The Connection Between Human and Companion Animal Diabetes

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Honors Capstone

May 11, 2021

In the United States, nearly one and a half million people are diagnosed with diabetes each year (Statistics About Diabetes). This contributes to the 10.5% of our population or 34.2 million Americans that have diabetes. With millions of people being affected by diabetes, it is no wonder it is such a popular area of research. Lots of people are also affected by diabetes less directly. This can be through the owning of a companion animal that has diabetes. In the United States, cats and dogs are the most common companion animals. 38.4% of households own at least one cat and 35.4% of households own at least one dog. Together, these two groups create much of the diabetic burden faced in the United States. Research on these topics is of great importance because diabetes is becoming more prevalent in both humans and companion animals.

In the past thirty years, there have been alarming increases in the number of both humans and animals that have diabetes. Globally the diabetic burden has increased greatly with the incidence rate in humans going from 11.3 million people in 1990 to 22.9 million people in 2017 (Lin et al., 2020). The prevalence rate of diabetes has also increased in humans during this time from 211.2 million to 476 million (Lin et al., 2020). It has been predicted that this trend will continue similarly over the coming years. Similar increases have been seen in companion animals as well. In 1990, the prevalence of feline diabetes in North America was 1 in 400 cases. In 2007, just 17 years later, this prevalence doubled to approximately 1 in 200 cases. Canine diabetes shows a very similar prevalence to feline diabetes at 0.32-0.64%, which equates to 1 in 156.25 to 312.5 cases. While the increases on the companion animal side of this issue are not on the same scale, they show that prevalence increases in diabetes can be seen on a more universal scale.

Both diabetics and owners of diabetic animals alike face many challenges associated with this disease. While there has been much research done on diabetes in both humans and companion animals, one area that has not been particularly studied is how there might be a

connection between companion animals and humans in diabetes research. With diabetes becoming more prevalent in both humans and companion animals, one could see that combining research on these species might help us to come up with better treatment options for all. With how much research has been done on diabetes in humans though, it can be questioned why one would even investigate research about diabetic companion animals. This question can be answered in part by how research into companion animals might offer a new perspective to those trying to decide what the best options for humans are. With there being many similarities between diabetes in these two groups, studying the advances in one and applying it to the other could offer breakthroughs that would have otherwise taken much longer to get to. When looking at the best treatment option in both of these groups, applying information about different insulin types and the cost of insulin in one group could lead to new and better options in the other. The similarities of this disease in all animals make this research possible. If the effects of this disease were vastly different in these groups, advances based on information found in the other group could not be made.

In a previous study conducted it was seen that most modern research on companion animal diabetes makes claims about the effectiveness of various types of insulin, the differences between Type I and Type II diabetes, the cost of insulin, and the new advances made in the field of companion animal diabetes, all while showing the different effects these advances had on both the quality of life for animals and their owners. While not all of these claims can be directly related to human diabetes, many of them can. Similar claims have been made in this research of humans about how effective different types of insulin are, the differences between the two main types, and insulin cost, though many of the new advances in companion animal diabetes have come from technology already seen in human diabetes. Companion animal diabetes research has also impacted both animals and their owners while human diabetes research just improves the quality of life of the affected individual. Based on

the similarities seen in both these areas of research, it must be determined if insulin research advances in companion animals could show promise for advances in human diabetes research as well. To better evaluate this issue, the various forms of insulin used in humans and companion animals must be assessed. In companion animals, it has been found that ultra-long-lasting insulin offers better control of blood sugar than long-acting insulin (Bloom and Rand, 2014). In humans, it has been found that ultra-long-acting insulin could provide a stable lower glucose level in individuals with Type II diabetes (Heise et al., 2011) and was able to give similar control as other types of insulin in Type I diabetics (Birkeland et al., 2011). By determining if the effects of ultra-long-acting insulin could fully be seen in humans as they are in companion animals, we could provide human diabetics with not only a better glycemic control but a better quality of life through this.

