis B and C virus infection in a Brazilian Eastern Amazon region. *Arq Gastroenterol* 2010; 47: 35-41.

72. Aquino JA, Pegado KA, Barros LP, Machado LF. Seroprevalence of hepatitis B virus and hepatitis C virus infections among individuals in the State of Para. [Portuguese]. *Revista Da Sociedade Brasileira de Medicina Tropical* 2008; 41: 334-7.

73. Ivantes CA, Silva D, Messias-Reason I. High prevalence of hepatitis C associated with familial history of hepatitis in a small town of south Brazil: efficiency of the rapid test for epidemiological survey. *Braz J Infect Dis* 2010; 14: 483-8.

74. Gonzalez SA, Keeffe EB. IL-28B As a Predictor of Sustained Virologic Response in Patients with Chronic Hepatitis C Virus Infection. *Gastroenterol Hepatol (NY)* 2011; 7: 366-73.

75. Ridruejo E, Solano A, Marciano S, Galdame O, Adrover R, Cocozzella D, Delettieres D, et al. Genetic variation in interleukin-28B predicts SVR in hepatitis C genotype 1 Argentine patients treated with PEG IFN and ribavirin. *Ann Hepatol* 2011; 10: 452-7.

76. Burguete-Garcia A, Conde-Gonzalez C, Jimenez-Mendez R, Juarez-Diaz Y, Meda-Monzon E, Torres-Poveda K, et al. Hepatitis C virus surveillance study among primary care attention clients in Mexico: A public health opportunity for an emerging disease. *Pharmacoepidemiology and Drug Safety* 2011; 20: S186-187.

77. Malbran C. Taller de Actualización en Hepatitis virales: ¿El conocimiento actual es aplicable en Argentina? Malbran C 2010; Available from: http://www.hepatitisviral.com.ar/presentaciones/reunion_19/101018epidanlis.ppt.

78. Ridruejo E, Adrover R, Cocozzella D, Fernandez N, Reggiardo MV. Efficacy, tolerability and safety in the treatment of chronic hepatitis C with combination of PEG-Interferon-Ribavirin in daily practice. *Ann Hepatol* 2010; 9: 46-51.

79. Lampe E, Espirito-Santo MP, Martins RM, Bello G. Epidemic history of Hepatitis C virus in Brazil. *Infect Genet Evol* 2010; 10: 886-95.

80. Sawada L, Pinheiro AC, Locks D, Pimenta AS, Rezende PR, Crespo DM, Crescente JA, et al. Distribution of hepatitis C virus genotypes among different exposure categories in the State of Para, Brazilian Amazon. *Rev Soc Bras Med Trop* 2011; 44:8-12.

81. Campiotto S, Pinho JRR, Carrilho FJ, Da Silva LC, Souto FJD, Spinelli V, Pereira LMMB, et al. Geographic distribution of hepatitis C virus genotypes in Brazil. *Brazilian J Medical and Biological Research* 2005; 38: 41-9.

82. Romano CM, de Carvalho-Mello IM, Jamal LF, de Melo FL, Iamarino A, Motoki M, Pinho JR, et al. Social networks shape the transmission dynamics of hepatitis C virus. *PLoS ONE* 2010; 5: e11170.

83. Mora MV, Romano CM, Gomes-Gouvea MS, Gutierrez MF, Carrilho FJ, Pinho JR. Molecular characterization, distribution, and dynamics of hepatitis C virus genotypes in blood donors in Colombia. *J Med Virol* 2010; 82: 1889-98.

84. Burguete-Garcia AI, Conde-Gonzalez C, Jimenez-Mendez R, Juarez-Diaz Y, Meda-Monzon E, Torres-Poveda K, Madrid-Marina V. Hepatitis C seroprevalence and correlation between viral load and viral genotype among primary care clients in Mexico. *Sal Pub Mex* 2011; 53(Supl. 1): S7-S12.