Typical insulin administration for companion animal diabetics includes injecting intermediate-acting insulin twice a day, once in the morning before mealtime and once at night before mealtime. For humans, intermediate-acting insulin can be given twice a day the same as in companion animals, or long-acting insulin can be given once a day, typically at night. Some people need extra support in their insulin control and are also provided with a rapid-acting or short-acting insulin right before mealtime. In current research into human and companion animal diabetes, there are no approved insulin therapies that could be administered at a once-a-week rate by the FDA. There has been much more research on the companion animal side though of the benefits of insulin therapies like this. The new ultra-long-acting insulin would lead to better control of companion animal diabetes by reducing the administration of shots to once a week. This is supported by the knowledge that some pets become quite confrontational when receiving their shots, so reducing the number of injections would improve the quality of life for both the animals and their owners (Niessen et al., 2012). While humans may not become confrontational when faced with having to give

themselves shots daily, there are other benefits that once-a-week insulin injections could provide. If an ultra-long-acting insulin with similar effects to that which it has in companion animals was used in humans, we might see similar benefits in glycemic control. Animals treated with ultra-long-acting insulin also had better glycemic control than those treated with long-acting insulin (Bruyette and Keiler, 2013). The extent to which ultra-long-acting insulin improves glycemic management in companion animals must be evaluated to determine if this would be a feasible option in humans. On one hand, it could easily be seen that diabetes affects companion animals and their owners as well as people who have diabetes themselves in the same way. One issue seen with companion animals is that the owners often have to change their schedules so that they can administer insulin shots to their animals. Individuals who have diabetes themselves must also often have to change their schedules or be interrupted during other tasks so that they can administer their insulin shots. Schaper et al. (2017) pointed out that it is recommended for insulin to be injected within thirty minutes before a meal. This means that individuals must be prepared to give themselves injections before every meal to achieve adequate glycemic control, implying that if they do not have insulin available, they would have to change their plans to accommodate this. Numerous other impacts of diabetes have been discussed concerning both of these groups. On the companion animal side, it can be seen that while the owners work life can be greatly affected by the time management associated with this disease, there are also many other impacts to the owner including increased stress levels due to worrying about their animal, feeling like they have less control of their animal due to having to consult a vet for most decisions, and not being able to leave their animal for extended periods due to not having someone to take care of their animal who knows how to administer shots. These are all great examples of the toll that pet diabetes takes on the owners. On the human side of things, there are also many other impacts than their time management of when they must inject themselves. Diabetes often

affects a person's life in general, making them have to change how they eat and exercise for starters. Diabetes can also put individuals at a greater risk for heart disease and strokes which can be very problematic. There is also a possibility of damage to the central nervous system and the integumentary system (Pietrangelo and Olson, 2020). On the other hand, diabetes in these two groups could be seen as very different from each other. Most issues with companion animal diabetes come from what the owner faces and not what the animal with diabetes goes through. Just as some pets might be hassle-free and not need ultra-long-acting insulin, humans might be the same too with multiple injections a day not bothering them. Therefore, it is clear while some individuals, both human and companion animals, might not need ultra-long-acting insulin, it could provide greater glycemic management for those that do. Even though this greater glycemic control could be provided through this type of insulin, it is not likely that even all companion animals would be able to access it, let alone humans. In companion animals, this is due to it not being approved by the FDA, so they must meet qualification criteria to be prescribed ultra-long-acting insulin. Access in humans is also a tricky subject due to FDA approval and doctors prescribing insulins that have been around for years because they know that individuals can be regulated on them even if they have to inject much more often than they would with a newer type of insulin. As such, if researchers are looking for a solution that provides longer-term control of diabetes than current insulin is providing, then ultra-long-acting insulin in companion animals and similar technologies in humans could provide this control with more research involving clinical trials.

To better evaluate this issue, it must first be understood how all of the different forms of insulin compare to each other. Six different types of insulin can be used in the treatment of diabetes. These include rapid-acting, short-acting, intermediate-acting, long-acting, ultra-long-acting, and mixed insulin. These can be differentiated from each other by how quickly they take to start working and how long they can provide glycemic control in the

individual. Rapid-acting insulin starts almost immediately after you take it, typically ranging from two and a half to twenty minutes after it has been injected (Diabetes and insulin, 2019). This type of insulin reaches its peak performance between one and three hours after injection, though it can last up to five hours. It must be noted though that rapid-acting insulin should only be injected right before a meal so that blood sugar levels do not drop too low.

Short-acting insulin lowers glucose levels within thirty minutes of injection. (Diabetes and insulin, 2019) This requires individuals to inject themselves thirty minutes before eating to properly control glucose levels after a meal. The short-acting insulin peak occurs two to five hours after it has been injected and can last up to eight hours. These differ from intermediate-acting, long-acting, and ultra-long-acting insulin which are basal insulins. Basal insulin, also known as background insulin, is often taken in the absence of food to keep blood glucose levels stable. Intermediate-acting insulin starts to work around 60 minutes after it has been injected and peaks between four and twelve hours, lasting a max of twenty-four hours (Diabetes and insulin, 2019).

Long-acting insulin starts to work even slower than intermediate-acting, releasing steadily over twenty-four hours and has no peak.

Ultra-long-acting insulin has an even slower onset than long-acting and releases insulin at a steady place for longer than twenty-four hours. The onset and peaks of the previously listed insulins are described in Table 1 and depicted in Figure 1. Mixed insulin usually contains intermediate-acting insulin combined with either rapid-acting or short-acting insulin

Table 1. Onset and peak of the different types of insulin assessed in this study.

Type of Insulin	Onset after Injection	Peak
Rapid-acting	2 ½ to 20 minutes	1 to 3 hours
Short-acting	Within 30 minutes	2 to 5 hours
Intermediate-acting	60 minutes	4 to 12 hours
Long-acting	Several hours	None, releases steadily over 24 hours
Ultra-long-acting	Several hours	None, releases steadily over more than 24 hours

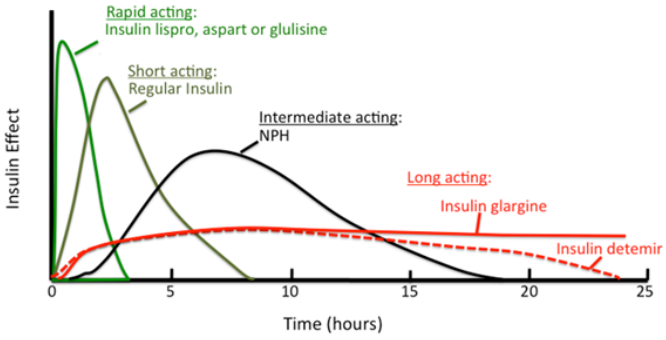

Figure 1. Graph illustrating the relative insulin effects over time of rapid-acting, short-acting, intermediate-acting, and long-acting insulin. (Insulin Regimens, 2017)

and contains the benefits of both (Diabetes and insulin, 2019). In companion animals, rapid-acting and short-acting insulin are not used because their peak is far too short to provide adequate glycemic control. These two types of insulin are used in humans for mealtime glycemic control though an intermediate-acting or long-acting insulin is typically prescribed in conjunction with it for proper glycemic control as they cannot often provide it alone. Adequate glycemic control can be achieved in humans as well though by basal insulins alone. Based on this information about different types of insulin and basal insulins being able to provide glycemic control, ultra-long-acting insulin could be a viable option for the treatment of diabetes in companion animals and humans.

In both companion animals and humans, multiple studies have found that there are many benefits to ultra-long-acting insulin which have contributed to it being on the market in both groups. One form of ultra-long-acting insulin that has proven effective in companion animals is Glargine. Bruyette and Keiler (2013) included more information about the ultra-long-acting insulin and how it affects felines. They stated that cats who were treated with Glargine, an effective form of ultra-long-acting insulin that was originally used as long-acting insulin in humans to provide basal insulin concentrations, offered not only better glycemic control, but also a greater likelihood of remission than felines treated with Protamine zinc (PZI), a long-acting insulin, or Lente, an intermediate-acting insulin (Bruyette and Keiler, 2013). While Glargine can provide basal insulin concentration in humans, it does not offer this even greater glycemic control or likelihood of remission in humans since it only acts as a long-acting insulin. McInnes et al. (2020) found that some patients with early Type II diabetes who were provided with Glargine for a short-term intervention were able to sustain a diabetes remission, though this data was not statistically significant. A type of ultra-long-acting insulin that has shown promise in humans though is Degludec. Zinman et al. (2011) found that when compared with Glargine, Degludec offered a comparable basal

insulin control without the adverse effects seen in Glargine. Some of these adverse effects include low blood sugar, weight gain, edema, and injection site reactions. Degludec, being an ultra-long-acting insulin, also allows for a reduced dosing frequency of once a day or three times a week. Glargine must be administered in human patients once a day so the possibility of going from seven days a week of injections to having to inject less than half the days in the week could greatly decrease the burden of shot administration. Research conducted by Heise et al. (2011) added to this, stating that Degludec had similarly low rates of hypoglycemia to Glargine, but its post-dinner plasma glucose control was much better. The ultimate goal of insulin therapy is to achieve diabetic remission, which is the ability to maintain euglycemia without insulin for 2 to 4 weeks after insulin therapy has been discontinued, without the reappearance of clinical signs of diabetes. While this is the ultimate goal though, it is not always achievable, which is especially the case in humans. Therefore, a better goal of treatment would be to achieve glycemic control for the longest period possible. In companion animals and humans, ultra-long-acting insulin would be a more viable option to achieve this. While different types of ultra-long-acting insulin are being used in these groups, ultra-long-acting insulin, in general, has shown to provide the same or better glycemic control for a longer time than other types of insulin, providing a more efficient treatment in these groups.