85. Sanchez JL, Sjogren MH, Callahan JD, Watts DM, Lucas C, Abdel-Hamid M, Constantine NT, et al. Hepatitis C in Peru: risk factors for infection, potential iatrogenic transmission, and genotype distribution. *Am J Trop Med Hyg* 2000; 63: 242-8.

86. Pujol FH, Loureiro CL. Replacement of hepatitis C virus genotype 1b by genotype 2 over a 10-year period in Venezuela. *J Clinical Gastroenterology* 2007; 41: 518-20.

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**Appendix 1.** Search strategy.

| | | |
|---|---|---|
| 1 | Exp hepatitis C/or exp hepatitis C virus/ | 109556 |
| 2 | exp INCIDENCE/ | 340425 |
| 3 | exp PREVALENCE/ | 406350 |
| 4 | exp EPIDEMIOLOGY/ | 1226445 |
| 5 | or/2-4 | 1498788 |
| 6 | 1 and 5 | 19651 |
| 7 | exp Hepatitis C/ | 91455 |
| 8 | (hepatitis adj c).mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 121802 |
| 9 | (hepacvirus or hepatitis-c or HCV).mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 128013 |
| 10 | ("chronic hepatitis" adj5 c).mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 26998 |
| 11 | or/7-10 | 128384 |
| 12 | exp incidence/ | 340425 |
| 13 | exp prevalence/ | 406350 |
| 14 | exp epidemiology/ | 1226445 |
| 15 | or/12-14 | 1498788 |
| 16 | 11 and 15 | 22491 |
| 17 | 6 or 16 | 22496 |
| 18 | limit 17 to yr = "1995-current" | 20666 |
| 19 | 18 and mexic $.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 168 |
| 20 | remove duplicates from 19 | 127 |
| 21 | 18 and brazi$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 435 |
| 22 | remove duplicates from 21 | 342 |
| 23 | 18 and argentin$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 88 |
| 24 | remove duplicates from 23 | 69 |
| 25 | 18 and colombia$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 26 |
| 26 | remove duplicates from 25 | 17 |
| 27 | 18 and peru$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 34 |
| 28 | remove duplicates from 27 | 27 |
| 29 | 18 and venezuel$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 37 |
| 30 | remove duplicates from 29 | 27 |
| 31 | 18 and ecuad$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 10 |
| 32 | remove duplicates from 31 | 6 |
| 33 | 18 and chile$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 26 |
| 34 | remove duplicates from 33 | 16 |
| 35 | 18 and urugua$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 11 |
| 36 | remove duplicates from 35 | 8 |
| 37 | 18 and paragua$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 4 |
| 38 | remove duplicates from 37 | 2 |
| 39 | 18 and boliv$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 9 |
| 40 | remove duplicates from 39 | 6 |
| 41 | 18 and guyan$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 0 |
| 42 | 18 and surinam$.mp. [mp=ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 2 |
| 43 | remove duplicates from 42 | 2 |
| 44 | 18 and hondura$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 5 |
| 45 | remove duplicates from 43 | 4 |
| 46 | 18 and beliz$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 2 |
| 47 | remove duplicates from 45 | 1 |
| 48 | 18 and guatemal$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 2 |
| 49 | remove duplicates from 47 | 1 |
| 50 | 18 and el salvad$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 5 |
| 51 | remove duplicates from 49 | 4 |
| 52 | 18 and costa rica$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 4 |
| 53 | remove duplicates from 51 | 3 |
| 54 | 18 and panam$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 0 |
| 55 | 18 and nicaragu$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 9 |
| 56 | remove duplicates from 54 | 6 |
| 57 | 18 and south americ$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 67 |
| 58 | remove duplicates from 56 | 55 |
| 59 | 18 and latin americ$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 58 |
| 60 | remove duplicates from 58 | 45 |
| 61 | 18 and central americ$.mp. [mp = ti, ab, sh, hw, tn, ot, dm, mf, ps, rs, nm, ui] | 36 |
| 62 | remove duplicates from 60 | 32 |