Since it has been determined that ultra-long-acting insulin provides the best control for companion animals and humans, the different forms of ultra-long-acting insulin must be assessed. Similar to Glargine, there is another ultra-long-acting insulin used in companion animals that can be considered a form of long-acting insulin in humans. This form of insulin is called Detemir. No significant differences in the efficacy of these two forms of insulin were found in a study done by Bruyette and Keiler (2013). The overall remission rate of cats that were administered Glargine was 84% for patients treated within 6 months of diagnosis and

35% for patients treated after 6 months of diagnosis, while cats treated Detemir showed remission rates of 81% and 42%, respectively (Bruyette and Keiler, 2013). Based on modern evidence, only Glargine or Detemir appear to be viable options for treating feline diabetes, a fact that may be extended to other companion animals. Glargine and Detemir both meet the goal of achieving insulin control for the longest period possible in felines. Additionally, if they can achieve remission in an animal, they would provide the longest period of insulin control by returning blood sugar to a normal level for at least two weeks. In humans, on the other hand, Glargine and Detemir are only used as long-acting insulins so they do not provide the same control. Ultra-long-acting insulins that are used in humans include the previously listed Degludec as well as Icodec which is a new investigational insulin. Gordon (2020) found that in trials, Icodec has offered a similar reduction in insulin levels as glargine. Icodec, though, is the only insulin that has shown effectiveness at a once-a-week level which is the typical dosing period of all companion animal ultra-long-acting insulins. Icodec has been modified so that it can bind to albumin and circulate through the body in the same way that the insulin our body typically produces would. This modification has also allowed it to clear the body more slowly, giving it a half-life of about 196 hours which allows it to cover a full week of insulin requirements, revolutionizing the control of diabetes in humans (Nishimura et al., 2020).

New advances are currently being made in the realm of human diabetes. New trials are being conducted on the previously discussed insulin Icodec which is the first human insulin that has shown the ability to provide week-long insulin control. In companion animals, once-a-week injections have been around for years. Forms of insulin that only provide daily control in humans provide week-long control in these companion animals. One might assume that the difference in mass between humans and companion animals might be why this discrepancy occurs. This would not be correct though because Total Daily Insulin

(TDI) requirements are calculated in humans as 25% of their body weight in pounds of 55% of their weight in kilograms. The number calculated from this gives individuals how many units of insulin they need a day. Based on specific insulin resistance or sensitivity individuals may need a higher or lower dose, respectively. Insulin dosage is similar in companion animals. If their baseline blood glucose concentration is less than 20 mmol/L then they will receive a fourth of their body weight in kilograms. If their baseline blood glucose concentration is greater than 20 mmol/L then they will receive half of their body weight in kilograms. If the effectiveness of insulin injections in companion animals was based on mass then these two values would be a higher percentage per weight than humans rather than lower. This points to an unknown cause for why long-acting insulin provides ultra-long-lasting effects in companion animals. Minimal research has been found on this issue, but it must be considered what effects human ultra-long-acting insulin would have in companion animals. If long-acting insulin in humans has shown ultra-long-lasting effects in companion animals, then would ultra-long-acting insulin in humans provide ultra-ultra-long-lasting effects in companion animals and if so, how long would these effects last? Oda et al. (2020) found that Degludac has a duration of action that is greater than 42 hours. Being a newer insulin with minimal studies in companion animals, the exact duration has not yet been determined but it does not appear to last as long or longer than Glargine or Detemir which were what had been expected. Degludac did improve glycemic control in companion animals though so it could provide treatment even though it might not be the most beneficial. More research does need to be done though before it is fully determined that Glargine and Detemir have greater efficacy. More research must also be done on Icodec in human trials to see if it is worth it to conduct trials in companion animals. If Icodec continues to hold promise in humans, then it is possible that like Glargine and Detemir it could provide an even longer-lasting control in companion animals. Additionally, if it were determined why

insulin persists longer in companion animals, that knowledge could be applied to create a new form of insulin that could provide the longest period of glycemic control in humans. This could provide a form of insulin that is similar to Icodec in its modifications. It is also possible that if the modifications made to make Icodec insulin were applied to existing insulin formulas, their half-lives could be expanded as well.

One important factor when treating anyone with diabetes is starting treatment early. In companion animals, early treatment with ultra-long-acting insulin is vital to achieving remission. The benefits of ultra-long-lasting insulin are also much greater overall if this remission is achieved. Ultra-long-acting insulin not only allows the owners to achieve good glycemic control of the animal which would improve their quality of life, but it also reduces the number of times the owner must inject their pet. If remission is achieved, the number of injections the owner needs to administer drops to zero. This shows just how beneficial the use of ultra-long-acting insulin is. While 25-30% of cats who have achieved remission relapse, the vast majority do not and no longer require injections (Bruyette and Keiler, 2013). This would give owners even more freedom when using ultra-long-acting insulin because they would no longer have to change their schedules to revolve around injections if their animal achieved remission. The effects of early treatment can be seen to be beneficial to both companion animals and their owners.

Early treatment in humans with diabetes also has many benefits, though all are related to them directly. Detecting diabetes early in humans and starting treatment greatly reduces the risk of serious complications seen with this disease. Herman et al. (2015) found that the time it takes for a treatment to be initiated after diagnosis and how soon diabetes is diagnosed after it has developed is more important than the intensity of treatment. For individuals diagnosed with Type II diabetes, if healthy lifestyle changes are started soon after the disease has developed it is possible to reverse it and reach normal blood sugar levels again without a need

for medication. This is also a situation where research into companion animals could be extended to humans. While there is the possibility of remission with healthy lifestyle changes, not all can reach remission this way. Ultra-long-acting insulin usage early on has shown the possibility for remission in companion animals. While research into ultra-long-acting insulin in humans is relatively new, there is the possibility that these same effects could be found. Using the research found in companion animals to develop similar studies in humans, researchers could see if there is a correlation between early ultra-long-acting insulin treatment and remission. If this was found, it could revolutionize the treatment of human diabetics. Changing towards a healthier lifestyle would still be emphasized, but for those who don't see reversal with this technique, ultra-long-acting insulin could provide that help. These individuals are already being given insulin so changing their form of insulin to one that could cause remission would only be more beneficial. With the high remission rates ultra-long-lasting insulin provides in companion animals, it is not unlikely that it could provide remission in humans too. Other than living a healthier lifestyle, there have not been any other treatments that have shown remission in human Type II diabetics. Therefore, finding an alternative treatment option that can lead to remission in humans would offer glycemic control that no other insulin has given to humans. Combining the research between these groups could not only benefit humans who might also achieve remission through this treatment but more information on this topic, in general, could help us to understand why this phenomenon exists.

Many factors play into the disease of diabetes. One of the most important factors is what type of diabetes the individual has. This information can play a role in the implications that this disease will have on that individual as well as how they are treated for diabetes. As mentioned before, there are three different types of diabetes. Type I diabetes is classified as an animal that is insulin-dependent. The cause of this is damage or destruction of pancreatic

islets by beta-cells which leads to the animal having an absolute insulin deficiency (Bloom and Rand, 2014). Type II diabetes is the form of diabetes that occurs in an animal that is noninsulin-dependent. This type of diabetes is classified by an animal that has insulin resistance or an insulin deficiency from the beta-cell dysfunctions, which can be reversible with rapid glycemic control. Bruyette and Keiler (2013) further classified Type II diabetes into a third form known as Type III diabetes. This form of diabetes, which is similar to impaired glucose tolerance in humans, can be caused by medications or diabetogenic hormones which lead to glucose intolerance, though the cause of this resistance is not always known. In companion animals and humans, diabetes can be obtained in several ways including gaining weight and becoming obese, genetic predisposition, physical inactivity, increasing age, and medications. Many other factors can play a role in the development of diabetes, but these are some of the most important.

While Type I and Type II diabetes are similar, they have different implications on those with diabetes because of the different effects that they have on these individuals. This is why some things, like the possibility of remission, may be seen in Type II diabetics and not in Type I diabetics. Type I and Type II diabetes are generally the most recognized, but they are not the only ones that exist. Another form of diabetes that must be considered is Type III. Type III diabetes mellitus classifies an impaired glucose tolerance that is caused by insulin resistance. With this information, it must be questioned how to properly treat humans and companion animals with these different types. While there are differences seen in the effect of diabetes between humans and companion animals, the types remain the same between these two groups. The different types must still be understood though because not all require insulin for treatment.