**Appendix 2.** Estimates of the prevalence of HCV among adults from the general population.

| Country | Sample | HCV Measure | Year of data collection | Prevalence (%) |
|---|---|---|---|---|
| **Published studies** | | | | |
| Brazil | • 5,542 serological samples from the state of Para (> 6 million residents in 2000), tested by the Viral Hepatitis, Division of Medical Biology laboratory.[72] | ELISA *(Teknika version 4.0)*, LIA *(Teknika version 3.0)* | 2002-2005 | 3.6 |
| | • A random sample (n = 1,059) from the municipality of Sao Paulo (> 10 million residents in 2000).[28] | Not specified | 1999 | 1.4 |
| | • A convenience sample of 243 patients at one of 13 health care units in Buriticupu (> 63,000 residents in 2010).[71] | ELISA *(Hemagen)* | 2010 | 5.8 |
| | • A cross-sectional survey of 816 residents of Tamboara (population, < 5,000 in 2010), a town with high endemicity of HCV infection.[73] | HCV rapid test *(Bioeasy)*, PCR *(Roche version 2.0)*, CIA *(Abbott)* | 2007 | 4.3 |
| | • A random sample of 1,308 residents from one of the 30 sentinel areas in the city of Salvador (2.3 million residents in 1998).[29] | ELISA *(Abbott)*, RIBA *(Chrion version 3.0)*, PCR *(unspecified)* | 1998 | 1.5 |
| Chile | • A random sample of 959 residents from La Florida, Santiago (~329,000 residents in 1992).[30] | ELISA *(Abbott version 3.0)*, RIBA *(Chiron version 3.0)*, PCR *(Roche version 2.0)* | 1993 | 1.2 |
| Mexico | • A consecutive sample of 20,534 patients with > 1 risk factor for HCV seeking care at 4 family medicine clinics of the Instituto Mexicano del Seguro Social (Mexican Social Security Institute), covering ~50% of individuals with private insurance (or > 25 million Mexicans in 2006).[76] | ELISA *(unspecified)* PCR *(unspecified)* | 2006-2007 | 1.5 |
| | • 300 consecutive patients attending a family practice unit in Mexico City (> 17 million residents in 2003).[32] | PCR *(Roche version 2.0)* | 2003 | 2.0 |
| | • The National Health Survey (Encuesta Nacional de Salud); a random sample of 21,271 residents from throughout Mexico (> 100 million residents in 2000).[31] | ELISA *(Abbott version 3.0)*, RIBA *(Roche)*, RT-PCR *(Roche)* | 2000 | 1.4 |
| **Publically available unpublished data** | | | | |
| Brazil | • A cross-sectional national survey of 31,000 residents aged 10 to 60 years, from Brazilian State capitals and the Federal District.*[27] | ELISA *(Abbott version 3.0)*, PCR *(unspecified)* | 2005-2009 | 0.9 – 1.9 |
| Argentina | • The Sistema Nacional de Vigilancia Epidemiológica passive surveillance system, composed of sentinel health units that report newly identified cases of HCV, in Argentina (> 36 million residents in 2000).** | ELISA *(unspecified)*, RT-PCR *(unspecified)* | 2000-2001 | 1.3 – 1.7 |
| | • A cluster survey of Derqui residents (population, 5,500 in 2003), a representative community of Buenos Aires province.[23] | ELISA *(unspecified)* | 2003 | 0.9 |

CIA: chemiluminescence immunoassay. ELISA: enzyme-linked immunosorbent assay. HCV: hepatitis C virus. LIA: line immunoassay. PCR: polymerase chain reaction. RT: reverse transcriptase. RIBA: recombinant immunoblot assay. *Methods published in Ximenes, 2010.[26] **Estimates based on unpublished, but publically available data from government reports.[25]