When considering how to treat diabetes in both of these groups, similarities can be seen with the type of diabetes the individual has. In the case of Type I diabetes, the animal

must be treated with insulin. No other therapy has proven effective in treating an individual who is insulin-dependent. With the only option for treatment being insulin, ultra-long-acting insulin would provide effective treatment for companion animals, and long-acting or ultra-long-acting insulin could effectively treat humans. Type II diabetes on the other hand must be treated differently. In animals with Type II diabetes, dietary changes, weight loss, and oral medications are usually the first line of treatment. Insulin therapy is not always used in these animals until after these methods have failed, though it has been shown that early insulin therapy can lead to remission. As discussed previously, early treatment initiation is key. Not only could early treatment with insulin result in remission, but lifestyle changes could lead to normal blood sugar levels as well. The final type of diabetes being discussed here, Type III, cannot be treated with insulin at all. Due to insulin resistance, treatment with insulin will have no effects on these individuals. Since their cells do not respond to insulin the other treatment options, including dietary changes, weight loss, and oral medications, must be used.

Other factors that play into the treatment of diabetes include the effects that this disease plays on owners of diabetic animals and humans with diabetes. Owners and diabetic humans alike are mainly in control of how they are treating this disease. While physicians do come into play, and the possibility of a guardian if the human with diabetes is not yet an adult, the individual who is most involved is either the person with diabetes or the person caring for an animal with diabetes. Niessen et al. (2012) also pointed out the challenges associated with caring for an animal with diabetes including the impact of diagnosis and treatment along with the cost of treatment. They found that 60% of families worried about the cost of their pet's diabetes to their family. It was found that the average it costs these diabetic companion animal owners between $43 and $231 a month just to care for the animal's diabetes which equates to between $2,236 to $12,012 a year (Leanny, 2020). This cost

includes things like insulin, needles, and regular diabetic vet costs but does not include any of the other costs a regular companion animal owner would spend on things like food and toys. Cost also plays a major role for diabetic humans. On average the medical expenses for someone with diabetes is $16,752 per year which is 2.3 times the health care costs someone without diabetes would accumulate in a year on average. With this evidence, it can be inferred that humans with diabetes are most likely facing similar worry when it comes to trying to afford the cost of treatment. If both groups are facing a cost issue, either directly or indirectly, it must be addressed which form of treatment in both groups is the most cost-effective for the quality of life that it provides.

To assess the issue of the cost of diabetes, we must first take a step back and examine where these costs are coming from. The cost of diabetes starts with the diagnosis of this disease. Practitioners make very important decisions after they have diagnosed a person or a companion animal with diabetes. These include the diet the individual should have, the type of insulin and the dosage that is required, how they should be monitored and how intense this monitoring should be, and the accompanying therapy. While these guidelines set by the practitioner do help the individual treating the companion animal's diabetes or their own diabetes, it does not give them much choice in the issue. This leads to a challenge that is often seen with diabetes which is of the practitioner having to make the best treatment plan for their patient while recognizing what that individual might be capable of affording. Another challenge faced around is the time it takes to treat diabetes. The amount of time it takes to meet these guidelines so that an individual may properly treat diabetes at home and the financial burden that comes from doctor/vet visits and insulin itself can add up. When an individual is newly diabetic or owns a newly diabetic the time portion of this issue will often be greater. With treatment mastery and efficiency, this can be diminished, but it cannot be fully discounted. Cost cannot be fully diminished either but finding an affordable insulin

option can take away some of the burdens. Therefore, it is important to look into the cost of insulin and see if there are possible cheaper options that could provide the same quality.

One large discrepancy seen between the effects of diabetes in humans and companion animals is the cost. While treatment between these groups seems to be relatively similar, both following different therapies for the different types and only differing in the effectiveness of some forms of insulin, the cost of insulin can be very different. Cost can play a large role for both diabetic companion animal owners and human diabetics when they are purchasing insulin. Many different types of insulin can be used, but it is usually determined by the practitioner which one is the best for every situation. Human diabetics and companion animals differ a little here. It is often seen that treatment in companion animals who are insulin-dependent requires only one type of insulin to be used while in humans, multiple types of insulin may be needed to maintain blood sugar levels. Having to buy multiple types of insulin to achieve the same control along with higher doses due mainly to increased body weight makes the cost of being a human diabetic higher in general, but there are also cost discrepancies seen between similar types of insulin in the two groups. When determining what type of insulin to buy in each situation if, given the choice, owners of diabetic animals and human diabetics must compare the prices so that they can lessen the financial burden of diabetes on themselves.

The three main types of insulin previously discussed (Glargine, Detemir, and Degludec) were analyzed here. The results which are shown in Figure 2 indicate that there is a large difference in the cost of 10mL vials of the same type of insulin in humans and companion animals. Glargine had the

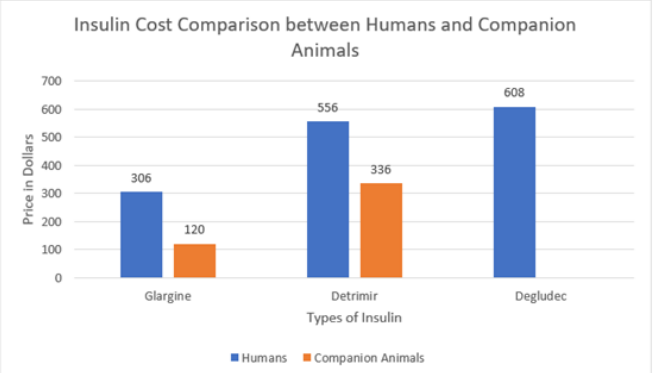

Figure 2: Graph interpreting the cost (in US dollars) of a 10mL vial of Glargine, Detemir, and Degludec for Humans and Companion Animals from GoodRx. Note: no prices for Degludec were found in companion animals. March 2021.

lowest cost for both groups, but the insulin sold to humans was still staggeringly higher. In the same brand of insulin even, Glargine was $186 more for one vial of insulin in humans than companion animals. Similarly, Detemir was $220 more per vial between these groups. The cost of Detemir was also much higher than Glargine in general with the cost of the companion animal vial of Detemir being greater than the cost of the human vial of Glargine. Degludec had the highest price of any of the insulin vials for humans. Thompson et al. (2015) pointed to the costs of this insulin also being less for companion animals, however, a specific value was never stated. With this information in mind, it can be seen that when comparing long-acting insulin in humans which is ultra-long-acting insulin in companion animals that Glargine is more cost-effective than Detemir. Since they both provide similar glycemic control it can be inferred that Glargine would be a more beneficial insulin choice since its financial burden is lower. When comparing Degludec to Glargine and Detemir, it can be seen that Degludec costs almost double that of Glargine which would initially make many people wary of using Degludec. If it is considered that Degludec has the possibility of being administered at less than half the rate of Glargine, this price does not seem as daunting. Before determining if Degludec would be a viable cost-effective option it must be determined how well Degludec works for the individuals. If Degludec only provides glycemic control for twenty-four hours it would not be as financially feasible to use this type of insulin. However, if Degludec provided glycemic control for a longer period and only needed to be administered three times a week it would cost less than Glargine per dose. Based on use, Degludec's price for the same number of days as Glargine if it provided this longer glycemic control would be just over $260 compared to Glargines $306. Therefore, in this case, it could be inferred that Degludec would be the most beneficial insulin choice in humans. With comparable insulin control and the minimization of adverse effects, Degludec could be a very viable insulin option with a decreased financial burden. The use of Glargine in animals and

Degludec in humans that have shown longer-lasting results further support the idea that ultra-long-acting insulin can provide the best form of insulin therapy in companion animals and humans.

While there is a role of insurance coverage when it comes to the cost of insulin for humans which decreases the price some depending on the company, it must still be questioned why insulin with the same chemical formula has different costs for these groups. Animals have often been prescribed insulin that is made for humans, so why does it cost less? While there are some insulin types used in animals that are of porcine or bovine origin, many of the types used are the same as those used in humans so this discrepancy should not exist. Along with the difference in costs between insulin labeled for humans and insulin labeled for companion animals, there is a large inflation from the cost of production to the price of the product. Torres (2021) predicted that the production of one vial of human insulin costs $2.28-$3.42 and one vial of analog insulin, which imitates the body's natural insulin release pattern, costs $3.69-$6.16. While some forms of insulin could cost more to produce and the exact prices of insulin production are not released, this shows that there is a monopoly on this product. The price far outweighs production and makes the financial burden much bigger on individuals affected by this disease. Since diabetics and owners of diabetics face a price inflation issue, more research should be done to find if there is a way this cost could be reduced. Reducing this cost would lessen the financial burden on these individuals even more and make it so that price was not as big of a consideration in what the best treatment option for an individual is. If this were not able to be done though, it could be found why companion animal insulin costs less than insulin for humans. Studying how the price has been reduced in companion animals or inflated in humans could provide information to those in human diabetes research on what could be done to make their insulin more affordable. Research has not yet been done on this topic, but it could be quite important though as it has been found

that some people without insurance have been using animal-grade insulin as a substitute (MacLeod, 2019). This is not an uncommon phenomenon as many have found glycemic control with animal-grade insulins. Being able to control human diabetes with animal-grade insulin further shows how the same insulin is being used in both of these groups with vastly different prices. The reuse of costly needles has also been seen in many diabetics. Therefore, decreasing the financial burden of diabetes would have effects that extend far beyond an individual's bank account. They would be at less of a health risk in the case of needle reuse and they could also incur less stress due to a decreased cost. With the price of insulin increasing dramatically every year, something needs to be done now to figure out a way to decrease the cost before it is too late. Many individuals already cannot afford insulin and if the trend continues this way many more will join this group, possibly resorting to unsafe techniques to reduce their financial burden.

Diabetes is becoming a more complex issue every year in companion animals and humans. With the increases in prevalence seen in both groups, research into the best treatment options is vital. Additionally, due to the similarities in this disease in both groups, combining research could potentially give us new advances that improve the quality of life for all individuals affected too. Many factors played into finding these treatment options in both groups. One of the most important was the type of diabetes that a person or companion animal had. Whether an individual has Type I, Type II, or Type III diabetes plays a large role in how they can be treated, complicating the issue of what the best treatment option is. As the types were the same for both groups though, it could be seen that effective treatments found for diabetes in one group could be effectively applied to the other. For both humans and companion animals who had Type I diabetes or Type II diabetes, not including those that are insulin resistant, insulin administration has been deemed the most viable treatment option. In companion animals, it has been seen in studies that ultra-long-acting insulin shows the

greatest promise in comparison to other types of insulin. This is due to the many benefits it has including dramatically decreasing the number of shots that must be administered to once-a-week, providing longer-lasting glycemic control, and giving companion animals a greater possibility for remission. In humans, long-acting insulin has been widely used to control blood sugar levels, though some types of ultra-long-acting insulin have made their way into the market. Insulins like Degludec have provided a decreased administration rate with longer-lasting glycemic control. While this administration rate is under half what that of long-acting insulin was, it is not at the same once-a-week rate seen in animals. Just in the past year though, a newer form of insulin, Icodec, has shown this once-a-week promise. Trials are currently being conducted on a form of insulin that could change the game for humans affected by this disease. Insulins that have provided this once-a-week rate in companion animals have also shown the possibility of remission. Therefore, if looking for a way to help Type II human diabetics achieve remission, more research should be done into ultra-long-acting insulins in humans. Using similar research techniques as those conducted in companion animals, it could be found that ultra-long-acting insulin could have the same effect in humans. This shows how valuable combining these two areas of research could be. Other than making changes for a healthier lifestyle, there has been no evidence for something that could provide humans a possibility of remission. As making these healthier changes does not help everyone achieve remission, this new treatment option could provide people with an opportunity to reverse something that greatly changed their life. The cost of insulin also plays a large role in determining the best treatment for these groups and is another area where combined research could benefit both groups. There has been a large inflation from the cost of production to the price of insulin for all individuals. Finding ways to decrease the price of insulin could decrease the financial burden of this disease and improve the lives of all individuals affected. Needle reuse would not be as large of a problem and humans might not

resort to using insulin prescribed to animals to lessen their burden. Decreasing the price, in general, would benefit both groups, but one must also consider why there is a cost difference between companion animals and human insulin. Using research to determine why insulin cost less for companion animals could also help to decrease the price for humans. This advance would make it so that the best form of insulin for treatment was based more on what provided the best glycemic control and not what the individual could afford. Based on current costs though, it was determined that ultra-long-acting insulin was the most cost-effective for companion animals. A similar cost analysis in this review showed that Degludec, an ultra-long-acting insulin, also cost less for how much it had to be administered as long as it provided greater glycemic control than long-acting insulin which is found on an individual basis. The new Icodec could also provide even less of a financial burden on these individuals as it would be able to be administered at a seventh of the rate of long-acting insulins. As long as it cost less than seven times that of Glargine, the most cost-effective long-acting insulin, and less than half of Degludec it would be a very cost-effective choice for human diabetics. Despite the cost-effectiveness ultra-long-acting insulin has, it is not a viable treatment option for Type II and Type III diabetics who are insulin resistant due to their inability to respond to insulin therapy. This is where other treatment options come into play. Therapies like dietary changes, weight loss, and oral medications would be the most effective. In humans, it has been seen that some of these changes have led to remission when treatment was started early. If this research was applied to companion animals there is a possibility that the same effects could be seen in them as well. With more research into how companion animals and human diabetes relate to each other, applying the advances in one group to the other could help them reach the same, making the issues faced by both much easier to manage.

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